Supplement 1

S3-Leitlinie der Deutschen Gesellschaft für Ernährungsmedizin (DGEM)

Evidenztabellen

1 Indikation und Kontraindikation

1.1 Heimenterale Ernährung (HEE)

Empfehlung 1

HEE sollte mangelernährten Patienten oder Patienten mit einem Ernährungsrisiko angeboten werden, die ihren Nährstoffbedarf nicht durch die orale Nahrungsaufnahme decken können und über einen ausreichend funktionierenden Gastrointestinaltrakt verfügen, mit dem Ziel, das Körpergewicht, den funktionellen Status und die Lebensqualität zu verbessern bzw. zu erhalten..

Empfehlungsgrad B

1. Schuetz P, Fehr R, Baechli V et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. The Lancet 2019; 393: 2312-2321. doi:10.1016/s0140-6736(18)32776-4 [15]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+ ROB 4/7	**Countries:** Switzerland **Centers:** University Clinic in Aarau, the University Hospital in Bern, the Cantonal hospitals in Lucerne, Solothurn, St Gallen, Muensterlingen, and Baselland, and the hospital in Lachen **Setting:** n/a **Funding Sources:** The Swiss National Science Foundation	**Total no. Patients:** 2088 **Inclusion criteria:** at least 18 years at nutritional risk of 3 or greater expected to stay in hospital for more than 4 days if they were willing to provide informed consent within 48 h of hospital admission for any reason **Exclusion criteria:** patients who were initially admitted to intensive care units or surgical units; unable to ingest oral nutrition; already	Patients were randomly assigned (1:1) to receive either individualized nutritional support (intervention group) or standard hospital food (control group). In the intervention group, nutritional support was initiated as soon as possible after randomization and within 48 h after hospital admission. Patients received individualized nutritional support (figure 1) to reach protein and caloric goals, according to a previously published consensus protocol19 that follows 2018 inter-national guidelines.7 Briefly, individualized nutritional goals were defined for each patient on hospital admission by a trained registered dietitian. Caloric requirements were predicted using the weight adjusted Harris-Benedict equation.20 Daily protein intake was set at 1·2–1·5 g/kg of bodyweight to adjust for increased protein breakdown during acute disease,21 with lower targets for patients with acute renal failure (0·8 g/kg of bodyweight). To reach these goals, an individual nutritional plan

	and the Research Council of the Kantonsspital Aarau, Switzerland **Dropout rates:** 2.9% **Study limitations:** Risk of Bias: high Inconsistency: n/a Indirectness: moderate Impreciseness: low Publication bias: n/a Trial was pragmatic, and masking of participants and personnel was deemed to be impractical, thus observer bias might occur, nutrition in the control group represented the reality of standard Swiss hospital food, which might not be unconditionally generalizable to other health-care systems, no investigation on costs	receiving nutritional support on admission; with a terminal condition; admitted to hospital because of anorexia nervosa, acute pancreatitis, acute liver failure, cystic fibrosis, or stem- cell transplantation; after gastric bypass surgery; with contraindications for nutritional support	was developed by a trained registered dietitian for each patient. Patients in the control group received standard hospital food according to their ability and desire to eat, with no nutritional consultation and no recommendation for additional nutritional support.
Notes	**Author's Conclusion:** Understanding the optimal use of nutritional support is complex because timing, route of delivery, and the amount and type of nutrients might all affect clinical outcomes. In our trial, we asked the basic question of whether nutritional support during the hospital stay improves outcomes in medical patients at nutritional risk, compared with standard hospital food. This trial showed that early use of individualized nutritional support to reach protein and caloric goals in medical inpatients at nutritional risk is effective in increasing energy and protein intakes, and in lowering the risk of adverse outcomes and mortality within 30 days. Our findings strongly support the concept of systematically screening medical inpatients on admission to hospital for nutritional risk, irrespective of any underlying conditions, followed by a nutritional assessment and introduction of individualized nutritional support in at-risk patients.		
Outcome measures/results	adverse clinical outcome within 30 days		- During the hospital stay, caloric goals were reached in 800 (79%) and protein goals in 770 (76%) of 1015 patients in the intervention group. - By 30 days, 232 (23%) patients in the intervention group experienced an adverse clinical outcome, compared with 272 (27%) of 1013 patients in the control group (adjusted odds ratio [OR] 0·79 [95% CI 0·64–0·97], p=0·023). - By day 30, 73 [7%] patients had died in the intervention group compared with 100 [10%] patients in the control group (adjusted OR 0·65 [0·47–0·91], p=0·011).

		- There was no difference in the proportion of patients who experienced side-effects from nutritional support between the intervention and the control group (162 [16%] vs 145 [14%], adjusted OR 1·16 [0·90–1·51], p=0·26).

2. Gomes F, Baumgartner A, Bounoure L et al. Association of Nutritional Support With Clinical Outcomes Among Medical Inpatients Who Are Malnourished or at Nutritional Risk. JAMA Network Open 2019; 2: e1915138. doi:10.1001/jamanetworkopen.2019.15138 [16]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review and Meta-Analysis 1++ AMSTAR 2 10/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** SNSF (SNSF Professorship, PP00P3_150531) and the Forschungsrat of the Kantonsspital Aarau (1410.000.058 and 1410.000.044) to Dr Schuetz. **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: Low Risk of bias of single studies: moderate Inconsistency: moderate Indirectness: moderate Impreciseness: low Publication bias: low Several of the included studies had a high or unknown risk of bias, small sample sizes, and short study duration	**Total no. Studies:** 27 **Inclusion criteria:** randomized and nonrandomized clinical trials that allocated non–critically ill medical inpatients who are malnourished or at nutritional risk to a nutritional support intervention or a control group **Exclusion criteria:** studies conducted in outpatient care settings, nursing homes, long-term care facilities, or intensive care units and trials focusing on surgical patients, patients with pancreatitis (because of their particular nutritional needs and the management of this condition), and those receiving palliative care.	Assessment of the association of nutritional support with clinical outcomes in medical inpatients who are malnourished or at nutritional risk.

Notes	**Author's Conclusion:** This updated systematic review and meta-analysis found that use of nutritional support interventions was associated with clinically significant improvements of important clinical outcomes in the medical inpatient population, in whom malnutrition is highly prevalent. This analysis supports the current practice guidelines issued by the European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society for Parenteral and Enteral Nutrition (ASPEN), advocating a proactive, screening-based approach for initiating nutritional support during the hospital stay of medical inpatients who are malnourished or at nutritional risk.	
Outcome measures/results	Primary outcome: mortality Secondary outcomes: nonelective hospital readmissions, length of hospital stay, infections, functional outcome, daily caloric and protein intake, and weight change	Primary outcome: - the mortality rate was 8.3% (230 of 2758) among the intervention group patients compared with 11.0% (307 of 2787) among the control group patients (OR, 0.73; 95% CI, 0.56-0.97, P = .03). This significant reduction in mortality associated with the nutritional support was different from the nonsignificant association observed in the original meta-analysis (OR, 0.96; 95% CI, 0.72-1.27) Secondary outcomes - Compared with the control group, nutritional support interventions were associated with a significant reduction of nonelective hospital readmissions (14.7% [280 of 1903] in the intervention vs 18.0% [339 of 1880] in the control group; RR, 0.76; 95% CI, 0.60-0.96; P = .02) - Compared with the control group, the intervention group patients had no differences in rates for infections (4.8% [88 of 1817] vs 5.6% [102 of 1825]; OR, 0.86; 95% CI, 0.64-1.16), functional outcome at follow-up (17.3 vs 16.9 points; mean difference in Barthel index score, 0.32 points; 95% CI, −0.51 to 1.15), or LOS (11.5 days vs 12.0 days; mean difference, −0.24 days; 95% CI, −0.58 to 0.09) - nutritional support interventions were associated with a significantly higher energy intake (1618 kcal in the intervention group vs 1331 kcal in the control group; mean difference, 365 kcal; 95% CI, 272-458 kcal) and protein intake (59 g in the intervention group vs 48 g in the control group; mean difference, 17.7 g; 95% CI, 12.1-23.3 g). In addition, there was a significant increase in body weight (0.63 kg in the intervention group vs −0.19 kg in the control group; mean difference, 0.73 kg; 95% CI, 0.32-1.13 kg).

<u>Empfehlung 2</u>

Patienten, bei denen ein hohes Risiko für Mangelernährung bzw. eine Schluckstörung besteht, sollte vor der Entlassung aus dem Krankenhaus die Möglichkeit einer Ernährungstherapie mit oraler Nahrungssupplementation (ONS) (sofern die Schluckstörung keine Kontraindikation für ONS darstellt) oder eine HEE empfohlen werden.

Empfehlungsgrad B

Empfehlung 3

Eine HEE kann auch bei Patienten mit Demenz durchgeführt werden, wenn eine medizinische Indikation vorliegt, wobei Schweregrad der Erkrankung und ethische Aspekte auf individueller Ebene zu berücksichtigen sind.

Empfehlungsgrad 0

3. de Luis DA, Aller R, de Luis J, Izaola O, Romero E, Terroba MC, et al. Clinical and biochemical characteristics of patients with home enteral nutrition in an area of Spain. Eur J Clin Nutr. 2003;57(4):612-5. [20]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** Spain **Centers:** Seccione de Endocrinologia y Nutricion Clinica Hospital u. Rio Hortega **Setting:** Tertiary care **Funding Sources:** n/a **Dropout rates:** none **Study limitations:** no generalizability	**Total no. Patients:** n=102 **Inclusion criteria:** adult patients living in Valladolid West area, were discharged from hospital on HEN **Exclusion criteria:** patients with normal oral tolerance	4 conditions had to be fulfilled to recommended HEN: (1) enteral nutrition had to be initiated in the hospital, shown to be well-tolerated for a period of 10 days and the patient or a close relative had to be fully trained in the use of HEN (2) the familial home environment had to be compatible with safe HEN delivery (3) the patient's disease had to be sufficiently controlled and stable to allow home treatment (4) the expected duration of HEN had to be at least one month Patients divided in 2 Groups: 1. Group 1: oral tolerance with supplements 2. Group 2: NGT, PEG or jejunostomy
Notes	HEN was indicated for patients with oral failure, defined as an involuntary reduction in oral intake below the minimal amount necessary to maintain protein – energy equilibrium (< 50% of daily adjusted by age and sex) with a functioning gut. During HEN, physicians supervised the home patients and the patients themselves or their close relative were asked to contact the nutrition team if any problem occurred **Author's Conclusion:** In conclusion, HEN is a valid and safe technique for nutrition support, with a good clinical outcome.		
Outcome measures/results	- Information for each patient was prospectively recorded by the dietitian: age, sex, body mass index, triceps skinfold, midarm circumference, underlying disease, exitus, dates of initiation and discontinuation of HEN, nutrient formula, mode of administration and complications of HEN		- distribution of patients by diseases was: 71 (69.6%) had a head and neck cancer; 14 (13.7%) had a neurological disorder affecting swallowing (cerebrovascular accident and/or dementia); 6 (5.9%) had tumors in different locations with anorexia; and 11 (10.8%) had one of several miscellaneous diseases inducing dysphagia or anorexia

	- Finally, the yearly incidence of HEN was calculated each year on the basis of the estimated population in our area of recruitment, assuming almost all HEN patients were reported	- HEN was administered orally in 81 patients (79.4%), via a nasogastric tube (NGT) in 15 patients (14.7%), via a percutaneous gastrostomy (PEG) in five patients (4.9%), and via a jejunostomy in one patient (1%) - The mean duration of HEN was 101±46.9 days - During the course of HEN, six patients had diarrhea (5.9%), and four (3.9%) constipation, and two vomiting (2%) that did not require cessation of HEN - Albumin, prealbumin, transferrin and lymphocytes improved in all the groups, when comparing the first review with the last - After the follow-up (3 y) with review, each 3 months, 10 of the 102 patients (9.8%) had died, and 92 (90.2%) were alive → Survival probability was influenced by the access route, with the worse outcome in patients with no oral nutrition (NGT, PEG and jejunostomy; hazard ratio: 24.9; 95% CI: 4.1 – 52), adjusted by age, sex and diagnosis

4. De Luis DA, Izaola O, Cuellar LA, Terroba MC, Cabezas G, De La Fuente B. Experience over 12 years with home enteral nutrition in a healthcare area of Spain. J Hum Nutr Diet. 2013;26 Suppl 1:39-44. [22]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** Spain **Centers:** Unit of Endocrinology and Nutrition, Hospital University "Rio Hortega", Institute of Endocrinology and Nutrition, Medicine School, Valladolid, Spain **Setting:** Tertiary care **Funding Sources:** no funding **Dropout rates:** none **Study limitations:** n/a	**Total no. Patients:** n=891 (n=460 were males) **Inclusion criteria:** adult patients living in Valladolid West area, were discharged from hospital on HEN **Exclusion criteria:** n/a	3 conditions had to be fulfilled to recommended HEN: (1) enteral nutrition had to be initiated in the hospital, shown to be well-tolerated for a period of 5 days and the patient or a close relative had to be fully trained in the use of HEN (2) the familial home environment had to be compatible with safe HEN delivery (3) the patient's disease had to be sufficiently controlled and stable to allow home treatment Patients divided in 2 Groups: A. Group 1: oral tolerance with supplements B. Group 2: NGT, PEG or jejunostomy
Notes	HEN was indicated for patients with oral failure, defined as an involuntary reduction in oral intake below the minimal amount necessary to maintain protein – energy equilibrium (< 50% of daily adjusted by age and sex) with a functioning gut. During HEN, physicians supervised the home patients and the patients themselves or their close relative were asked to contact our nutrition team if any problem occurred **Author's Conclusion:** HEN has a high incidence in our area and it is a valid and safe technique for nutrition support.		

Outcome measures/results	- Information for each patient was prospectively recorded by the dietitian: age, sex, weight, height, body mass index, triceps skinfold, midarm circumference, underlying disease, exitus, dates of initiation and discontinuation of HEN, nutrient formula, mode of administration and complications of HEN - Finally, the yearly incidence of HEN was calculated each year on the basis of the estimated population in our area of recruitment, assuming almost all HEN patients were reported	- Group 1: HEN was administered orally in 472 patients (68.28%) - Group 2: n=219: nasogastric tube in 168 patients (24.30%), a percutaneous enteral gastrostomy tube in 47 patients (6.80%) and a jejunostomy in four patients (0.60%) - Distribution of diseases: 34.1% had head and neck cancer, 10.3% had human immunodeficiency virus infection, 30.6% had a neurological disorder affecting swallowing (cerebrovascular accident and/or dementia), 7.7% had diseases in the digestive tract (fistulae, pancreatic disease, inflammatory bowel disease), 5.9% had tumors in different locations with anorexia, 1.3% had head trauma, and 12.1% had one of several miscellaneous diseases inducing dysphagia or anorexia - During the course of HEN, 31 patients had diarrhea (4.5%), 17 patients had constipation and 12 patients had nausea - mean (SD) duration of HEN: 159.9 (97) days - In multivariable analysis, an independent factor associated with death was age (hazard ratio = 1.03; 95% confidence interval - 1.01–1.05), adjusted by sex, route and diagnosis - Prealbumin and transferrin were higher in group 2 than in group 1 - improvement of weight, triceps skinfold and midarm circumference in both groups; Weight and mid-arm circumference were higher in group 1 than in group 2 - No differences were detected in biochemical and anthropometric parameters among different groups of diseases

5. Schneider SM, Raina C, Pugliese P, Pouget I, Rampal P, Hebuterne X. Outcome of patients treated with home enteral nutrition. JPEN J Parenter Enteral Nutr. 2001;25(4):203-9. [25]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** France **Centers:** Alpes-Maritimes Département of France **Setting:** HEN and its benefits	**Total no. Patients:** n=417 **Inclusion criteria:** oral failure **Exclusion criteria:** n/a	HEN in patients with an involuntary reduction in oral intake below the minimal amount necessary to maintain protein-energy equilibrium but with functioning and accessed gut. 5 conditions to recommend HEN:

	Funding Sources: in France HEN is fully funded since 1989 **Dropout rates:** 1,9% (n=8 stopped HEN because of HEN intolerance) **Study limitations:** n/a		1. Expected duration of HEN had to be at least 1 month 2. Enteral nutrition had to be initiated in the hospital and shown to be well tolerated for a period of one week 3. Patient´s disease had to be sufficiently controlled and stable to allow home treatment 4. Patient or caregiver had to be fully trained in the use of HEN 5. Social and familial home environments had to be compatible with safe HEN delivery
Notes	**Author's Conclusion:** HEN provides well-tolerated long-term nutritional support in many patients. However, because of their likelihood of being old and the nature of the underlying disease, these patients as a group tend to have a modest prognosis. This calls for the determination of more accurate selection criteria and the measurement of the impact of HEN on quality of life.		
Outcome measures/results	- Information concerning HEN program for each patient was prospectively recorded by one of the dietitians of the team: sex, age, BMI, underlying disease, dates of initiation and discontinuation of HEN, nutrient formula, mode of administration - Survival probabilities - Conditions associated with survival		- Mean age: 64 ±25 - Incidence: 1996 111 patients/million inhabitants - Prevalence rose: 1990 19 patients/million inhabitants; 43 in 1991; 57 in 1992; 104 in 1993; 153 in 1994; 142 in 1995; 162 in 1996 - During course of HEN almost all patients had digestive complaints that did not require cessation of HEN; 54% reported at least 1 problem with the tube - Daily cost: $9 - Mean duration of HEN: 242±494 days; 24 to 103 months follow-up - Probabilities of being alive at: - 1month: 80% - 1year: 41.7% - 5 years: 25% - Factors associated with death: dementia, neurologic diseases, head and neck cancer, AIDS, Age over 70 years - 5.5% of patients remained dependent on HEN - 32.6% resumed full oral nutrition - 20.2% of patients died during the first month of HEN; 35% died after more than 1 month - 6.7% of the patients stopped HEN for other reasons

6. Deutz NE, Matheson EM, Matarese LE et al. Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial. Clin Nutr 2016; 35: 18-26. doi:10.1016/j.clnu.2015.12.010 [29]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1++	**Countries:** United States **Centers:** n/a **Setting:** Inpatient and posthospital discharge **Funding Sources:** Abbott Nutrition **Dropout rates:** 4.6% **Study limitations:** limited generalizability; patients represent a selected hospitalized population.	**Total no. Patients:** 652 **Inclusion criteria:** aged ≥ 65 years with a recent hospital admission (within 72 h) with a primary diagnosis of CHF, AMI, PNA, or COPD. Patients were required to have a Subjective Global Assessment (SGA) class of B (moderate or suspected malnutrition) or C (severe malnutrition) **Exclusion criteria:** diabetes mellitus (type 1 or 2) due to product composition not intended for patients with diabetes mellitus; current active or treated cancer, and impaired renal or liver function.	Standard-of-care plus HP-HMB (n = 328) or a placebo supplement (n 1⁄4 324), 2 servings/day. During hospitalization, patients received the individual hospitals' standard nutritional care at the discretion of the attending physicians. Patients were instructed to consume 2 servings of their allocated study intervention (i.e., HP-HMB or placebo) each day. During the 90-day post discharge period, patients were instructed to continue to supplement their regular dietary intake with 2 servings daily of their allocated intervention, which was provided to the patients without charge.
Notes	**Author's Conclusion:** This double-blind, ITT, randomized, placebo-controlled study showed that a specialized, nutrient-dense ONS containing high protein and HMB did not alter the primary composite endpoint of hospital readmission rates and mortality in this specific population of malnourished, older adults hospitalized for CHF, AMI, PNA, or COPD. However, early administration (within 72 h of hospitalization) of HP-HMB in addition to the current nutritional care was associated with decreased post discharge mortality and improved nutritional status. Further analyses are required to understand the mechanism(s) leading to these observed effects.		
Outcome measures/results	90-day post discharge incidence of death or nonelective readmission, 30- and 60-day post discharge incidence of death or readmission, length of stay (LOS), SGA class, body weight, and activities of daily living (ADL)		- 90-day post discharge incidence of death or nonelective readmission was similar between HP-HMB (26.8%) and placebo (31.1%). - No between-group differences were observed for 90-day readmission rate, but 90-day mortality was significantly lower with HP-HMB relative to placebo (4.8% vs. 9.7%; relative risk 0.49, 95% confidence interval [CI], 0.27 to 0.90; p = 0.018). - The number-needed-to-treat to prevent 1 death was 20.3 (95% CI: 10.9, 121.4). - Compared with placebo, HP-HMB resulted in improved odds of better nutritional status (SGA class, OR, 2.04, 95% CI: 1.28, 3.25, p = 0.009) at day 90, and an increase in body weight at day 30 (p = 0.035). - LOS and ADL were similar between treatments.

7. Orlandoni P, Peladic NJ, Di Rosa M et al. The outcomes of long term home enteral nutrition (HEN) in older patients with severe dementia. Clin Nutr 2019; 38: 1871-1876. doi:10.1016/j.clnu.2018.07.010 [30]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2+ JBI 6/8	**Countries:** Italy **Centers:** Clinical Nutrition Unit of INRCA geriatric hospital **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: moderate Impreciseness: low Publication bias: n/a	**Total no. Patients:** 585 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	The assessment of the harmful effects of home enteral nutrition administered via the nasogastric tube and percutaneous endoscopic gastrostomy in patients with advanced dementia in terms of mechanical, gastrointestinal and metabolic complications, to estimate the survival, to explore the risk factors for mortality and to compare the outcomes of patients with advanced dementia with those of patients without dementia.
Notes	**Author's Conclusion:** The discussion on the appropriateness of enteral nutrition in patients with severe dementia is still open. Our results show that, if there is a medical prescription for tube-feeding and a patient's surrogate decision-makers express free and informed consent to the tube-feeding of the patient, enteral nutrition should not be contraindicated a priori if the patient has severe dementia. Regular follow-up is mandatory to guarantee adherence to the therapy and achieve its initial aims and to ensure that the principles of beneficence and nonmaleficence are respected.		
Outcome measures/results	Incidence rates of mechanical, gastrointestinal and metabolic complications and survival rates		- There was no difference between the incidence rates of complications in patients with severe dementia and those in patients without dementia. - The incidence of mechanical complications was 1.35/ 1000 days for patients without dementia vs. 1.53/1000 days for patients with dementia ($p = 0.270$), the incidence of gastrointestinal complications was 1.30/1000 days for patients without dementia vs. 1.35/ 1000 days for patients with dementia ($p = 0.984$) and the incidence of metabolic complications was 0.36/ 1000 days for patients without dementia vs. 0.35/1000 days for patients with dementia ($p = 0.252$). - The Kaplan Mailer analyses showed that there was no evidence to support the theses on poorer prognosis of survival of patients with dementia (median survival was 193 days for patients without dementia vs. 192 days for patients with dementia, ($p > 0.05$)). - The female gender, advanced age, nasogastric tube, diabetes mellitus and chronic renal failure were identified as risk factors.

		- Subjects whose Geriatric Nutritional Risk Index values were higher had a lower risk of mortality.

1.2 Heimparenterale Ernährung (HPE)

Empfehlung 4

HPE sollte denjenigen Patienten empfohlen werden, welche ihren Nährstoffbedarf nicht ausreichend über den oralen und/oder enteralen Weg decken können und welche außerhalb des Krankenhauses sicher behandelt werden können

Empfehlungsgrad B

Empfehlung 5

HPE kann bei Patienten über 65 Jahren sicher angewendet werden, auch bei erhöhter Komorbidität.

Empfehlungsgrad B

8.	**Schuetz P, Fehr R, Baechli V et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. The Lancet 2019; 393: 2312-2321. doi:10.1016/s0140-6736(18)32776-4 [15]**
→ see No. 1	

9.	**Staun M, Pironi L, Bozzetti F et al. ESPEN Guidelines on Parenteral Nutrition: Home Parenteral Nutrition (HPN) in adult patients. Clin Nutr 2009; 28: 467-479. doi:10.1016/j.clnu.2009.04.001 [37]**
Guideline **Relevant recommendations/ statements**	- Home parenteral nutrition support should be used in patients who cannot meet their nutritional requirement by enteral intake, and who are able to receive therapy outside an acute care setting - Long-term PN is indicated for patients with prolonged gastrointestinal tract failure that prevents the absorption of adequate nutrients to sustain life. As it is a life-saving therapy for patients with irreversible intestinal failure, it does not require evaluation of efficacy by randomized controlled trial. Its ability to maintain quality of life and promote rehabilitation supports the use of home treatment. - Prognosis in HPN is mainly governed by the underlying disease, but poor outcomes related to the HPN itself come from problems with catheters and the associated vessels. It is important to preserve lines and to protect the vessels as best possible. Reference should be made to the ESPEN

	guidelines on central venous catheters. In line sepsis in HPN a conservative approach with antibiotics is normally advocated before removing the catheter. - Underlying disease related factors must be strictly controlled, by treating inflammation and minimizing the dosage of bone damaging drugs.

Empfehlung 6

HPE sollte als primäre und lebensrettende Therapie für Patienten mit transient-reversiblem oder permanent-irreversiblem Darmversagen aufgrund einer nicht bösartigen Erkrankung verordnet werden, sofern die Indikation nach Empfehlung 4 zutrifft.

Empfehlungsgrad B

10. Pironi L, Forbes A, Joly F, Colomb V, Lyszkowska M, Van Gossum A, et al. Survival of patients identified as candidates for intestinal transplantation: a 3-year prospective follow-up. Gastroenterology. 2008;135:61-71. [58]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** 9 European countries **Centers:** 41 HPN centers **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** 15 % **Study limitations:** n/a	**Total no. Patients:** 473 **Inclusion criteria:** patients with intestinal failure **Exclusion criteria:** n/a	- survival on home parenteral nutrition or after transplantation was analyzed in 153 (97adult, 56 pediatric) candidates for transplantation and 320 (262 adult, 58 pediatric) noncandidates
Notes	**Author's Conclusion:** The results confirm home parenteral nutrition as the primary therapeutic option for intestinal failure and support the appropriateness and potential life-saving role of timely intestinal transplantation or patients with parenteral nutrition failure.		
Outcome measures/results	survival of the patients		- the 3-year survival was 94% (95% CI, 92%–97%) in non-candidates and 87% (95% CI, 81%–93%) in candidates not receiving transplants (P=.007) - survival was 80% (95% CI, 70%– 89%), 93% (95% CI, 86%–100%), and 100% in parenteral nutrition failure, high-risk primary disease, and high-morbidity intestinal failure, respectively (P=.034) - 15 candidates underwent transplantation. 6 died, including all 3 of those who were in hospital, and 25 % of those who were at home at time of transplantation (P=.086) - survival in the 10 patients receiving a first isolated small bowel transplant was 89% (95% CI, 70%–100%), compared with 85% (95% CI,

		74%–96%) in the candidates with parenteral nutrition failure not receiving transplants because of central venous catheter complications, or 70% (95% CI, 53%– 88%) in those with parenteral nutrition–related liver failure (P=.364)

Empfehlung 7

HPE kann bei Patienten mit chronischem Darmversagen aufgrund einer bösartigen Erkrankung verordnet werden.

Empfehlungsgrad 0

11. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clinical nutrition (Edinburgh, Scotland). 2017;36:11-48. [7]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline **Relevant recommendations/statements**	- Nutrition and metabolic interventions aim to maintain or improve food intake and mitigate metabolic derangements, maintain skeletal muscle mass and physical performance, reduce the risk of reductions or interruptions of scheduled anticancer treatments, and improve quality of life. - If nutrient intake remains inadequate, supplemental or complete nutrition by the oral, enteral or parenteral route may be indicated, depending on the level of function of the gastrointestinal tract. Parenteral nutrition may be indicated in instances of complete bowel obstruction or failure. - Nutritional therapy in cancer patients who are malnourished or at risk of malnutrition has been shown to improve bodyweight and energy intake but not survival. - In cases of severe intestinal insufficiency due to radiation enteritis, chronic bowel obstruction, short bowel syndrome, peritoneal carcinosis, or chylothorax, nutritional status can be maintained by parenteral nutrition. - Nutritional support should receive special consideration if patients are receiving palliative anti-cancer treatment. There is agreement that unconditional artificial nutrition in all patients undergoing anticancer therapy is associated overall with more harm than benefit.		

12. Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurcher G, Muscaritoli M. ESPEN Guidelines on Parenteral Nutrition: non-surgical oncology. Clinical nutrition (Edinburgh, Scotland). 2009;28:445-54. [10]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline	- A standard nutritional regimen may be recommended for short-term parenteral nutrition, while in cachectic patients receiving intravenous feeding for several weeks a high fat-to-glucose ratio may be advised because these patients maintain a high capacity to metabolize fats - Perioperative parenteral nutrition is only recommended in malnourished patients if enteral nutrition is not feasible		

Relevant recommendations/statements	- In non-surgical well-nourished oncologic patients, routine parenteral nutrition is not recommended because it has proved to offer no advantage and is associated with increased morbidity - In incurable cancer patients home parenteral nutrition may be recommended in hypophagic /(sub) obstructed patients (if there is an acceptable performance status) if they are expected to die from starvation/under nutrition prior to tumor spread. - Total daily energy expenditure in cancer patients may be assumed to be similar to healthy subjects, or 20–25 kcal/kg/day for bedridden and 25–30 kcal/kg/day for ambulatory patients - Supplemental PN is recommended in patients if inadequate food and enteral intake (<60% of estimated energy expenditure) is anticipated for more than 10 days

13. Bozzetti F, Amadori D, Bruera E, Cozzaglio L, Corli O, Filiberti A, et al. Guidelines on artificial nutrition versus hydration in terminal cancer patients. European Association for Palliative Care. Nutrition (Burbank, Los Angeles County, Calif). 1996;12:163-7. [61]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline **Relevant recommendations/statements**	- In an attempt to reach a decision on the type of treatment support (artificial nutrition vs. hydration) which would best meet the needs and expectations of the patient, they propose a three-step process: Step I: define the eight key elements necessary to reach a decision; Step II: make the decision; and Step III: reevaluate the patient and the proposed treatment at specified intervals. - Parenteral nutrition is very expensive and its use at home requires specific training of the patient and family and the periodic surveillance by health care providers experienced in the administration and monitoring of nutritional support.		

14. August DA, Huhmann MB. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. JPEN Journal of parenteral and enteral nutrition. 2009;33:472-500. [62]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline **Relevant recommendations/statements**	- Patients with cancer are nutritionally-at-risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. - Nutrition support therapy should not be used routinely in patients undergoing major cancer operations. - Nutrition support therapy is appropriate in patients receiving active anticancer treatment who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time - The palliative use of nutrition support therapy in terminally ill cancer patients is rarely indicated - Patients should not use therapeutic diets to treat cancer.		

15. Bozzetti F, Cotogni P, Lo Vullo S, Pironi L, Giardiello D, Mariani L. Development and validation of a nomogram to predict survival in incurable cachectic cancer patients on home parenteral nutrition. Annals of oncology : official journal of the European Society for Medical Oncology. 2015;26:2335-40. [65]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** no details on either qualitative or quantitative composition of nutritional admixtures at the start of HPN	**Total no. Patients:** 579 **Inclusion criteria:** an incurable malignancy and absence of any oncologic treatment **Exclusion criteria:** patients with ascites or pleural effusion; patients with uncontrolled symptoms	- all patients received HPN, which was randomly split into a training and a testing sample - a nomogram was built in the training sample, in order to estimate median survival or survival probability at 3 and 6 months according to individual patient characteristics - in order to assess the clinical impact implied, they previously conducted a survey of incurable cancer patients receiving HPN, which shows that survival was markedly affected by Karnofsky performance status (KPS), tumor spread, Glasgow prognostic score (GPS) and tumor site
Notes	**Author's Conclusion:** An increasing number of patients are expected to receive HPN. In such a setting, tools for predicting the survival outcome may play a role toward personalized medicine and for investigating novel experimental therapies.		
Outcome measures/results	survival of the cancer patients		- in the training sample, median survival was 3.2 (95% CI 3.0–3.7) months - GPS, KPS, tumor site and spread were confirmed to be significant prognostic factors - significant interaction was also shown between the site and spread

<u>Empfehlung 8</u>

HPE sollte bei Patienten mit CIF aufgrund einer fortgeschrittenen bösartigen Erkrankung verordnet werden, wenn ansonsten ein vorzeitiger Tod durch Unterernährung droht.

Empfehlungsgrad B

16. Hyltander A, Drott C, Unsgaard B et al. The effect on body composition and exercise performance of home parenteral nutrition when given as adjunct to chemotherapy of testicular carcinoma. Eur J Clin Invest 1991; 21: 413-420. doi:10.1111/j.1365-2362.1991.tb01389.x [74]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Sweden **Centers:** n/a **Setting:** n/a **Funding Sources:** Swedish Cancer Society (93-B89-22XA, 2014-B88-01XA, 2147-B89-04XA), the Medical Research Council (B89-17X- 00536-25A, B89-17K-08712-01A), Tore Nilson Foundation, Assar Gabrielsson Foundation (AB Volvo), Jubileumskliniken Foundation, Inga-Britt & Arne Lundberg Research Foundation, Axel & Margaret Ax:son Johnson Foundation, Swedish and Gothenburg Medical Societies and the Medical Faculty, University of Gothenburg. **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 33 **Inclusion criteria:** male patients with testicular carcinoma **Exclusion criteria:** n/a	Patients were randomized to receive either TPN (n= 19) or spontaneous oral intake (n= 14) during PVB/PEB treatment. All patients received PVB/PEB treatment (cisplatinum, vinblastine/etoposid and bleomycine).
Notes	**Author's Conclusion:** In conclusion, this study demonstrates that TPN is insufficient to protect either body composition, whole body nitrogen sparing or working capacity when given daily for more than eight weeks as adjunct to chemo- therapy in patients with oral food intake reduced by 25-30%. Fat accumulation was the only measurable benefit. It is proposed that this is another example of the inefficiency of artificial nutrition to protect lean body mass in various groups of patients with upcoming or established undernutrition		
Outcome measures/results	Energy balance, weight, total protein intake, body nitrogen, adaption to undernutrition, maximal exercise capacity		- TPN patients were in overall positive energy balance (+850 Kcal day^{-1}), while the control group was in negative balance (-532 Kcal day^{-1}). This led to weight gain in the TPN group (+2.2k1.0kg) while the control group lost significant weight (-4.2 ± 1.1 kg).

		- The average spontaneous oral caloric intake was 1014 ± 153 Kcal day^{-1} in the TPN group and 1484 ± 200 Kcal day^{-1} in the control group; total protein intake corresponded to 1.5 g protein kg day^{-1} in the TPN group and 0-7 kg day^{-1} in the control group. - Weight gain in TPN-treated patients consisted only of fat accumulation without significant water retention, and they lost body nitrogen to the same extent as the control patients. - The adaptation to undernutrition was better preserved in the control patients determined by indirect calorimetry. - Maximal exercise capacity decreased during chemotherapy in both groups to the same extent from around 180 watts to 137 watts (P<0.001), but the relationship between oxygen uptake and submaximal work was not significantly influenced by chemotherapy or TPN in either of the two groups.

17.	**Lundholm K, Daneryd P, Bosaeus I et al. Palliative nutritional intervention in addition to cyclooxygenase and erythropoietin treatment for patients with malignant disease: Effects on survival, metabolism, and function. Cancer 2004; 100: 1967-1977. doi:10.1002/cncr.20160**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Sweden **Centers:** Department of Surgery, Sahlgrenska University Hospital, Goteborg University (Gothenburg, Sweden) **Setting:** n/a **Funding Sources:** the Swedish Cancer Society (2014), the Swedish Research Council (08712), the Assar Gabrielsson Foundation (AB Volvo), the Jubileumskliniken Foundation, the Inga Britt and Arne Lundberg Research Foundation, the Swedish Medical Society, the	**Total no. Patients:** 309 **Inclusion criteria:** insidious (3–5% over 3 months) or ongoing weight loss due to generalized malignant disease and solid tumor type, disease for which effective tumor treatment was not available; they had not received tumor therapy < 2–3 months before inclusion; and they had an expected survival time of > 6 months as estimated by the clinician. **Exclusion criteria:** brain metastases; expected survival of < 6 months; manifest impairment of kidney function, with serum creatinine levels > 200 µmol/L; body	Patients with malignant disease who experienced progressive cachexia due to solid tumors (primarily gastrointestinal lesions) were randomized to receive a COX inhibitor (indomethacin, 50 mg twice daily) and EPO (15–40,000 units per week) along with specialized, nutrition-focused patient care (oral nutritional support and home total parenteral nutrition [TPN]) provided on a patient-by-patient basis to attenuate inflammation, prevent anemia, and improve nutritional status. Control patients received the same indomethacin and EPO doses that study patients received without the added nutritional support. All patients were treated and followed until death.

	Gothenburg Medical Society, and the Medical Faculty of Gothenburg University. **Dropout rates:** n/a **Study limitations:** n/a	temperature/recurring fever > 37.8 °C; and persistent cholestasis, with serum bilirubin concentration above the normal level (21 µmol/L).	
Notes	**Author's Conclusion:** The results of the current study strongly support that nutrition is a limiting factor influencing survival and that nutritional support protects integrated metabolism and metabolic function in patients with progressive cachexia secondary to malignant disease.		
Outcome measures/results	food intake, energy balance, body composition, and maximum exercise capacity		- Home TPN was provided to approximately 50% of the study patients without severe complications. - Over the entire observation period, rhEPO prevented the development of anemia in both study patients and control patients. - Intention-to-treat analysis revealed an improvement in energy balance for nutritionally supported patients ($P < 0.03$); no other significant differences in outcome between study patients and control patients were observed. - As-treated analysis demonstrated that patients receiving nutrition experienced prolonged survival ($P < 0.01$), which was accompanied by improved energy balance ($P < 0.001$), increasing body fat ($P < 0.05$), and a greater maximum exercise capacity ($P < 0.04$). - A trend toward increased metabolic efficiency at maximum exercise ($P < 0.06$) for study patients relative to control patients also was observed.

18. Lundholm K, Korner U, Gunnebo L et al. Insulin treatment in cancer cachexia: effects on survival, metabolism, and physical functioning. Clin Cancer Res 2007; 13: 2699-2706. doi:10.1158/1078-0432.CCR-06-2720 [76]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Sweden **Centers:** Department of Surgery, Sahlgrenska University Hospital, Goteborg University (Gothenburg, Sweden) **Setting:** n/a **Funding Sources:** Swedish	**Total no. Patients:** 138 **Inclusion criteria:** manifest weight loss due to generalized malignant disease and solid tumor type **Exclusion criteria:** tablet- or insulin-dependent diabetes, brain metastases, expected survival of <6 months, impaired kidney function	Patients with mainly advanced gastrointestinal malignancy were randomized to receive insulin (0.11 F 0.05 units/kg/d) plus best available palliative support [anti-inflammatory treatment (indomethacin), prevention of anemia (recombinant erythropoietin), and specialized nutritional care (oral supplements + home parenteral nutrition)] according to individual needs. Control patients received the best available palliative support according to the same principles.

	Cancer Society (2014), the Swedish Research Council (08712), Assar Gabrielsson Foundation (AB Volvo), Jubileumskliniken Foundation, Inga Britt and Arne Lundberg Research Foundation, Novo Nordisk Scandinavian AB, Swedish and Goteborg Medical Societies, and the Medical Faculty, Goteborg University. **Dropout rates:** n/a **Study limitations:** various combinations of interventions interact differently among patients; a fact difficult to compensate for in statistical computations on cohorts with a limited number of patients	(serum creatinine >200 µmol/L), increased body temperature to 37.8 °C, and persistent cholestasis (serum bilirubin >21 µmol/L).	
Notes	**Author's Conclusion:** In conclusion, the present study shows that daily insulin treatment in catabolic cancer patients had significant effects towards improved micronutrient intake and intermediary fat metabolism, which caused increased net retention of body fat associated with improved metabolic efficiency during a close to maximum workload, without indications that insulin stimulated disease progression. The present observations show that insulin treatment is a powerful complement in multimodal palliative care of weight-losing cancer patients as suggested half a century ago.		
Outcome measures/results	food intake, body composition, exercise capacity, metabolic efficiency during exercise, and spontaneous daily physical activity		- Patient characteristics at randomizations were almost identical in study and control groups. - Insulin treatment for 193 ± 139 days (mean ± SD) significantly stimulated carbohydrate intake, decreased serum-free fatty acids, increased whole body fat, particularly in trunk and leg compartments, whereas fat-free lean tissue mass was unaffected. - Insulin treatment improved metabolic efficiency during exercise but did not increase maximum exercise capacity and spontaneous physical activity. - Tumor markers in blood (CEA, CA-125, CA 19-9) did not indicate the stimulation of tumor growth by insulin; a conclusion also supported by improved survival of insulin-treated patients ($P < 0.03$).

19.	Obling SR, Wilson BV, Pfeiffer P et al. Home parenteral nutrition increases fat free mass in patients with incurable gastrointestinal cancer. Results of a randomized controlled trial. Clin Nutr 2019; 38: 182-190. doi:10.1016/j.clnu.2017.12.011 [77]		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+ ROB 5/7	**Countries:** Denmark **Centers:** Odense University Hospital Denmark **Setting:** n/a **Funding Sources:** Danish Cancer Society (R90- A6191), the Region of Southern Denmark, Odense University Hospital (12/26914), Baxter Healthcare Corporation **Dropout rates:** n/a **Study limitations:** Risk of Bias: high Inconsistency: n/a Indirectness: moderate Impreciseness: high Publication bias: n/a Challenge of inclusion, with a large group of patients not wanting to participate, difficult to predict if study population is representative, population studied was remarkably fragile and before the end of study more than half of the patients were dead	**Total no. Patients:** 47 **Inclusion criteria:** histologically confirmed incurable gastrointestinal cancer (locally advanced or metastatic), age > 18 years, performance status (PS) 0 - 2 [17], nutritionally at risk according to NRS 2002 score ≥ 2 **Exclusion criteria:** functional or actual short bowel syndrome	Patients with incurable gastrointestinal cancer, nutritionally at risk, were randomly assigned to either; a) best practice nutritional care and dietetic counselling (non-sHPN) or b) dietetic counselling and supplemental home parenteral nutrition (sHPN group). Treatment duration was 24 weeks with visits every six weeks for five scheduled visits.
Notes	**Author's Conclusion:** Findings from this study suggest that sHPN temporally have a preventive effect on loss of FFM in patients with incurable gastrointestinal cancer. sHPN may have a positive effect on overall QoL and it may be considered if sHPN should be offered in carefully selected patients		

	with incurable cancer. We found no increased risk of adverse events or death when offering sHPN but on the other hand a significant advantage in function or overall survival was not identified. However, with a small sample size, caution must be applied, as the findings might not be solid.	
Outcome measures/results	Primary outcome: gain in bioelectrical impedance analyses (BIA) estimated FFM Secondary outcomes: muscle strength, quality of life and survival	- Median age was 66.9 (41.5 - 88.2), BMI 21.3 (14.8 - 35.7) and (91%) were receiving palliative chemotherapy. - Median FFM and fat free mass index increased in the sHPN group. - At 12 weeks a significant difference ($p < 0.01$) was found between the groups; in the sHPN group 69% of the patients (versus 40%) increased their FFM. - Handgrip strength increased in both groups but without significance between the two. - Quality of life at 12 weeks was significantly better ($p < 0.05$) in the sHPN group. No difference was noticed in survival, median 169 (CI 88 - 295) days versus 168 (CI 80 - 268) days. - Study completion was accomplished by 36%; 60% died before end of study.

1.3 Kombinationen

<u>Empfehlung 9</u>

Sowohl HEE als auch HPE sollen mit oraler Ernährung kombiniert werden, wenn die orale Ernährung möglich, aber nicht hinreichend zum Erhalt bzw. zur Verbesserung des Ernährungszustandes und der ernährungsabhängigen Lebensqualität ist.

Empfehlungsgrad A

<u>Empfehlung 10</u>

HPE sollte in Kombination mit HEE bzw. oraler Ernährung verordnet werden, wenn HEE oder orale Ernährung möglich aber nicht hinreichend zum Erhalt bzw. zur Verbesserung des Ernährungszustandes und der ernährungsabhängigen Lebensqualität ist.

Empfehlungsgrad B

1.4 Kontraindikationen für HEE bzw. HPE

Empfehlung 11

Eine HEE/HPE sollte nur durchgeführt werden, wenn eine Verbesserung des Ernährungszustands, des funktionellen Status oder der Lebensqualität zu erwarten oder ein Status quo nicht anders zu erhalten ist.

Empfehlungsgrad B

20.	**Schuetz P, Fehr R, Baechli V et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. The Lancet 2019; 393: 2312-2321. doi:10.1016/s0140-6736(18)32776-4 [15]**
→ See No. 1	

21.	**Kaegi-Braun N, Tribolet P, Gomes F et al. Six-month outcomes after individualized nutritional support during the hospital stay in medical patients at nutritional risk: Secondary analysis of a prospective randomized trial. Clin Nutr 2021; 40: 812-819. doi:10.1016/j.clnu.2020.08.019 [92]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+ ROB 4/7	**Countries:** Switzerland **Centers:** 8 Swiss hospitals **Setting:** n/a **Funding Sources:** The Swiss National Science Foundation (SNSF) (PP00P3_150531) and the Research Council of the Kantonsspital Aarau **Dropout rates:** 2% **Study limitations:** Risk of Bias: high Inconsistency: n/a Indirectness: moderate Impreciseness: low Publication bias: n/a The intervention focused mainly on the hospital stay	**Total no. Patients:** 2028 **Inclusion criteria:** NRS total score of 3 points or more was mandatory, expected length of hospital stay of ≥ 5 days. **Exclusion criteria:** initial admission to an intensive care unit or surgical unit, inability to ingest oral nutrition, ongoing nutritional treatment before trial inclusion, terminal conditions, anorexia nervosa, acute pancreatitis and liver failure, cystic fibrosis or stem cell transplantation, history of gastric bypass surgery, and any contraindications for nutritional support	We randomly assigned patients to receive protocol-guided individualized nutritional support to reach protein and energy goals (intervention group) or hospital food as usual (control group) during the hospital stay. The intervention was discontinued at hospital discharge and further nutritional support was based on the discretion of the treating team.

	and only a minority of patients received nutritional support in the outpatient setting after discharge; EFFORT was a pragmatic trial, and blinding of participants and personnel was deemed to be impractical; control group received hospital food as usual, which may vary from hospital to hospital and within countries. Forth, our trial design does not allow to make firm conclusions regarding the underlying reasons for lack of effect at long-term		
Notes	**Author's Conclusion:** Understanding the optimal use of individual nutritional support to effectively prevent and treat malnutrition is highly complex. Particularly, the optimal timing of nutritional support in regard to best time to start nutrition and optimal duration of the intervention have not well been established. The EFFORT trial showed that a nutritional intervention to reach protein and energy goals in medical inpatients at nutritional risk that focuses on the inpatient setting effectively reduces the risk of adverse outcomes and mortality within 30 days, but there is no apparent legacy effect. There is now a strong need to study effects of outpatient nutritional support interventions (possibly combined with other strategies to increase muscle mass, such as increased physical activity) in the nutrition- ally vulnerable population of medical patients.		
Outcome measures/results	primary outcome: all-cause mortality at 6-months secondary outcomes: non-elective hospital readmissions, functional outcome and quality of life		- At 6-month, 231 of 994 (23.2%) intervention group patients had died compared to 246 of 999 (24.6%) control group patients, resulting in a hazard ratio for death of 0.90 (95%CI 0.76 to 1.08, p = 0.277). - Compared to control patients, intervention group patients had similar rates of hospital readmission (27.3% vs. 27.6%, HR 1.00 (95%CI 0.84 to 1.18), p = 0.974), falls (11.2% vs. 10.9%, HR 0.96 (95%CI 0.72 to 1.27), p = 0.773) and similar quality of life and activities of daily living scores.

2 Strukturelle Voraussetzungen

2.1 Häusliche Voraussetzungen

Empfehlung 12

Die Eignung des Umfeldes und die Sicherstellung der nötigen Unterstützung für Patienten, die HEE/HPE erhalten, kann durch den zuständigen Arzt bzw. das NST überprüft werden. Ziel ist die sichere Durchführung der HEE/HPE Therapie.

Empfehlungsgrad 0

22. Vashi PG, Virginkar N, Popiel B et al. Incidence of and factors associated with catheter-related bloodstream infection in patients with advanced solid tumors on home parenteral nutrition managed using a standardized catheter care protocol. BMC Infect Dis 2017; 17: 372. doi:10.1186/s12879-017-2469-7 [100]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective cohort study 2+ JBI 8/8	**Countries:** USA **Centers:** Cancer Treatment Centers of America **Setting:** cancer patients on HPN **Funding Sources: the** study was funded by Cancer Treatment Centers of America **Dropout rates:** n/a **Study limitations:** Risk of bias: low Inconsistency: n/a Indirectness: moderate Impreciseness: moderate Publication bias: n/a Data not primarily collected for research purposes, therefore, data on potential confounding variables is	**Total no. Patients:** 335 **Inclusion criteria:** patients with solid tumors receiving HPN between January 2012 and July 2015 while being treated at Cancer Treatment Centers of America® (CTCA) at Midwestern Regional Medical Center **Exclusion criteria:** n/a	Three types of venous access devices were used: peripherally inserted central catheters, tunneled central catheters, and ports.

	missing. The venous access devices were not specifically placed for the purpose of HPN. The study population consisted of heterogeneous non-hospitalized patients with solid tumors from a single institution.		
Notes	**Author's Conclusion:** We found a low incidence rate of CRBSI following a standardized catheter maintenance protocol in a high-risk oncology population undergoing HPN.		
Outcome measures/results	Primary outcome: incidence of catheter-related blood stream infections (CRBSI)		Of 335 patients, 15 (4.5%) patients experienced CRBSI. One patient experienced 2 episodes of CRBSI. As a result, for a total of 408 venous access devices, the number of CRBSI cases was 16 (3.9%). The overall incidence of CRBSI per 1000 HPN days was 0.54 (95% CI: 0.32 to 0.86). Of the 16 CRBSI cases, 8 occurred in ports, 7 in peripherally inserted central catheters and 1 in tunneled central catheters. There were no statistically significant differences in the incidence rates of CRBSI across the 3 types of venous access devices. No variables were found to be statistically significantly associated with CRBSI incidence. Type of venous access device had no effect on the incidence of CRBSI. Severely malnourished patients and those with metastatic disease had almost twice the risk of CRBSI compared to well-nourished and non-metastatic patients respectively; however, the results did not attain statistical significance. Similarly, serum albumin <3.5 g/dl was associated with almost thrice the risk of CRBSI compared to serum albumin > = 3.5 g/dl, however, the finding was not statistically significant.

23. Dreesen M, Foulon V, Vanhaecht K et al. Development of quality of care interventions for adult patients on home parenteral nutrition (HPN) with a benign underlying disease using a two-round Delphi approach. Clin Nutr 2013; 32: 59-64. doi:10.1016/j.clnu.2012.05.006 [105]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guidance paper **Relevant recommendations / statements**	Valid key interventions to assess the quality of care: - Ensuring the training takes place in an inpatient setting - Ensuring the training program includes pump use and care, catheter care and recognizing common problems - Making a checklist available of criteria for which competence of the patient is achieved - Making written information with clear messages available for all patients to take home after education		

	- Making visible information (images, photos, instruction DVD) available for all patients to take home after education - Ensuring education can be continued at home after the inpatient education Ensuring patients knowledge is checked periodically

24. Dreesen M, Foulon V, Vanhaecht K et al. Identifying patient-centered quality indicators for the care of adult home parenteral nutrition (HPN) patients. JPEN J Parenter Enteral Nutr 2014; 38: 840-846. doi:10.1177/0148607113495891 [110]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Patient interview / case series 3	**Countries:** Belgium **Centers:** University Hospital of Leuven **Setting:** n/a **Funding Sources:** The first author has an unconditional educational grant from the company Baxter Belgium **Dropout rates:** n/a **Study limitations:** Difficulty for patients to distinguish between HPN care (role and benefits of the different caregivers) and the HPN treatment "as such" concerning the outcome indicators. Reviewer bias.	**Total no. Patients:** 12 **Inclusion criteria:** new adult patients (experienced 1-180 days), treated at the University Hospital of Leuven, Belgium, between June 2011 and November 2011 **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** Using face-to-face, semi structured interviews, we developed quality indicators from the patients' perspective. In all, the quality indicators in Table 2 give an indication of what quality of care means for patients. This interesting set of indicators can be used to perform, evaluate, or improve current HPN care after checking if these indicators are followed in practice. In addition, they will assist us toward a more patient-centered care.		
Outcome measures/results	Experiences with HPN, role of health care professionals, optimization of care, Advice to new patients		Structure indicators: - Availability of contact person 24 hours a day - Availability of experienced and trained home nurse Process Indicators - Concerning family caregivers o Giving support to the patients - Concerning general practitioner o Being available for home nurses when questions occurs

		○ Being sufficiently informed on HPN ○ Giving confidence to patient ○ Referring the patient timely to the hospital ○ Be willing to listen to the patient - Concerning home nurses ○ Being accessible for questions/problems ○ Communicating sufficiently with patients ○ Exempting patients from technical operations ○ Following same protocol as taught to patients ○ Giving confidence to patient ○ Monitoring parameters ○ Managing problems proactively ○ Taking responsibility and initiative when problems occur ○ Taking enough time for patient and social aspects ○ Using aseptic techniques to manage catheter - Concerning patient ○ Sharing experiences with fellow HPN patients - Concerning physicians in hospital ○ Following the evolution of patient ○ Giving clear understandable information about purpose and plan of therapy ○ Informing GP on current state of patient ○ Be willing to listen and being sufficiently available - Concerning nutrition support team ○ Agreeing on clear aims for education with patient ○ Learning to patient what to do when problems occur ○ Providing general information in a clear and understandable manner ○ Providing information on practical problems ○ Ensuring nutrition needs are met - Concerning supplier of the material ○ Communicating well with patient ○ Performing correct delivery (timely, right place, right amount) ○ Giving confidence to patient ○ Respecting privacy of patient ○ Delivering orderly packaged material and enough material for aseptic management of catheter

2.2 Fachliche Voraussetzungen / Ernährungsteams

Empfehlung 13

Krankenhäuser, die Patienten mit HEE/HPE entlassen, sollten mindestens eine spezialisierte Ernährungsfachkraft beschäftigen oder über ein multidisziplinäres NST (Arzt, spezialisierte Pflegefachkraft, Ernährungsfachkraft, Apotheker, u. a.) verfügen, welches sich u. a. um die Rezeptur und das Entlassungsmanagement kümmert.

Empfehlungsgrad B

25. Silver HJ, Wellman NS, Galindo-Ciocon D et al. Family caregivers of older adults on home enteral nutrition have multiple unmet task-related training needs and low overall preparedness for caregiving. J Am Diet Assoc 2004; 104: 43-50. doi:10.1016/j.jada.2003.10.010 [125]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Caregiver interviews / case series 3	**Countries:** USA **Centers:** n/a **Setting:** Home enteral nutrition **Funding Sources:** grant number R03 HS11276 from the Agency for Health care Research and Quality, a dissertation grant from Nestle´ Clinical Nutrition, Deerfield, IL, and the National Policy and Resource Center for Nutrition and Aging, Miami, FL **Dropout rates:** 66% **Study limitations:** small sample size, varied diagnosis with comorbid conditions	**Total no. Patients:** 90 **Inclusion criteria:** first discharge on enteral nutrition, no paid or formal home health caregivers provide enteral nutrition care, but by a family caregiver, caregivers had to be 21 or older unpaid for caregiving, resided within 45 driving minutes of their care recipient's home, and speaking English or Spanish **Exclusion criteria:** n/a	structured interviews
Notes	**Author's Conclusion:** Despite some limitations, this study targeted a caregiver population that has received little attention. Investigations usually focus on the complication or mortality rates of the older adult on home enteral nutrition. This study provides insight into understanding the challenges and needs of		

	their caregivers. Being adequately trained and prepared may result in caregivers who feel competent, provide efficacious care, have lower health care use, and ultimately help contain health care costs.	
Outcome measures/results	demographic and descriptive information, administration of the Home Enteral Nutrition Caregiver Task checklist, caregiver overload, preparedness, competence, self-assessment of effectiveness as caregiver	Caregivers performed an average of 19.7±8.1 of the 33 tasks daily. On the whole, the number of tasks for which caregivers reported needing training exceeded the number for which they reported having received training (17.9±5.4 vs 6.3±6.04 tasks, respectively). Although from half to 80% of caregivers performed technical tasks, less than half reported receiving training. Notably, they were not taught how to clean the tubing, manage tube clogs, use the infusion pump, check for formula residual, check tube placement, manage tube leaks, or perform an aseptic hand washing technique. A little more than half of caregivers reported managing stomach cramps, gas, diarrhea, constipation, nausea, and vomiting. Yet nutrition-related tasks were least common in caregiver training because over 90% reported needing training for managing gastrointestinal symptoms. Likewise, reported training needs were unmet for monitoring for signs of infection, body weight changes, and dehydration. Mean preparedness for caregiving score was low (1.72±0.77). Although 21 (70%) caregivers rated their effectiveness as caregivers as "fair" or "good," only 14 agreed "very much" with "You feel that you are a good caregiver." Less than one-third agreed "very much" that they feel "competent" or "self-confident" as caregivers. Just over half (n=17) of the caregivers reported that they telephoned health care professionals 1 or 2 times per week for further instructions.

26. Dinenage S, Gower M, Van Wyk J, Blamey A, Ashbolt K, Sutcliffe M, et al. Development and evaluation of a home enteral nutrition team. Nutrients. 2015;7(3):1607-17. [120]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case control study 2-	**Countries:** UK **Centers:** n/a **Setting:** HEN Team, cost-effectiveness **Funding Sources:** local funding to form a HEN Team, after that further 12 months of funding totaling 84.071 pounds was awarded **Dropout rates:** n/a	Total no. Patients: n=70 (70% female) Inclusion criteria: >18 years, gastrostomy tubes Exclusion criteria: n/a	HEN Team: dietitians, nurses and a speech, language therapist, homecare company nurse, nutrition nurse was developed with the aim of delivering a quality service for people with gastrostomy tubes living at home

	Study limitations: time since insertion of tube was not considered in calculation of cost savings, no control group possible, calculated cost savings were crude estimates, pre-post design didn´t allow temporal variations in care environment to be evaluated → changes maybe without introduction of the team		
Notes	**Author's Conclusion:** This service evaluation demonstrated that the establishment of a dedicated multi-professional HEN Team focused on achievement of key objectives improved patient experience and, although calculation of cost savings was estimates, provided evidence of cost-effectiveness.		
Outcome measures/results	- care pathway embedded into practice: stages of management for people concerning their feeding tubes, how referrals be created, timeframes for assessment and review, discharge from service (provision of a framework for activity, point of reference) - schedule of training - → impact of the HEN team on patients´ outcome was assessed in a pre-post test evaluation design Outcomes: - malnutrition risk of patients: MUST - number of patients carers, healthcare stuff, nursing home trained in gastrostomy tube care - number of patients who had tubes removed - estimates of costs: enteral feed prescription, thickening agents for dysphagia - frequency and length of hospital admission, transport costs for ETF related problems (for n=28)	- age: 61 years (range 19-90); nearly 70% lived in their own homes - 70% percutaneous gastrostomy tube - Most frequent medical condition causing the need of a tube: cerebrovascular accident (25%) - proportion of patients at medium or high risk of malnutrition (MUST score greater than 0) was reduced from 41% to 25% suggesting reduced risk of malnutrition - Patients and carers reported improved support in managing their ETF - Cost savings were realized through: - (1) prevention of hospital admission and related transport for ETF related issues - (2) effective management and reduction of waste of feed and thickener - (3) balloon gastrostomy tube replacement by the HEN Team in the patient's home, and optimization of nutritional status - fewer hospital admissions for tube-related problems recorded in 2012 compared to 2010/2011 - All respondents (30% of the population) stated that they were extremely satisfied with the services provided by the HEN Team, with 100% of respondents rating the overall service received as good or excellent	

27. Landeiro MJ, Peres HH, Martins TV. Evaluation of the educational technology "Caring for dependent people" by family caregivers in changes and transfers of patients and tube feeding. Rev Lat Am Enfermagem. 2016;24:e2774. [130]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Controlled trial 2+	**Countries:** Portugal **Centers:** Medicine services of a hospital in Porto, Portugal **Setting:** HEN education for caregivers vs. control **Funding Sources:** n/a **Dropout rates:** 12.2% (n=9, death, disease, institutionalization) **Study limitations:** power of education considered as a facilitator in the teaching and learning process related with the information about home care → access to technology is expensive	**Total no. Patients:** n=74 (n=65 analyzed) **Inclusion criteria:** family caregivers pf patients with functional dependence, Acceptation to participate, age ≥18 years, internet access at home, basic skills to handle information technology/support of a family member/ significant other meeting these conditions and having under their responsibility one dependent person with recent hospitalization **Exclusion criteria:** n/a	1. Intervention (IG): n=32 (n=36 at beginning) → interactive educational technology at home 2. Control (CG): n=33 (n=38 at beginning) family caregivers → The assessment in both groups had two moments: initial, during hospitalization and one month after discharge → Both groups had the same procedure except that the interactive educational technology was not presented to the control group, nor provided a guide for navigation → After the second evaluation, the CG was granted access to the tool
Notes	• First evaluation of baseline: patients still in hospital; second evaluation: during home visit (1 month after clinical discharge) • To prevent the participants of the CG to had contact with those of the IG, it was decided to carry out the selection of participants in both groups in different services and during the first 70 days of the start of data collection **Author's Conclusion:** these results confirm the improvement of interactive educational technologies and in the training of family caregivers to care for dependents. This technology successfully met the technical quality and learning needs of caregivers and was considered easy and stimulating.		
Outcome measures/results	- Sociodemographic data - Satisfaction - Evaluation of knowledge questionnaire: how to feed by nasogastric tube, positioning and transferring the dependent person - Functional dependence assessed by Barthel index → both groups underwent two stages of evaluation with a set of tools that allowed assessing the knowledge	- Mean age: IG → 57.69 years vs. CG → 56.64 years - Regarding the occupation of the 65 family caregivers, 25 (38,5%) were in retirement or preretirement situation, 23 (35,4%) were active, 16 (24,6%) unemployed and 1 (1,5%) handicapped - Majority of family caregivers were daughters and spouses (18.5%) - Main reasons for hospitalization: respiratory, cardiac, urinary problems - 72.3% of patients were totally dependent; main cause: behavioral disorders like Alzheimer´s and dementia (31%), nervous system disease like Parkinson (7.5%), diseases of circulatory system like stroke (16.9%)	

		- There were no statistical differences in the distribution of age, gender, educational level of family caregivers, time being caregiver and age of the dependent person, between IG and CG - IG had a larger increase in knowledge related to the use of the educational technology; initial assessment of groups → equivalent knowledge of the different areas - In the control group the knowledge did not differ in the two evaluation time points - There was a moderate positive correlation between educational status and total knowledge before the intervention (r = 0,528; p = 0,000) and also with the total knowledge after the intervention (r = 0,407; p = 0,002). - time spent by family caregivers with the use of technology education varied: 18 (56,3%) spent from 1 to 4 hours, 13 (40,6%) spent from 4 to 10 hours and 1 (3,1%) more than ten hours

Empfehlung 14

HEE/HPE sollte grundsätzlich und entsprechend etablierter Standards von einer spezialisierten Ernährungsfachkraft oder einem multidisziplinären NST eines Krankenhauses oder einer ambulanten Einrichtung koordiniert werden, da dies die Qualität der Maßnahmen erhöht, die Komplikationsraten reduziert und damit einen wesentlichen Beitrag zur Verbesserung der Lebensqualität der Patienten sowie zur Kosteneffizienz der Maßnahmen leistet.

Empfehlungsgrad B

28.	**Silver HJ, Wellman NS, Galindo-Ciocon D et al. Family caregivers of older adults on home enteral nutrition have multiple unmet task-related training needs and low overall preparedness for caregiving. J Am Diet Assoc 2004; 104: 43-50. doi:10.1016/j.jada.2003.10.010**
→ see No. 25	

29. Soifer NE, Borzak S, Edlin BR et al. Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial. Arch Intern Med 1998; 158: 473–477 [132]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
Ib	randomized, controlled, prospective	Intervention group: intravenous therapy Control group: Care by nursing staff	3 months	clinic	875 catheters in 441 patients	n/a	peripher intravenous catheter	Decrease of inflammation: 7.9 % (intervention group) vs. 21 % control group	Intravenous therapy reduces complications

30. Goldstein M, Braitman LE, Levine GM. The medical and financial costs associated with termination of a nutrition support nurse. JPEN J Parenter Enteral Nutr 2000; 24: 323-327. doi:10.1177/0148607100024006323 [133]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
retrospective review 2+	**Countries:** USA **Centers:** tertiary care community hospital **Setting:** patients receiving total parenteral nutrition **Funding Sources:** n/a **Dropout rates:** **Study limitations:**	**Total no. Patients:** 1,093 **Inclusion criteria:** patients receiving total parenteral nutrition **Exclusion criteria:** n/a	period with nutrition support nurse vs. period without nutrition support nurse
Notes	**Author's Conclusion:** Adequate staffing of a nutrition support team reduced inappropriate TPN and complications of TPN. Financial savings of the same order of magnitude as the nurse's compensation accompany substantial decreases in patient morbidity.		
Outcome measures/results	(1) the percentages of patients receiving TPN inappropriately, (2) the number of days of inappropriate TPN, (3) catheter-related sepsis,~ 7 and (4) the amount of TPN wastage		Overall, during the years when the nutrition support nurse was present, 61 of 713 (8.6%) patients receiving TPN had a functional gastrointestinal tract. In comparison, 46 of 380 TPN patients (12.1%) had a functional gastrointestinal tract when the nutrition support nurse was absent, a risk difference of 3.5% points (95% CI, -0.6 to 8.3; p = .069). More patients had a greater number of days of inappropriate TPN in the years when there was no nutrition support nurse (p < .05). During the years when the nutrition support nurse was present, 63 of 713 (8.8%) TPN patients developed line sepsis compared with 50 of 380 (13.2%) when there was no nutrition support nurse, a risk difference of 4.4% points (95% CI, 0.06 to 9.2; p = .028, Table II).

		During years of transition the number of TPN bags discarded increased from none, (nutrition support nurse present) to 8 bags (nutrition support nurse absent). Subsequently wastage decreased from 11 bags (nutrition support nurse absent) to 5 bags nutrition support nurse present). There was $4333 in excess charges for TPN wastage during the 2 years that the nutrition support nurse was absent. Using the minimum estimate of $1400 per episode of sepsis,8 total preventable charges more than doubled, an increase of $89,158 the year after the nutrition support nurse position was eliminated. Preventable charges decreased by $79,582 from FY 1994 to FY 1995, the year the nutrition support nurse position was reinstated. Applying these ratios to our estimated charges during the year after the termination of the nutrition support nurse, a potential cost savings between $38,148 and $194,285 (depending on the estimate for sepsis) results. Similarly, the ratio was 0.4282 and 0.4230 when the nutrition support nurse position was reinstated, resulting in a decrease in costs of between $34,485 and $156,654. The financial outlay of the hospital was the nutrition support nurse's total salary of $40,000 plus 22% benefits per annum ($48,800 total). Using the minimum cost estimate for sepsis, the institution's employment cost for the nutrition support nurse are of the same order of magnitude as total preventable costs. Using the maximum cost estimate for sepsis, preventable costs were 3 to 4 times NSN compensation.

2.3 Schulungen

<u>Empfehlung 15</u>

Das Schulungsprogramm für den Patienten und/oder das häusliche Pflegepersonal sollte von kundigem Fachpersonal (z. B. Ernährungsfachkräfte oder Pflegefachkräfte eines klinischen NST oder eines beauftragten „Provider" bzw. Homecare-Unternehmens) durchgeführt werden.

Empfehlungsgrad B

31. Silver HJ, Wellman NS, Arnold DJ et al. Older adults receiving home enteral nutrition: enteral regimen, provider involvement, and health care outcomes. JPEN J Parenter Enteral Nutr 2004; 28: 92–98 [142]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	observation study	interviews at home during first 3 months with HEN	n/a	at home	30 (20 male, 10 female)	68.4 years	HEN for max. 3 months, BMI 20.04 ± 5.12 kg/m^2, 17 with BMI < 18.5 kg/m^2	Energy intake: 1596 ± 553 kcal/d, GI complications at 6.3%, with 1/3 each of tube obstruction, leaky tubes, displacement of tubes, water intake 53 ±3 7% of required amount ↓urinary excretion, Weight ↓: -4.35 ± 8.40 kg.	more complications in women, lower energy intake, lower BMI, complications associated with unplanned nursing facility visits and readmissions.

32.	Silver HJ, Wellman NS, Galindo-Ciocon D et al. Family caregivers of older adults on home enteral nutrition have multiple unmet task-related training needs and low overall preparedness for caregiving. J Am Diet Assoc 2004; 104: 43-50. doi:10.1016/j.jada.2003.10.010 [125]
→ see No. 25	

33.	Soifer NE, Borzak S, Edlin BR et al. Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial. Arch Intern Med 1998; 158: 473–477 [132]
→ see No. 29	

Empfehlung 16

Alle Informationen im Zusammenhang mit der Schulung zur HEE/HPE sollten nicht nur mündlich, sondern auch schriftlich oder über E-Health zur Verfügung gestellt werden.

Empfehlungsgrad B

Empfehlung 17

Ausgewählte Patienten bzw. deren Angehörige können die Nährlösungen nach adäquater Schulung und Eignung selbst herrichten, mischen sowie an- und abhängen, was eine Unabhängigkeit von Fachpersonal ermöglicht und eine Verbesserung der Lebensqualität sowie Kostenersparnis bewirken kann.

Empfehlungsgrad 0

34. Park JY. Implementing a central venous catheter self-management education program for patients with cancer. Eur J Oncol Nurs 2016; 25: 1-8. doi:10.1016/j.ejon.2016.08.010 [163]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** Korea **Centers:** tertiary hospital in Seoul **Setting:** patients with cancer **Funding Sources:** **Dropout rates:** **Study limitations:** number of times when subjects' practices on themselves was not controlled. outcome parameters were self-reported, selection bias	**Total no. Patients:** 45 **Inclusion criteria:** aged 20 or above, diagnosed with cancer, able to speak and write in Korean, willing to participate, and had their first central venous catheter(CVC) insertion during the study period **Exclusion criteria:** history of CVC insertion	central venous catheter self-management education program (CVC S-MEP) vs. usual care
Notes	**Author's Conclusion:** The CVC S-MEP helped improve patients' ability to resolve problems and adequately respond to CVC-related emergency situations by fostering greater self-care ability using methods such as face-to-face education, training with models, and feedback from healthcare professionals. In contrast to existing one-time group trainings, this program progresses in accordance with patients' own educational needs, which are identified through face-to-face discussions and consideration of the patients' condition and degree of understanding. Furthermore, examples of tasks presented through videos and physical models for practice were effective. Additionally, providing practical information for CVC self-management in a gradual and repetitive manner had a notable positive effect on patients.		
Outcome measures/results	CVC self-management knowledge, CVC self-management attitude, CVC self-management behaviors, Catheter-related complications	The CVC S-MEP significantly influenced CVC self-management knowledge and attitude. The group x time interaction on CVC self-management knowledge was statistically significant ($p < 0.007$), indicating that the CVC S-MEP influenced participants' knowledge over time. CVC S-MEP participants' attitude score similarly demonstrated a significant increase over time ($p < 0.001$).	

		When comparing the CVC management preformed at home between the groups, the experimental and control groups scored 8.29 and 6.92, respectively, indicating that the CVC S-MEP led to an improvement in CVC self-management. We observed 4 (19.0%) and 12 cases (50.0%) of CVC-related complications in the experimental and control groups, respectively, which were significant differences (p ¼ 0.030). Specifically, in the experimental group, we observed 1 (4.8%), 3 (14.3%), and 0 incidents of CVC-related infection, occlusion, and catheter damage, respectively; in the control group, the numbers of such incidents were 3 (12.5%), 8 (33.3%), and 1 (4.2%), respectively. Regarding the incidence of catheter-related infection, the rate in the experimental group (0.62 per 1000 catheter-days) appeared to indicate a low infection rate, while the rate of catheter-related infection in the control group (1.63 per 1000 catheter-days) indicated a noticeably higher infection rate. Furthermore, the incidence of occlusion was 1.87 per 1000 catheter-days in the experimental group, and 4.45 per 1000 catheter-days in the control group.

35. Bond A, Teubner A, Taylor M et al. Assessing the impact of quality improvement measures on catheter related blood stream infections and catheter salvage: Experience from a national intestinal failure unit. Clin Nutr 2018; 37: 2097-2101. doi:10.1016/j.clnu.2017.10.002 [117]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective observational study 2+ JBI 6/8	**Countries:** UK **Centers:** n/a **Setting:** home parenteral nutrition **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: high Impreciseness: low Publication bias: n/a Retrospective character of the study, cases admitted to other hospitals could have	**Total no. Patients:** 559 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	Training at home vs. training in the hospital (historical cohort)

	been missed, truncation bias by the start date		
Notes	**Author's Conclusion:** Our findings reveal that a very low CRBSI rate can be maintained when HPN patients are trained in their own home rather than in hospital. It also highlights that those with dedicated nursing care of their CVC have lower CRBSI rates and lower recurrent CRBSIs, suggesting that it may be reasonable to ask self-caring patients with recurrent CRBSIs to consider home care nursing. Our data also demonstrate that high CVC salvage rates can be achieved for CNS-related CRBSIs managed with a 10-day antibiotic salvage protocol, and that MSSA-related CRBSIs may be successfully salvaged without the need for catheter removal.		
Outcome measures/results	CVC type, the primary carer responsible for the CVC at the time of CRBSI (self, nurse, non-medical carer (e.g. family member)), isolated microorganism, duration of salvage therapy and success of salvage therapy		A total of 134 CRBSIs were recorded in 92 patients (62 patients with a single CRBSI and 30 patients with more than 1 CRBSI). The overall CRBSI rate was 0.31 per 1000 catheter days. 63% of CRBSI occurred in female patients. For those patients with >1 CRBS, the median time between the first and second event was 278 days. Of those with more than one CRBSI event, 70% were self-caring, 26.6% by nurses and 3.4% by a relative. The CRBSI rate for our cohort between 1993 and 2011, when patients were trained in hospital to manage their catheter, was 0.38 per 1000 catheter days. The CRBSI rate for 2012e2016, when patients were primarily trained at home, was 0.316 per 1000 catheter. 89% of infection episodes were associated with a single microorganism. days. Of the 100 cases where salvage was attempted, bacterial eradication was achieved in 67 cases based on negative peripheral and central blood cultures 48 h after completion of the salvage protocol. For those patients with a salvaged CVC and a subsequent CRBSI identified on follow-up (n = 16), the mean time from their initial successful salvage to the subsequent CRBSI was 305 days (range 11 - 810 days).

2.4 Besonderheiten bei Patienten in Pflegeeinrichtungen

<u>Empfehlung 18</u>

Bei geriatrischen Patienten und im Palliativbereich sollte unter ambulanten Bedingungen eine leichte bis mittelschwere Dehydratation, die nicht oral kompensierbar ist, mittels Infusion von Flüssigkeit in das Subkutangewebe behandelt werden.

Empfehlungsgrad B

36. O'Keeffe ST, Lavan JN. Subcutaneous fluids in elderly hospital patients with cognitive impairment. Gerontology 1996; 42: 36–39 [189]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
IIa	controlled	intravenous (IV) vs. subcutaneous (SC) parenteral liquids for at least 48 h	≥ 48 h/ treatment	hospital	60 (IV 30, SC 30)	80 years	Mild dehydration or low oral intake and cognitive impairment (MMSE ≤ 20 points).	Volume of fluid prescribed over 48 h =: IV 3.3 L vs. SC 3.6 L; serum urea =; keratinin =; anxiety before infusion SC 37% vs. IV 80%; cost of cannula: SC £6.80 vs. IV £28.70; local edema: SC 2	

37. Slesak G, Schnürle JW, Kinzel E et al. Comparison of Subcutaneous and Intravenous Rehydration in Geriatric Patients: A Randomized Trial. J Am Geriatr Soc 2003; 51: 155-160. doi:10.1046/j.1532-5415.2003.51052.x									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
Ib	Randomized, controlled	subcutaneous (SC) or intravenous (IV) rehydration with semi-isotonic glucose solution	as long as clinically necessary, 6 d (average); total study: 20 months.	Geriatric wards	96 (SC 48, IV 48)	85.3 ±6.7	Weak to moderate dehydration → parenteral fluid administration necessary	Increase in risk assessment: SC +1.82 vs. IV +0.53; volume administered: SC 750 mL/d vs. IV 1000 mL/d; failed punctures: SC and IV 0; Time/cannulation: SC 3min vs IV 5min; Feasibility: nurses: no difference, physicians: SC significantly better. Discomfort =, ADL ↑: same in SC and IV.	Change from SC to IV: 13 times change from IV to SC: 17 times, with SC and IV only few negative reactions

3 Zugangswege und Pumpen

3.1 Sonden und Pumpen für HEE

Empfehlung 19

Die HEE soll bevorzugt über eine PEG oder, falls indiziert, eine perkutane endoskopische Jejunostomie (PEJ) appliziert werden.

Empfehlungsgrad A

38. Corry J, Poon W, McPhee N, Milner AD, Cruickshank D, Porceddu SV, et al. Prospective study of percutaneous endoscopic gastrostomy tubes versus nasogastric tubes for enteral feeding in patients with head and neck cancer undergoing (chemo)radiation. Head Neck. 2009;31:867-76. [193]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Randomized study / prospective cohort study 2-	**Countries:** Australia **Centers:** n/a **Setting:** PEG vs. NGT in head and neck cancer patients **Funding Sources:** n/a **Dropout rates:** 3% didn´t complete RT dose **Study limitations:** different number of patients in the groups	**Total no. Patients:** n=105 **Inclusion criteria:** squamous cell carcinoma of head and neck, radical radiotherapy (RT) or radical chemoradiation, were required or expected to require enteral nutrition **Exclusion criteria:** n/a	Comparison between: 1. PEG tubes: n=32 - Vs. 2. NGT: n=73
Notes	- Patients who had whole oral cavity irradiation, accelerated hyper fractionated RT regimens, or concurrent chemotherapy and RT(chemoradiation) were advised that they would require a feeding tube → criteria used for insertion of a feeding tube were oral intake of less than 50% of calculated daily nutritional requirements, and/ or >5 kg weight loss from the commencement of treatment. - Fine bore NGT insertion was usually performed by the nursing staff. Stomach contents were aspirated and tested with litmus paper, and all patients had a chest X-ray to document correct placement - Prophylactic antibiotics were used on the day of and for 24 hours after PEG tube insertion. The technique used was the ‘‘push’’ technique as has been described by Tucker et al - Patients receiving NGTs were permitted to commence enteral feeding on an outpatient basis, but the vast majority of patients required a short stay hospital admission. Discharge criteria were the same as for the PEG tube patients. **Author’s Conclusion:** PEG tube use should be selective, not routine, in this patient population.		

Outcome measures/results	- adequacy of nutritional support: - median weight loss (proportion of patients who lost >10% body weight) - assessment of fat to muscle loss: mid arm circumference, triceps skinfold thickness - → after 6 weeks - Complications - Patients satisfaction: modified EORTC QLQ-H&N35 quality of life assessment - Cost - Others: primary disease site, TNM stage, WHO performance status, CTC (mucositis grade) v2.0 dysphagia grade → after 6 months posttreatment	- age: 60 years (range: 22-83) - no significant differences between the 2 groups: age, sex, primary site, TNM stage, performance status, or dysphagia grade - 97% in both groups completed the planned RT dose - median radiation dose received at the time of tube insertion was similar in both groups: 47 Gy (range, 22–70 Gy) for the NGT group and 46 Gy (range, 0–66 Gy) for the PEG group - PEG patients: - -significantly less weight loss at 6 weeks post-treatment (median 0.8 kg gain vs 3.7 kg loss, p < .001), - -had a high insertion site infection rate (41%) - -longer median duration of use (146 vs 57 days, p < .001) - -more grade 3 dysphagia in disease-free survivors at 6 months (25% vs 8%, p= 0.07) - Patient self-assessed general physical condition and overall quality of life scores were similar in both groups - Overall costs were significantly higher for PEG patients.

39. Nugent B, Lewis S, O'Sullivan JM. Enteral feeding methods for nutritional management in patients with head and neck cancers being treated with radiotherapy and/or chemotherapy. Cochrane Database Syst Rev. 2013(1):Cd007904. [195]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1++	**Countries:** n/a **Centers:** n/a **Setting:** PEG vs. NG in head and neck cancer patients receiving radiotherapy/ chemotherapy **Funding Sources:** n/a **Dropout rates:** 50% (n=1 of 2 eligible studies) **Study limitations:** blinding not possible, only 1 study eligible, small number of	**Total no. Studies:** n=1 (n=33 patients, 72% male) **Inclusion criteria:** RCT comparing one method of enteral feeding with another (NG, PEG, head and neck cancer patients receiving radiotherapy/chemoradiotherapy, >18 years **Exclusion criteria:** when there was no comparison between two methods of enteral feeding; patients excluded if they did not require enteral feeding, NG tube inserted	Comparison between one method of enteral feeding with another. Following possibilities were accepted: - Prophylactic percutaneous endoscopic gastrostomy (PEG) versus nasogastric tube (NG) - Prophylactic PEG versus PEG - Prophylactic PEG versus radiological inserted gastrostomy (RIG) - Prophylactic RIG versus NG - Prophylactic RIG versus PEG - Prophylactic RIG versus RIG - PEG versus NG - PEG versus RIG - RIG versus NG → only 1 study met inclusion criteria: study compared:

	patients, high degree of bias was identified in the study	instead of a PEG in error, PEG inserted instead of NG tube in error, patients unfit for PEG	1. PEG: n=15 2. NG: n=18
Notes	- 2 authors independently assessed trial quality and extracted data - One randomized controlled trial met the criteria for inclusion in this review. No further studies were identified when we updated the searches in 2012 - The greatest concern regarding bias is in relation to the five patients allocated a PEG who actually received a NG tube, due to patient refusal. The authors feel that this causes bias in favor of the PEG, as two patients refusing a PEG would influence patient satisfaction **Author's Conclusion:** There is not sufficient evidence to determine the optimal method of enteral feeding for patients with head and neck cancer receiving radiotherapy and/or chemoradiotherapy. Further trials of the two methods of enteral feeding, incorporating larger sample sizes, are required.		
Outcome measures/results	Primary outcomes: - Change in or maintenance of the nutritional status of the patient, measured by percentage body weight difference and/or anthropometry measurement changes such as triceps skin fold thickness, mid arm muscle circumference or by hand grip strength difference, during and post-treatment period Secondary outcomes: - Complications arising from the enteral feeding device, e.g. infection, tolerance of feeding device, death - Time enteral feeding device placed in relation to treatment delivered - Quality of life, health economics, user satisfaction of feeding device - Number of unscheduled treatment breaks/gaps during radiotherapy, prolongation of radiotherapy, non-completion of radiotherapy - Length of time (in days) enteral feeding is required - Reason for discontinuation of enteral feeding		- 33 patients were eligible for analysis as the trial was terminated early due to poor accrual - Number of patients with stage III/IV disease was similar in both groups (95% NG and 86% PEG) - Weight loss was greater for the NG group at six weeks post-treatment than for the PEG group (P = 0.001) - At six months post-treatment: no significant difference in weight loss between the two groups - Anthropometric measurements recorded six weeks post-treatment demonstrated lower triceps skin fold thickness for the NG group compared to the PEG group (P = 0.03) - No statistically significant difference between the two different enteral feeding techniques in relation to complication rates or patient satisfaction - Duration of PEG feeding was significantly longer than for the NG group (P = 0.0006) - cost of PEG feeding was 10 times greater than that of NG →was not significant - There was no difference in the treatment received by the two groups; four PEG fed patients and two NG fed patients -required unscheduled treatment breaks of a median of two and six days respectively - no studies of enteral feeding involving any form of radiologically inserted gastrostomy (RIG) feeding or comparing prophylactic PEG versus PEG were found for inclusion in the review - Quality of life was not measured

40. Paleri V, Roe JW, Strojan P, Corry J, Gregoire V, Hamoir M, et al. Strategies to reduce long-term postchemoradiation dysphagia in patients with head and neck cancer: an evidence-based review. Head Neck. 2014;36(3):431-43. [196]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review 2-	**Countries:** n/a **Centers:** n/a **Setting:** dysphagia, head and neck cancer, chemoradiation **Funding Sources:** Mr. J. Roe is funded by a grant from the Oracle Cancer Trust **Dropout rates:** n/a **Study limitations:** heterogeneity of the studies (methods, therapy)	**Total no. Patients:** 1. N=6 Studies (3 of them: RCT) 2.n=6 (n=4 retrospective, n=1 prospective, n=1 RT) **Inclusion criteria:** n/a **Exclusion criteria:** n/a	1. Prophylactic swallowing exercises→ to reduce long-term swallowing related morbidity; early implementation of protective exercise → important intervention 2. Gastrostomy tubes: Data from prospective studies suggest that patients tend to retain G-tubes longer than NG tubes.[35–37]. On this basis, some centers have moved away from prophylactic G-tubes, with the assumption that patients avoid oral intake earlier, if an alternative feeding route is available 3. IMRT: strategy to avoid dysphagia based on the established relationship between functional status of the swallowing-related structures and the pattern of irradiation dose distribution in these structures and on the ability of the IMRT to shape the high-dose volume in accord with the 3-dimensional outline of the target(s)
Notes	- importance of the dose–volume relationships found for structures involved in swallowing, the emerging role of IMRT planning has been underlined by several authors - disadvantages associated with IMRT, including a more inhomogeneous dose distribution, an increased risk of a marginal miss, increased total body dose, and increased time and expense **Author's Conclusion:** Given the findings of this review, we believe that there is a clear trend for better swallow outcomes to be experienced. Clearly, more prospective studies from several settings, considering the drawbacks of the studies published so far, need to be performed analyzing each of the 3 strategies discussed here to generate more confidence in the results reported earlier.		
Outcome measures/results	1. Prophylactic swallowing exercises 2. Use of gastrostomy tubes 3. IMRT as a strategy to reduce swallowing dysfunction		1. Prospective and randomized studies with small cohorts show a trend toward benefits for a preventative exercise program addressing oral and pharyngeal structures Examples: - pretreatment swallowing exercise (n=25) → improvement in MDADI score (p=0.002) -Significant differences in epiglottic inversion (p= 0.02) and tongue base position during the swallow (p= 0.025) were observed in the prophylactic exercise group over the control group -patients in the control group reported significantly fewer swallowing difficulties than those in the study group, with a proportional odds ratio (OR) of 2.3 (95% confidence interval [CI]: 1.3–4.0)

		2. Prospective and retrospective data indicate that better swallowing outcomes are likely when nasogastric tubes are used in preference to gastrostomy tubes to supplement enteral nutrition during chemoradiation. -significant differences in MDADI scores between the 2 groups in all domains of the questionnaire (p < .001), with superior outcomes in the NG group -Additionally, prophylactic G-tube was associated with a significantly higher incidence of late esophageal stricture compared with those who did not have prophylactic G-tube (30% vs 6%, p < .001) -there were 4 of 15 patients in the G-tube group with grade 3 dysphagia compared with only 1 of 18 in the NG-tube group (p 1⁄4 .15) 3. Emerging prospective data with mature results on small cohorts support the hypothesis that radiation dose restriction to swallowing structures using intensity-modulated radiation therapy techniques leads to better swallow outcomes. -muscular components of the swallowing apparatus, critical to the development of dysphagia in irradiated patients, can be spared by IMRT

41. Wang J, Liu M, Liu C, Ye Y, Huang G. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for patients with head and neck cancer: a systematic review. J Radiat Res. 2014;55(3):559-67. [197]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** Australia (n=3), UK (n=3), India (n=1), Pakistan (n=1), France (n=1) **Centers:** n/a **Setting:** Head and neck cancer patients with enteral feeding **Funding Sources:** n/a **Dropout rates:** 75% (n=32 studies, only 8 met eligibility criteria) **Study limitations:** heterogeneity of the studies, lack of carefully designed	**Total no. Studies:** n=8 (n=818 patients) **Inclusion criteria:** RCT, non-experimental studies (Cohort study, case control study), head and neck cancer patients, comparing PEG, PFG with NG, full-length English articles **Exclusion criteria:** according to QUOROM statement	Comparing 1. percutaneous endoscopic gastrostomy (PEG) and percutaneous fluoroscopic gastrostomy (PFG) with 2. Nasogastric tube feeding (NG) In Head and neck cancer patients

	RCTs, methodological weakness of observational studies → affects reliability, many uncontrolled factors may affect results, publication bias may have an influence, low number of studies		
Notes	- Patients undergo radical radiotherapy or radical chemoradiotherapy, with or without surgery - Including and excluding of studies according to QUOROM statement - Of 8 studies: 4 were prospective, 4 were retrospective **Author's Conclusion:** It became apparent from our studies that both feeding strategies have advantages and disadvantages. We recommend that a baseline nutritional assessment should be carried out by a dietitian for patients who receive tubes before treatment or at the time of diagnosis, taking the estimated time of tube feeding and the psychological characteristics of patients into consideration. (Further research required)		
Outcome measures/results	- Nutritional status (body weight, mid-arm circumference, triceps skin fold thickness, hemoglobin level, serum albumin level) - Duration of feeding - Complications - Radiotherapy delays - Disease-free survival - Overall survival	- Nutritional status: percutaneous gastrostomy and NGT have equivalent outcomes with regard to weight maintenance in patients with HNC → percutaneous gastrostomy feeding is advantageous over NGT feeding - no differences in serum albumin levels - Complications: - Infections: no significant difference in the infection rate between percutaneous gastrostomy and NGT feeding [RR = 1.13, 95% CI (0.08, 16.43), P = 0.93] - Tube dislodgement: incidence of tube dislodgement was lower for percutaneous gastrostomy than for NGTs [RR = 0.17, 95% CI (0.07, 0.40), P < 0.001] - Dysphagia: NGT causes less problems than percutaneous gastrostomy [OR=0.81, 95% CI (0.04, 18.25), P=0.90] - Survival: varying results; randomized effects model → no statistically significant difference in overall survival (RR=0.45, 95% CI = 0.10 to 2.06) - Duration: enteral feeding with a gastrostomy is significantly longer than with NGT - Days of radiotherapy delays: no differences - Quality of life: significantly higher incidence of pain was associated with gastrostomy tubes in the first week of insertion, whereas more patients felt they experienced an altered body image with an NGT, which was also seen as significantly more inconvenient than a gastrostomy	

42. Gomes CA, Jr., Andriolo RB, Bennett C, Lustosa SA, Matos D, Waisberg DR, et al. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. Cochrane Database Syst Rev. 2015:Cd008096. [194]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 1++	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** no funding **Dropout rates**: 45% (n=20 studies eligible) **Study limitations:** small number of participants in majority of studies (due to high costs?!); different length of follow-up; different requirements/techniques for endoscopy and its use; clinical differences between trials (different diseases); high bias	**Total no. Studies:** n=11 (n=735 patients) **Inclusion criteria:** randomized controlled trials comparing PEG vs. NGT, adults ≥ 18 years, swallowing disturbances or dysphagia, indication of nutritional support, any underlying disease **Exclusion criteria:** studies with radiologically inserted gastrostomy (PRG), nasojejunal tubes, jejunal tube percutaneous endoscopy gastrostomy (JET-PEG)	Intervention of enteral nutrition: Intervention group: PEG (performed by any method); n=373 Control group: NGT (irrespective of technique); n=362 Subgroup analysis of endoscopic gastrostomy technique: Group 1: Push Group 2: Pull Group 3: not reported
Notes	- Standard methodological procedures of Cochrane collaboration were used; computerized literature search - 2 review authors; assessment of risk of bias; For continuous and dichotomous data, we carried out available case analysis. In this update, for mean values of outcome data with missing standard deviations, we calculated this from the difference between means **Author's Conclusion:** PEG was associated with a lower probability of intervention failure, suggesting the endoscopic procedure may be more effective and safer compared with NGT. There is no significant difference in mortality rates between comparison groups, or in adverse events, including pneumonia related to aspiration. Future studies should include details of participant demographics including underlying disease, age and gender, and the gastrostomy technique.		
Outcome measures/results	Primary outcome: intervention failure → e.g. feeding interruption, blocking or leakage of the tube, no adherence to treatment Secondary outcome: - nutritional status (any method: mid-arm circumference, upper-arm skinfold thickness, body weight, serum albumin level, hemoglobin) - mortality - adverse events (aspiration, hemorrhage, pneumonia, wound infection, sinusitis, fistula)		- primary outcome „intervention failure": occurred in lower proportion of participants with PEG compared to NGT (RR 0.18, 95% CI 0.05 to 0.59, eight studies, 408 participants, low quality evidence) →statistically significant - Subgroup analysis: - Pull subgroup: significant difference favoring PEG (RR 0.07, 95% CI 0.01 to 0.35, three studies, 90 participants); - push subgroup contained only one clinical trial and the result favored PEG (RR 0.05, 95% CI 0.00 to 0.74, one study, 33 participants) techniques

	- time on enteral nutrition - Quality of life (any valid instrument) - Length of hospital stay - Costs, economic issues	- no technique reported: no statistically significant difference (RR 0.43, 95% CI 0.13 to 1.44, four studies, 285 participants). - secondary outcomes no differences between the groups in - mortality: RR 0.86, 95% CI 0.58 to 1.28, 644 participants, nine studies, very low-quality evidence - overall reports of any adverse event at any follow-up time point (ITT analysis, RR 0.83, 95% CI 0.51 to 1.34), 597 participants, 6 studies, moderate quality evidence - specific adverse events including pneumonia (aspiration) (RR 0.70, 95% CI 0.46 to 1.06, 645 participants, seven studies, low quality evidence) - nutritional status including weight change from baseline, and mid-arm circumference at endpoint; although there was evidence in favor of PEG for meta-analyses of mid-arm circumference change from baseline (MD 1.16, 95% CI 1.01 to 1.31, 115 participants, two studies), and levels of serum albumin were higher in the PEG group (MD 6.03, 95% CI 2.31 to 9.74, 107 participants) - enteral nutrition: MD 14.48, 95% CI -2.74 to 31.71; 119 participants, two studies - favored intervention PEG: - quality of life measures (n=4) (EuroQol) outcomes in two studies with 133 participants, for inconvenience (RR 0.03, 95% CI 0.00 to 0.29), discomfort (RR 0.03, 95% CI 0.00 to 0.29), altered body image (RR 0.01, 95% CI 0.00 to 0.18; P = 0.001) and social activities (RR 0.01, 95% CI 0.00 to 0.18), → fewer participants found the intervention of PEG to be inconvenient, uncomfortable or interfered with social activities - no significant differences between the groups for pain, ease of learning to use, or the secondary outcome of length of hospital stay (two studies, 381 participants) - time on enteral nutrition: 14.48 (-2.74 to 31.71)

43. Jaafar MH, Mahadeva S, Morgan K, Tan MP. Percutaneous endoscopic gastrostomy versus nasogastric feeding in older individuals with non-stroke dysphagia: a systematic review. J Nutr Health Aging. 2015;19:190-7. [200]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1++	**Countries:** Malaysia	**Total no. Studies:** n=9 (n=847 patients)	Comparison between: 1. Intervention group: PEG feeding; n=406

	Centers: Department of Medicine, University of Malaya, Kuala Lumpur **Setting:** PEG vs. NG in patients with dysphagia High Impact Research-Ministry of Education grant (UM.C/625/1/ HIRMOHE/ ASH/02), the Faculty of Medicine, University of Malaya **Funding Sources:** University of Malaya Research Grant (RP-010-2012), the Ministry of Science and Technology Science fund (SF017-2013) **Dropout rates:** 40% (n=6 of 15 potentially relevant articles excluded) **Study limitations:** only in 1 study blinding was possible, mostly poor-quality evidence, only 2 RCT, different follow-up duration	**Inclusion criteria:** RCT, non-RCTs which compared PEG and NG in non-stroke related dysphagia patients, ≥60 years, English language articles **Exclusion criteria:** any other methods of enteral feeding, articles that focused mainly on acute, sub-acute stroke or head and neck patients, review articles	2. Control group: NG tube feeding; n=441 → RCT: n=2; cohort studies: n=4, case control study: n= 1; retrospective studies: n=2
Notes	**Author's Conclusion:** Firm conclusions could not be derived on whether PEG feeding is beneficial over NG feeding in older persons with non-stroke dysphagia, as previously published literature was unclear or had a high risk of bias. A well-designed and adequately powered RCT, which includes carer strain and quality of life as outcome measures is therefore urgently needed.		
Outcome measures/results	Primary outcome: aspiration pneumonia - Other complications that can interrupt the nutritional status: tube clogging, tube dislodgement, diarrhea Secondary outcomes: - -mortality rate - -nutritional status: proportional body weight difference, serum albumin level, hemoglobin, anthropometry measurements (Triceps skinfold thickness, mid-arm circumference) - -time on enteral nutrition		- Mean age: 75 ±8.1 years - Main indications for enteral tube feeding: dementia, neurological disease - Duration of follow-up ranged from 4 weeks to 6 months - Pooled analysis indicated no significant difference in the risk of pneumonia [relative risk (RR) = 1.18, 95% confidence interval (CI) = 0.87-1.60] between PEG and NG feeding - No difference in overall complications [relative risk (RR) = 0.80, 95% confidence interval (CI) = 0.63-1.02] between PEG and NG feeding

	- -quality of life	- A meta-analysis was not possible for mortality and nutritional outcomes, but three studies suggested improved mortality outcomes with PEG feeding while two out of three studies reported PEG feeding to be better from a nutritional perspective

Empfehlung 20

Eine PEG sollte bei HEE einer chirurgischen Gastrostomie vorgezogen werden, vor allem wegen der geringeren Komplikationsrate, Kosteneffizienz und Operationszeit.

Empfehlungsgrad B

44. Bravo JG, Ide E, Kondo A, de Moura DT, de Moura ET, Sakai P, et al. Percutaneous endoscopic versus surgical gastrostomy in patients with benign and malignant diseases: a systematic review and meta-analysis. Clinics (Sao Paulo, Brazil). 2016;71(3):169-78. [207]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries:** Brazil **Centers:** n/a **Setting:** surgical vs. PEG in malignant disease **Funding Sources:** Gastrointestinal Endoscopy Unit, Gastroenterology Department, University of Sao Paulo Medical School **Dropout rates:** 61,1% (n=11 studies were not eligible) **Study limitations:** few randomized studies, lack of recent studies comparing the 2 techniques, lack of uniformity in surgical techniques, antibiotic use? small populations, lack of standardization regarding	**Total no. Studies:** n=7 (in total n=406 patients) **Inclusion criteria:** randomized controlled trials, retrospective studies, patients undergoing gastrostomy, compare PEG vs. SG **Exclusion criteria:** abstracts, letters, editorials, expert opinions, case reports, reviews, studies that did not consider desired outcomes, studies that compared other techniques	Comparison between following techniques: 1. surgical gastrostomy: n=174 - vs. 2. Percutaneous endoscopic gastrostomy: n=232

	major and minor complications		
Notes	• of 7 studies 5 were retrospective and 2 were randomized prospective studies • Review was conducted in accordance with PRISMA; publication bias was assessed by 2 independent reviewers • Minor complications are treated conservatively. Major complications may require hospitalization, blood transfusions, or endoscopic or surgical therapy; Period in which complications occur may be early (until 15 days) or late (after 15 days) • Main indications: neurological, traumatic, tumors of head and neck, stenosis, esophageal atresia; Technique: Gauderer-Ponsky or „pull" endoscopic gastrostomy (1980) **Author's Conclusion:** Separate analyses of retrospective and randomized studies revealed no differences between the methods in relation to mortality and major complications. Moreover, low levels of minor complications were observed among endoscopic procedures in randomized studies, with no difference observed compared with retrospective studies.		
Outcome measures/results	- Complications: - Minor complications: dislodged tubes, inadvertent removal of tubes, tube malfunction, other tube problems conservatively managed, peristomal leaks, peristomal infection, mild skin necrosis, wound granulation, minor wound bleeding, wound hematoma, post-procedure ileus, symptomatic pneumoperitoneum, subcutaneous emphysema, regurgitation, unsuccessful procedure - major complications: bowel perforations, gastrointestinal hemorrhage, gastrocutaneous fistula, intra-abdominal abscess, peristomal abscess, peritonitis requiring surgery, loss of catheter tract, aspiration pneumonia, sepsis, buried bumper syndrome, early inadvertent removal of tube - mortality	complications: - -no difference in major complications in retrospective (95% CI (-0.11 to 0.10)) or randomized (95% CI (-0.07 to 0.05)) studies - -minor complications: no difference was found in retrospective studies (95% CI (-00.17 to 0.09)), whereas a difference was observed in randomized studies (95% CI (-0.25 to -0.02)) → fewer complications: endoscopic gastrostomy - High heterogeneity (I^2=89%) mortality: - - related to procedure in retrospective studies: all deaths in SG; no trend favoring any group (risk difference analysis; 95 % CI (-0.15 to 0.03) - -related to procedure in randomized studies: no difference between PEG and SG (95 % CI (-0.05 to 0.03) - Main cause: aspiration pneumonia, peritonitis	

45. Ljungdahl M, Sundbom M. Complication rate lower after percutaneous endoscopic gastrostomy than after surgical gastrostomy: a prospective, randomized trial. Surg Endosc. 2006;20:1248-51. [208]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Sweden **Centers:** University Hospital; Uppsala **Setting:** SG vs. PEG technique **Funding Sources:** n/a	**Total no. Patients:** n=70 **Inclusion criteria:** swallowing disorders (neurologic impairment), patients eligible for both techniques (SG and PEG), need for long-term	Comparison: 1. PEG: n=35 - Vs. 2. SG: n=35

	Dropout rates: 2.8% (n=2 refused → 70 patients left) **Study limitations:** cause for enteral feeding was heterogeneous	(>4 weeks) enteral feeding irrespective of cause **Exclusion criteria:** previous surgeries in the upper gastrointestinal tract, endoscopy not possible (obstructions from tumors in pharyngoesophageal region)	→ all the patients were administered an intravenous single 1.5-g dose of cefuroxime in accordance with generally accepted recommendations
Notes	- Groups were comparable in terms of age, body mass index, underlying disease; Randomization was non-stratified - Study recruitment period: 45 months **Author's Conclusion:** The findings show PEG to be an efficient method for gastrostomy tube placement with a lower complication rate than SG. In addition, PEG is faster to perform and requires fewer medical resources. The authors consider PEG to be the primary procedure for gastrostomy tube placement.		
Outcome measures/results	- effectiveness - safety - complications were reported 7 and 30 days after operative procedure (minor and major); wound infection if at least 2 of the following conditions present: peristomal erythema, onduration, purulent discharge - mortality (patients followed for a minimum of 6 months) - basic laboratory: hemoglobin, coagulation, inflammatory parameters	- procedures were successfully completed for all patients - no perioperative complications/mortality - Median operative time was 15min for PEG and 35 min for SG ($p<0.001$) - rate of complications was lower for PEG (42.9%) than for SG (74.3%; $p < 0.01$) - -minor complications: dislocation of tube, wound infection, leakage at gastrostomy site - -Major complication: pneumonia , peritonitis (all successfully treated) - 30-day mortality rates were 5.7% for PEG and 14.3% for SG (nonsignificant difference); causes: restroke, gastrointestinal hemorrhage, aspiration pneumonia	

46. Rustom IK, Jebreel A, Tayyab M, England RJ, Stafford ND. Percutaneous endoscopic, radiological and surgical gastrostomy tubes: a comparison study in head and neck cancer patients. J Laryngol Otol. 2006;120:463-6. [209]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** UK **Centers:** Head and Neck surgery Department, Hull Royal Infirmary **Setting:** head and neck cancer, PEG vs. RIG vs. SUR	**Total no. Patients:** n=78 **Inclusion criteria:** squamous cell carcinoma of the upper aero-digestive tract **Exclusion criteria:** other cancers, no enteral feeding	Comparison of following techniques: 1. Percutaneous endoscopic gastrostomy (PEG) tube: n=40 2. Radiological gastrostomy (RIG) tube: n=28 3. Surgically gastrostomy (SUR) tube: n=10

	Funding Sources: **Dropout rates:** 21,4% (n=98 received gastrostomy tube; n=78 were reviewed) **Study limitations:** different numbers of patients between the groups		→ all patients received 2 g of intravenous cefotaxime or 1.2 g of co-amoxiclav 1 hour prior to procedure, except for patient receiving surgical gastrostomy tubes (antibiotic depended on individual surgeon´s choice)
Notes	**Author's Conclusion:** The PEG tube was considered superior to the RIG and SUR gastrostomy tubes, had fewer complications and was safer. Thus, PEG tube insertion is our first choice for head and neck cancer patients.		

Outcome measures/results	- Basic information: age, sex, primary diagnosis, type of tube inserted
	- Complications
	  - Minor or major (minor: peri-stomal leakage, superficial cellulitis, tube dislodgement, tube blockage, any combination; major: peritonitis, gastro-intestinal bleeding, pulmonary, cardiac and neurological events)
	  - Short-term (<30 days) or long-term (>30 days)
	- mortality
			- There were no significant demographic differences between the three groups
			- 36 patients (46 %) developed complications, 32 minor and 4 major
			- → major complications: peritonitis (n=3) all in RIG group; no major complications in PEG group
			- All three groups were similar in their rate of minor complications, with the dislodgement and blockage rate being lowest in the PEG group ($p > 0.05$)
			- 22% had long-term complications, 18% had short-term complications
			- The mortality rate was 4 % within 30 days of gastrostomy tube insertion; no deaths in the PEG group, 2 deaths in the RIG group (peritonitis) and 1 in the SUR group (bronchopneumonia)

47. Yuan Y, Zhao Y, Xie T, Hu Y. Percutaneous endoscopic gastrostomy versus percutaneous radiological gastrostomy for swallowing disturbances. Cochrane Database Syst Rev. 2016;2:Cd009198. [212]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries:** n/a **Centers:** n/a **Setting:** comparison of OEG vs. PRG in patients with swallowing disturbances **Funding Sources:** n/a **Dropout rates:** 100% → no RCTs available	**Total no. Studies:** n=0 RCTs **Inclusion criteria:** RCT comparing PEG and PRG, swallowing disturbances regardless of underlying disease, requiring enteral feeding, randomization to Peg or PRG **Exclusion criteria:** indication of decompression, retrospective	Comparison efficacy and safety: 1. Intervention: Percutaneous endoscopic gastrostomy (PEG) Vs. 2. Percutaneous radiological gastrostomy (PRG)

	Study limitations: no RCTs available	studies, case series, non-randomized controlled studies	
Notes	- Two authors independently evaluated the search results and assessed the quality of the studies. Data analyses could not be performed as no RCTs were identified for inclusion in this review. - Bias, heterogeneity was assessed **Author's Conclusion:** Both PEG and PRG are effective for long-term enteral nutritional support in selected individuals, though current evidence is insufficient to recommend one technique over the other. Choice of technique should be based on indications and contraindications, operator experience and the facilities available. Large-scale RCTs are required to compare the two techniques and to determine the optimal approach for percutaneous gastrostomy.		
Outcome measures/results	Primary outcome: mortality Secondary outcome: - success of tube placement - major complication rate: hemorrhage requiring blood transfusion or laparotomy, peritonitis, fistulas between the stomach and adjacent viscera, bowel perforation, aspiration of material in the airways, heart failure, respiratory failure, heart and respiratory failure, sepsis, necrotizing fasciitis, metastatic tumor implantation into the stoma, loss of catheter tract - Minor complication rate: abdominal pain with or without peritoneal involvement, wound infection, fever, peristomal leak, wound granulation or bleeding, gastroparesis, regurgitation or reflux, minor tube problems requiring minimal intervention - Duration of the procedure - Need for analgesia or sedation for the procedure • Improvement in malnutrition - Cost of the procedure - Length of hospital stay - Quality of life		- We identified no RCTs comparing PEG and PRG for percutaneous gastrostomy in individuals with swallowing disturbances - large body of evidence in this field comes from retrospective and non-randomized controlled studies and case series - Based on this evidence, both PEG and PRG can be safely performed in selected individuals, although both are associated with major and minor complications - A definitive RCT has yet to be conducted to identify the preferred percutaneous gastrostomy technique

48. Lim JH, Choi SH, Lee C, Seo JY, Kang HY, Yang JI, et al. Thirty-day mortality after percutaneous gastrostomy by endoscopic versus radiologic placement: a systematic review and meta-analysis. Intest Res. 2016;14:333-42. [213]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries:** UK, USA, France, Australia, Canada, New Zealand **Centers:** n/a **Setting:** PEG vs. RIG, 30-day mortality **Funding Sources:** n/a **Dropout rates:** 51.6% (n=16 from 31 eligible studies) **Study limitations:** heterogeneity of the studies, most studies were observational without randomization, groups weren´t matched, lack of RCT, no data on albumin or CRP levels, prophylactic use of antibiotics could not be controlled, mixed analysis of RCT and NRCT	**Total no. Studies:** n=15 (n=2 RCT) **Inclusion criteria:** patients with dysphagia or in need of prolonged tube feeding, RCT, other comparative studies comparing 30-day mortality, studies in peer-review journals, prospective and retrospective studies **Exclusion criteria:** preclinical studies, case reports, case series, review articles, studies with RIG placement after failure of PEG, studies with no cases of 30-day mortality, studies with no cases of 30-day mortality in either the PEG and the RIG group or duplicated reports from the same patient	Comparison: 1. PEG: n=1135 - Vs. 2. RIG: n=1048
Notes	- Review was conducted in accordance with PRISMA; Quality assessment of RCT using Jadad scale; Quality and risk of bias of nonrandomized comparative studies assessed using MINORS - Studies published from 1997-2015 **Author's Conclusion:** The present meta-analysis demonstrated that PEG is associated with a lower probability of 30-day mortality compared to RIG, suggesting that PEG should be considered as the first choice for long-term enteral tube feeding. Further prospective randomized studies are needed to evaluate and compare the safety of these two different methods of gastrostomy.		
Outcome measures/results	30-day mortality		- Jadad score RCTs: 2 and 3; mean MINORS score: 18.6 (95 % CI 17.27-19.95) - PEG was associated with a lower risk of 30-day mortality after tube placement compared with RIG (odds ratio, 0.60; 95% confidence interval [CI], 0.38–0.94; P =0.026) - pooled prevalence of 30-day mortality of PEG was 5.5% (95% CI, 4.0%–6.9%) and that of RIG was 10.5% (95% CI, 6.8%–14.3%); no difference between

		groups (OR 1.18; 95% CI 0.38-3.66; p=0.770) → high heterogeneity: χ^2=50.92, I^2=72.5%, P <0.001 - → pooled analysis with RCTs and NRCTs combined: statistically significant reduction of 30-day mortality rates in the PEG groups compared with the RIG groups (OR, 0.60; 95% CI, 0.44−0.82; P =0.001) (Fig. 2A) in a fixed effects model with moderate heterogeneity (heterogeneity χ^2=22.68, I^2=38.7%, P =0.063) - → 30-day mortality in patients with motor neuron disease: no difference between the groups - → 30-day mortality in patients with head and neck cancer: significantly reduced in the PEG group compared to the RIG group (OR, 0.09; 95% CI, 0.03−0.28; P <0.001) (Fig. 5A) with low heterogeneity (heterogeneity χ^2=0.51, I^2<0.1%, P =0.775 - No publication bias was noted

Empfehlung 21

Wenn eine PEG für die HEE nicht geeignet ist, kann eine perkutane

laparoskopisch assistierte Gastrostomie (PLAG) eine sichere und komplikationsarme Alternative sein.

Empfehlungsgrad 0

49. Serrano Aguayo P, Gros Herguido N, Parejo Campos J, Barranco Moreno A, Tous Romero MDC, Pereira Cunill JL, et al. New laparoscopic assisted percutaneous gastrostomy. Description and comparison with others gastrostomy types. Clin Nutr ESPEN. 2016;16:24-9. [211]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** Spain **Centers:** Virgen del Rocío University Hospital in Seville **Setting:** gastrostomy **Funding Sources:** n/a **Dropout rates:** no drop out	**Total no. Patients:** n=224 **Inclusion criteria:** patients in need of nutritional support (enteral feeding) **Exclusion criteria:** parenteral feeding, no need of enteral feeding	1. percutaneous endoscopic gastrostomy (PEG): n=106 2. percutaneous radiological gastrostomy (PRG): n=89 3. conventional surgical gastrostomy, Open Stamn or Laparoscopic Janeway (SG) n=9 4. percutaneous laparoscopic assisted gastrostomy (PLAG): n=20 → enteral feeding begun 6h after PEG, PRG and PLAG and 24h after SG

	Study limitations: small sample size of PLAG and SG does not allow statistical comparison with other groups, different disease severity		
Notes	- study period between January 2009 and October 2015 - Patients for one technique or another were selected by a nutritional support team physician → favored were PEG or PRG - SG was indicated: complete upper gastrointestinal tract obstruction, lack of transillumination, some anatomical abnormalities, interposition of colon or liver between the abdominal wall and the stomach - At least one-month follow-up after procedure and then every 3 months by the nutritional support team physician and nurse **Author's Conclusion:** We found lower complication rate in PLAG than any other technique. We believe that PLAG could be preferred technique for patients on whom it is not possible to perform PEG or PRG, as it is safe and easy.		
Outcome measures/results	- short term complications and long-term complications of PLAG technique - comparison PLAG complications rate with SG, PEG and PRG - efficacy of nutritional support		- diagnoses: head and neck cancer. Esophagus cancer, neurological dysphagia, miscellany (cystic fibrosis, achalasia, cerebral mucormycosis, tracheal-esophageal fistula, non-tumor induced esophageal stenosis) - follow-up time >30 days for all patients (except 6) - Many more complications were seen in the conventional gastrostomy group than in the other three groups, especially leakage of gastric content around the tube, with burning and irritation of the skin (66% compared with 2.83% in PEG and 0% in PLAG and PRG) - The group with the highest proportion of patients completely free of complications was PLAG (75%), whilst in the conventional surgical gastrostomy group, no patient was completely free of complications

<u>Empfehlung 22</u>

Als alternative Techniken für die Platzierung einer perkutanen endoskopischen Gastrostomie (PEG) können eine radiologisch insertierte Gastrostomie (RIG) bzw. perkutane radiologische Gastrostomie (PRG), verwendet werden, wenn eine endoskopisch geführte Sondenplatzierung nicht möglich ist.

Empfehlungsgrad 0

50. Burkitt P, Carter LM, Smith AB, Kanatas A. Outcomes of percutaneous endoscopic gastrostomy and radiologically inserted gastrostomy in patients with head and neck cancer: a systematic review. Br J Oral Maxillofac Surg. 2011;49:516-20. [150]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries**: n/a **Centers:** n/a **Setting:** enteral feeding in head and neck cancer patients **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** differences in sites and stages of cancer, heterogeneity of the studies	**Total no. Studies:** n=4 **Inclusion criteria:** patients requiring gastrostomy feeding, retrospective observational cohort studies **Exclusion criteria:** studies that evaluate only a single technique	Comparison: 1. PEG: n=190 - Vs. 2. RIG: n=109 3. Surgery: n=10
Notes	- Selected studies were assessed for their internal validity, generalizability - Assessment of Selection bias, performance bias, measurement bias **Author's Conclusion:** The comparison between outcomes of PEG and RIG seems to suggest on the evidence available that there is less risk of mortality and peritonitis if the gastrostomy is placed by the PEG technique rather than being inserted radiologically. This agrees with other studies. The analysis for infection suggests that there is little difference in the incidence of infection between the two techniques. The most likely complication is that of infection, and mortality with peritonitis is the least likely. Only one study reported complications that arose after surgical gastrostomy. This had a sample of only 10, one of whom died within 30 days.		
Outcome measures/results	- Complications: peritonitis, infection - mortality		- Mortality: overall RR of 0.13 (95% CI 0.05–0.36) for mortality in the PEG group compared with the RIG group - Peritonitis also gave a more favorable RR for the PEG group, with an overall RR of 0.24 (95% CI 0.05–1.16) relative to the RIG group - Infection has a RR of 0.89 (95% CI 0.23–3.54) for PEG compared with RIG - overall conclusions from this review must be considered in relation to the quality of each study and the size of the sample

51. Vidhya C, Phoebe D, Dhina C, Jayne S, Robert F. Percutaneous endoscopic gastrostomy (PEG) versus radiologically inserted gastrostomy (RIG): A comparison of outcomes at an Australian teaching hospital. Clin Nutr ESPEN. 2018;23:136-40. [214]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** Australia **Centers:** n/a **Setting:** enteral feeding, comparison PEG vs. RIG **Funding Sources:** no funding **Dropout rates:** no drop out **Study limitations:** retrospective data collection, difficult follow-up	**Total no. Patients:** n=137 **Inclusion criteria:** patients who need enteral feeding, head and neck cancer, stroke, post-trauma, neuromuscular pathologies **Exclusion criteria:** no PEG or RIG, other disease than mentioned in inclusion criteria	Comparison: 1. PEG: n=85 Vs. 2. RIG: n=52 → all patients were fasted for 12h prior to the procedure
Notes	**Author's Conclusion:** Although both PEG and RIG insertion techniques compare favorably in terms of the majority of peri and post procedural complications, the rates of tube dislodgement were significantly higher in the RIG group. The higher mortality rate at 1 year after RIG placement may be related to patient selection particularly as no differences were seen at 30 days.		

Outcome measures/results	- Demographic
	- Indication of gastrostomy
	- Procedural details
	- Peri- and post-procedural complications
	- Tube type
	- Tube dislodgement
	- mortality
			- Diseases (n):
			  - Head and neck cancer: PEG = 30;RIG = 21
			  - Stroke: PEG = 27, RIG = 11
			  - post-trauma: PEG = 6, RIG = 3
			  - neuromuscular pathologies: PEG = 9, RIG = 0
			- No differences in baseline characteristics (age, sex)
			- mean time from gastrostomy insertion to hospital discharge was 9 days in the PEG group (range 0e190) compared to 6 days in the RIG group (range 1e149), p = 0.69
			- Prophylactic antibiotics were given prior to the procedure in 52 (38%) of patients [PEG = 50 (58.9%), and RIG = 2 (3.8%)]
			- tube dislodgement rate: significantly higher in RIG (26.5%) compared to PEG (2.4%), $p < 0.001$
			- technical failure: 6 patients had a failed PEG insertion → successful RIG Insertion; 2 patients failed RIG insertion → successful PEG
			- 1-year mortality: significantly higher after RIG (46.2%) compared to the PEG group (16.7%), $p < 0.05$
			- other peri- and post-procedural complications: no differences between the groups

52. Odedra D, Nasirzadeh R, Menard A. Safety of Outpatient vs Inpatient Percutaneous Radiological Gastrostomy Tubes in Patients with Head and Neck Cancers. Can Assoc Radiol J. 2016;67:416-9. [215]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** Canada **Centers:** Department of diagnostic imaging Kingston General Hospital **Setting:** PRG vs. OP vs. IP in head and neck cancer patients **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** retrospective study → parameters not perfectly controlled, study was too small to break down complications based on stage of disease, no objective measure of patients´ clinical status	**Total no. Patients:** n=101 **Inclusion criteria:** all head and neck cancer patients who underwent PRG from January 2010 to Jun2 2013 **Exclusion criteria:** Patients with prior gastrostomy tube insertion	1. OP: n=50 2. IP: n=51
Notes	- OPs were transferred post procedure to the outpatient procedure unit - IPs were admitted prior to the procedure and observed overnight following the procedure - Previous to 2012, all PRGs in head and neck cancer patients were inserted as IPs. In early 2012, the practice in that hospital transitioned into a predominantly OP PRG insertion for head and neck cancer patients **Author's Conclusion:** Our study suggests that PRG can be safely and effectively performed as an OP procedure with similar complication and success rates as an IP setting in head and neck cancer patients. Further randomized prospective trials will be necessary to guide the clinical practice.		

Outcome measures/results	- mortality
	- complication rate:
	  - early: occurred within 15 days after procedure
	  - major: necessitating procedural intervention: deep infection/bacteremia, external leakage (requiring repeat procedure), pain (persistent), tube blockage or
			- mean age: OP 61.3 ±12.9 years vs. IP 66.0 ± 11.4 (p=0.053)
			- diabetes: IP n=8; OP n=5
			- more patients in IP group were symptomatic at the time of the procedure compared to OP group (31 in IP vs 15 in OP groups, P < .05)
			- most common stage of malignancy was IVa, with 60.4% and 66.0% of patients having stage IVa disease in IP and OP groups, respectively

	dislodgement (requiring repeat procedure), aspiration, peritoneal leakage - minor: Superficial infection, External leakage e (not requiring repeat procedure), Pain (transient), Tube blockage or dislodgement (not requiring repeat procedure) - demographical data: age, gender, diabetes status, symptomatic vs. Prophylactic status, type and stage of cancer	- most common primary malignancy was oropharyngeal cancer seen in 56.9% of IPs and 76% of the OP population. - Complications lower in OP group with 8 complications compared to 17 in IP group (p=0.051) - Major complications: IP n=3 and OP group n=4 (p>0.05) - Minor complications: OP group lower number of minor complications (4) vs. 14 in the IP group (p=0.018) - Number of early complications was similar between OP and IP (p>0.05) - Most common complication: tube dislodgement: 5 in IP and 3 in OP group - 15-day mortality was comparable between groups (p>0.05)

53. Yuan Y, Zhao Y, Xie T, Hu Y. Percutaneous endoscopic gastrostomy versus percutaneous radiological gastrostomy for swallowing disturbances. Cochrane Database Syst Rev. 2016;2:Cd009198. [212]
→ **See No. 47**

Empfehlung 23

HEE kann bei Patienten, die sie nur für kurze Zeit (maximal 6 Wochen) benötigen, über eine geeignete nasale Ernährungssonde verabreicht werden.

Empfehlungsgrad 0

54. Gomes CA, Jr., Andriolo RB, Bennett C, Lustosa SA, Matos D, Waisberg DR, et al. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. Cochrane Database Syst Rev. 2015:Cd008096. [194]
→ **See No. 42**

55. Paccagnella A, Baruffi C, Pizzolato D, Favaro V, Marcon ML, Morello M, et al. Home enteral nutrition in adults: a five-year (2001-2005) epidemiological analysis. Clin Nutr. 2008;27:378-85. [24]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+	**Countries:** Italy, North-East **Centers:** n/a	**Total no. Patients:** n=655 (44.3% males)	HEN

	Setting: Home Enteral Nutrition **Funding Sources:** costs of HEN were fully funded; no sources declared **Dropout rates:** n/a **Study limitations:** large number of elderly people → influences clinical outcomes; quality indicators of HEN are not completely valid due to the lack of specific follow-up	**Inclusion criteria:** age over 18 years, patients undergoing HEN therapy **Exclusion criteria:** children, no HEN therapy	
Notes	- clinical and organizational aspects are managed by a Nutritional Team (NT) specifically created for patients undergoing Artificial Nutrition - HEN program concerns patients discharged by the hospital or outpatients, on request of hospital physician or GP respectively - costs of HEN are fully funded and include home delivery of nutritional products, the infusion pump with relative support stand, the infusion set, syringes and the pick-up from the patient's home of left-over nutrients and materials according to a specific interventional certified system **Author's Conclusion:** Efficient organization means being able to look after a greater number of patients undergoing HEN, raising awareness regarding the nutritional treatment.		

Outcome measures/results	- following data were analyzed at the initiation of HEN: age, sex, pathology, Karnofsky index, type of enteral access device, presence of pressure ulcers, weight, body mass index, hematochemical tests, daily enteral intake
	- Length of therapy and patient survival
	- patients were divided according to pathology
	- outcome was based on:
	  - patient mortality
	  - patient's ability to resume oral nutrition
			- mean age: 77.4 years
			- HEN for pathologies: 26.7% neurovascular, 40.9% neurodegenerative, 11.5% head-neck cancer, 9.8% abdominal cancer, 1.5% head injury, 2.6% congenital anomaly, 7.0% other
			- average of 22.9% weight loss from past weight was observed across all indications for HEN before commencement of enteral feeding
			- Mean incidence (cases/10^6 inhabitants/year): 308.7 (range 80.7-355.6)
			- mean prevalence (cases/10^6 inhabitants): 379.8 (range 138.7-534.6)
			- The median length of HEN: 196 days
			- 7.9% of patients resumed oral nutrition
			- Of all the considered hematochemical data, only albuminemia and proteinemia values resulted statistically related to age ($p < 0.01$)
			- median survival rate: 9.1 months and resulted influenced by age (Odds ratio: 1.80; 95% Confidence Interval: 1.19-2.72), sex (0.22; 0.08-0.59), Karnofsky index (0.65; 0.43-0.97)
			- Resumption of oral nutrition was influenced by age (0.50; 0.36-0.68), sex (2.50; 1.23-5.06), Karnofsky index (1.55; 1.15-2.10) and type of enteral access device (0.44; 0.26-0.76)

		- 87% were fed by balanced artificial products in conjunction with a fiber rich product with average ratio of 60:40; rest: specific products for diabetes or hyperproteinic formula - Average daily enteral intake: 24.4±8.0 kcal/kg/day

Empfehlung 24

Um mechanische Komplikationen der HEE (Verstopfung, Dislokation) zu reduzieren, sollten bei langfristigem Bedarf (spätestens nach 6 Wochen) anstelle von Nasensonden perkutane Sonden verwendet werden.

Empfehlungsgrad B

56. Gomes CA, Jr., Andriolo RB, Bennett C, Lustosa SA, Matos D, Waisberg DR, et al. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. Cochrane Database Syst Rev. 2015:Cd008096. [194]
→ See No. 42

57. Ao P, Sebastianski M, Selvarajah V, Gramlich L. Comparison of complication rates, types, and average tube patency between jejunostomy tubes and percutaneous gastrostomy tubes in a regional home enteral nutrition support program. Nutr Clin Pract. 2015;30:393-7. [220]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** Canada **Centers:** Northern Alberta Home Enteral Nutrition Program **Setting:** Home Enteral Nutrition **Funding Sources:** no funding **Dropout rates:** no dropout **Study limitations:** limited sample size, retrospective study design, different routes of J-tube insertion → sample size insufficiently powered	**Total no. Patients:** n=129 from n=560 eligible **Inclusion criteria:** patients discharged from Northern Alberta Home Enteral Nutrition Support Program (NAHENSP) from January 2010 to December 2011 **Exclusion criteria:** total duration of tube feeding for <1 month or solely nasoenteral access device insertion	Patients were classified into 2 categories based on type of enteral access device: 1. J-tube 2. PEG tubes → A total of 64 J-tube patients were identified and compared with 65 PEG tube patients →Patients with both J-tube and PEG tube insertions during their enrollment in the NAHENSP were included in the J-tube cohort

	for a subgroup analysis based on route of insertion, no data at hand to determine if operator experience was correlated with feeding tube complications → Confounder?!; no clinical correlation between enteral access device complications in relation to patient nutrition outcomes		
Notes	**Author's Conclusion:** J-tubes are associated with higher complication rates requiring tube replacement compared with PEG tubes. The main causes of J-tube replacement are dislodgement and obstruction.		
Outcome measures/results	- Data collected from patient charts included patient demographics, indication for enteral feeding, route and size of feeding tube - Comparisons in terms of complications →complications are further subdivided: 1. tube complications (obstruction, leakage) 2. enteral access site complications (irritation, infection) 3. patient complications (nausea, vomiting, gastroesophageal reflux disease [GERD], aspiration pneumonia, hospitalizations)		- both cohorts were similar with respect to mean age, sex distribution, and presence of supplemental oral feeds to reach their nutrition goals - Patients with J-tubes had a significantly higher occurrence of previous GI surgery prior to placement of feeding tubes compared with patients with PEG tubes (70.3% vs 10.8%; P < .001) - Indications for enteral device placement were significantly different between the cohorts → most common indication for J-tube use was esophageal/gastric cancer at 45.3% compared with 10.8% in the PEG group (P < 0.001); head and neck cancer patients were most common indication at 43.1% in PEG cohort compared with 14.1% of J-tube patients (p<0.001) - Tube replacement rates for the J-tube group included 3.2 cases per 1000 patient days compared with 0.86 cases per 1000 patient days in the PEG group (P < 0.001) - The mean ± SEM duration to first tube replacement for J-tube and PEG tube patients was 160 ± 26.3 days and 331 ± 53.6 days, respectively (P = 0.010) - The most common causes for tube replacement in J-tube patients were dislodgement (35.6%) and obstruction (22.2%) compared with routine replacement (54.5%) and dislodgement (27.2%) in the PEG tube group

3.2 Parenteraler Zugang und Pumpen für HPE

Empfehlung 25

Der Zugang zur Vena cava superior sollte die erste Wahl für die ZVK-Platzierung sein, und zwar über die innere Jugularvene oder die Vena subclavia.

Empfehlungsgrad B

Empfehlung 26

Um das Thromboserisiko zu verringern, sollte der rechtsseitige Zugang dem linksseitigen vorgezogen werden.

Empfehlungsgrad B

Empfehlung 27

Die Spitze des ZVKs sollte auf der Höhe des Übergangs von der Vena cava superior zum rechten Atrium platziert werden.

Empfehlungsgrad B

58. Cadman A, Lawrance JA, Fitzsimmons L, Spencer-Shaw A, Swindell R. To clot or not to clot? That is the question in central venous catheters. Clinical radiology. 2004;59:349-55. [283]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review	**Countries:** n/a	**Total no. Patients:** 334	

2+	**Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** they did not review patient notes, so the study did not include clinically suspected venous thromboses that were not imaged; it was not possible to determine the exact location of the catheter tip from the chest radiograph	**Inclusion criteria:** malignant disease **Exclusion criteria:** n/a	428 CVC inserted into 334 patients
Notes	**Author's Conclusion:** Distal placement of tunneled CVC, either in the distal third of the SVC or proximal RA is optimal.		
Outcome measures/results	incidence of venous thrombosis		- venous thrombosis occurred in five out of 191 (2.6%) CVC in a distal position - five of 95 (5.3%) in an intermediate position - 20 of 48 (41.7%) in a proximal position - Significant difference in thrombosis rate between lines sited with the tip in a distal compared with a proximal position (p< 0,0005) - CVC with tips in a proximal position were 16 times more likely to thrombose than those in a distal position

59. Petersen J, Delaney JH, Brakstad MT, Rowbotham RK, Bagley CM, Jr. Silicone venous access devices positioned with their tips high in the superior vena cava are more likely to malfunction. American journal of surgery. 1999;178:38-41. [237]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case series 3	**Countries:** US **Centers:** Northwest Hospital in Seattle **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** none **Study limitations:** n/a	**Total no. Patients:** 141 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- series A (n=43): Groshong catheters, Hickman catheters, Port-A-Cath subcutaneous ports were used between September 1988 and August 1989 - series B, follow up series (n=98): same catheters as in series A

Notes	**Author's Conclusion:** Malfunctions can be minimized in silicone venous access catheters by locating the catheter tip as close to the superior vena cava/right atrial junction as possible, or slightly inside the right atrium.	
Outcome measures/results	position of the catheter tip	- catheter tip location was the only factor that was statistically predictive of malfunctions (coefficient 0.842, P<0.001) - a significant increase in malfunctions was observed in cases where the catheter tip was located greater than 4 cm superior to the junction of the right atrium and the superior vena cava (z-test of proportions, P=0.003) - malfunctions were minimized in those cases where the catheter tip was located in the right atrium - during follow up period: malfunctions occurred in 26 of the 141 cases (18.4%)

60. Verso M, Agnelli G, Kamphuisen PW, Ageno W, Bazzan M, Lazzaro A, et al. Risk factors for upper limb deep vein thrombosis associated with the use of central vein catheter in cancer patients. Internal and emergency medicine. 2008;3:117-22. [236]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 385 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- assessing the efficacy and safety of enoxaparin for the prophylaxis of CVC-related thrombosis - CVC-related thrombosis was screened by mandatory venography after 6 weeks of study treatment - n=191 enoxaparin group, 40 mg once daily in the prevention of CVC-associated VTE - n= 194 placebo group - total of 310 patients,155 in each treatment group, had an adequate venography and were included in the efficacy analysis
Notes	**Author's Conclusion:** An inadequate position of the CVC tip, left-sided CVC insertion and chest radiotherapy are independent risk factors for CVC-related thrombosis in cancer patients.		
Outcome measures/results	CVC-related thrombosis		- CVC-related thrombosis was found in 50 out of 310 patients (16.1%) - at multiple logistic regression analysis, CVC tip misplaced in the upper half of superior vena cava (OR 4.05, 95%CI 1.64–10.02), left-sided CVC insertion (OR 2.29, 95%CI 1.01–5.51) and chest radiotherapy (OR 7.01, 95%CI 1.42–34.66) were independent risk factors for thrombosis - the presence of distant metastases (OR 9.36, 95%CI1.53–57.05) increased the risk of thrombosis in patients who received placebo

Empfehlung 28

PICCs können verwendet werden, wenn die Dauer der HPE auf weniger als sechs 6 Monate geschätzt wird.

Empfehlungsgrad 0

61.	**Mateo-Lobo R, Riveiro J, Vega-Piñero B et al. Infectious Complications in Home Parenteral Nutrition: A Systematic Review and Meta-Analysis Comparing Peripherally-Inserted Central Catheters with Other Central Catheters. Nutrients 2019; 11. doi:10.3390/nu11092083 [243]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review & Meta-Analysis 1++ AMSTAR 2 11/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: Critically low Risk of bias of single studies: n/a Inconsistency: low Indirectness: high Impreciseness: moderate Publication bias: n/a Limitation in terms of statistical power. Further, the allocation of patients to one or another type of catheter was not randomized, and the selection of the catheters for each patient was performed on a clinical basis with a consequent risk of bias	**Total no. Studies:** 3 **Inclusion criteria:** English language articles; prospective observational studies or clinical trials (retrospective studies or cases-control studies were not eligible); the study must report the type of catheter studied (PICC vs. other CVCs); the study should report associated and adequate epidemiological data to allow further statistical analyses **Exclusion criteria:** we excluded studies that recruited pediatric patients; as our unit is dedicated only to adult patients, we have no experience with HPN in children	There is the possibility that peripherally inserted central catheters (PICCs) may diminish catheter-related blood stream infection (CRBSI) rates. Thus, studies reporting the rates of CRBSI with HPN were included.
Notes	**Author's Conclusion:** A meta-analysis of prospective studies showed that there is insufficient evidence to show a difference in CRBSI rates between PICCs and tunneled catheters. On the other hand, PICCs showed less CRBSI rates than ports. Further, there was no difference in the rate of catheter-related		

	thrombosis and mechanical complications. More prospective studies and randomized trials are needed to give specific recommendations for choosing between PICCs and tunneled central catheters to deliver HPN.	
Outcome measures/results	catheter-related blood stream infection (CRBSI) rates	- The relative risk of the CRBSI rate was 0.41 (0.14–1.17) for peripherally inserted central catheters (PICC) vs. tunneled catheters. - The relative risk of the CRBSI rate was 0.16 (0.04–0.64) for PICC vs. ports. - The relative risk of the thrombosis rate was 3.16 (0.20–49.67) for PICCs vs. tunneled.

62. Opilla M. Peripherally Inserted Central Catheter Experience in Long-Term Home Parenteral Nutrition Patients. Journal of the Association for Vascular Access 2017; 22: 42-45. doi:10.1016/j.java.2016.12.001 [249]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2-	**Countries:** United States **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** small number of subjects and devices. Furthermore, there are little published data available to compare results for very long-term PICC use for HPN	**Total no. Patients:** 19 **Inclusion criteria:** PICCs in place for >6 months **Exclusion criteria:** n/a	A retrospective review of medical records from January 2005 to April 30, 2016, for Peripherally Inserted Central Catheter (PICC) insertion date, duration of access, material type and size, and complications leading to removal.
Notes	**Author's Conclusion:** This group of patients demonstrated that PICCs are a viable option for very long-term HPN administration. The PICC over- all complication rate in our study was very low compared with other published reports. The most frequent complication of CRBSI was expected, but the rate was quite low. It is not clear from this small cohort whether the primary use of double- lumen PICCs removed for CRBSI was a contributing infection risk factor. This is the only HPN infusion study to date reporting 7 PICCs lasting 3 or more years, with 2 lasting >5 years without complications resulting in removal. Five PICCs were still in use at the completion of the study period. Patients received their prescribed therapy reliably and without interruption with this device. Larger studies are needed to confirm the efficacy of maintaining a PICC for very long-term HPN administration.		
Outcome measures/results	PICC days, overall complication rate, catheter related blood stream infection, symptomatic thrombosis, infusion related complications, alcohol or antibiotic lock therapy, alteplase, need for caregiver assistance	- 19 adult HPN patients had 26 PICC placements. - Total PICC days were 22,262 with a mean of 856 (265-2500) days. 7 PICCs were in place for 3 to greater than 5 years.	

		- The overall complication rate was 0.58/1000 CVC days. Catheter related bloodstream infection (CRBSI) was the main cause of PICC removal. - There was no evidence of symptomatic thrombosis. - Patients experienced no infusion related complications. - The PICCs were 88% polyurethane, 65% double lumen, and 54% were 5 Fr. - No patient received alcohol or antibiotic lock therapy, and 8 patients had successful alteplase administered at least one time. - All patients needed caregiver assistance for site care and dressing changes but were independent in HPN infusion and flushing.

Empfehlung 29

Die HPE soll aus Gründen der Sicherheit und Effektivität möglichst mittels einer Infusionspumpe verabreicht werden.

Empfehlungsgrad A

63.	**Ayers P, Adams S, Boullata J, et al. American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. parenteral nutrition safety consensus recommendations. JPEN J Parenter Enteral Nutr. 2014;38:296-333. doi: 10.1177/0148607113511992 [253]**
Guideline **Relevant recommendations/ statements**	- An interdisciplinary process should be employed for selecting and evaluating equipment and technological aids, such as smart pumps and barcoding to reduce errors in PN administration. - Protocols for safe operation of infusion pumps shall stipulate rules regarding alarm silencing, modification, and disabling. - Healthcare organizations should purchase infusion pumps with capacity to reduce errors due to incorrect programming. Whenever possible, infusion pumps should be standardized throughout the organization. - Protocols for safe operation of infusion pumps shall stipulate rules regarding alarm silencing, modification, and disabling. Healthcare organizations should purchase infusion pumps with capacity to reduce errors due to incorrect programming. Whenever possible, infusion pumps should be standardized throughout the organization. - Protocols for safe operation of infusion pumps shall stipulate rules regarding alarm silencing, modification, and disabling. - Healthcare organizations should purchase infusion pumps with capacity to reduce errors due to incorrect programming. Whenever possible, infusion pumps should be standardized throughout the organization.

Empfehlung 30

Eine tragbare, netzunabhängige Pumpe soll für mobile Patienten mit HPE verwendet werden, wodurch die Lebensqualität und die Mobilität dieser Patienten im Vergleich zu stationären Pumpen verbessert wird.

Empfehlungsgrad A

64. Saqui O, Fernandes G, Allard JP. Quality of life analysis during transition from stationary to portable infusion pump in home parenteral nutrition patients: a Canadian experience. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition. 2014;29:131-41. [255]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** US **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** n/a **Study limitations:** the small sample may be under-powered for the statistical tests; an over-estimation of the Quality of life changes	**Total no. Patients:** 20 **Inclusion criteria:** patients that were stable and had been on HPN for >6 months using a stationary pump **Exclusion criteria:** Those who would not require HPN for >3 months or had used a portable pump within the past 6 months	- patients receiving HPN with a pole-mounted pump - they completed Short Form 36 (SF-36®) and pump-specific questionnaires - Patients were then enrolled in a 2-month prospective crossover open study - randomized to use a pole-mounted pump or a portable pump - after 1 month, each arm crossed over - measurements were repeated at 4 and 8 weeks
Notes	**Author's Conclusion:** Our HPN patients reported improved happiness and satisfaction regarding ease of use and function with a portable vs pole-mounted pump.		
Outcome measures/results	quality of life		- they reported ease of movement between rooms (4.11 ± 0.21 vs 1.44 ± 0.20; P = .001); when traveling (5.00 ± 0.00 vs 3.00 ± 0.45; P < .02) (1 = very difficult, 5 = very easy); 5.0% were sleep disturbed with the portable compared to 42.1% with pole-mounted pump (P < .04) - patients were significantly happier with the portable vs pole-mounted pump (4.53 ± 0.19 vs 2.68 ± 0.22; P < .001) (1 = very unhappy, 5 = very happy)

65. Boutin J, Hagan E. Patients' preference regarding portable pumps. Journal of intravenous nursing : the official publication of the Intravenous Nurses Society. 1992;15:230-2. [256]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case reports 3	**Countries:** n/a **Centers:** n/a **Setting:** n/a	**Total no. Patients:** 23 **Inclusion criteria:** HPN patients **Exclusion criteria:** n/a	- HPN patients were surveyed

	Funding Sources: n/a **Dropout rates:** n/a **Study limitations:** n/a		
Notes	**Author's Conclusion:** HPN patients with portable pumps were more independent and mobile than those without portable pumps.		
Outcome measures/results	pump satisfaction		- the electrically operated pump system was not as versatile as the portable pump - the portable pump signifies independence through mobility and the patients have an emotional attachment to their pumps - pump malfunction only occurred in the portable pump - 70 % of the patients were able to walk due to their portable pump

4 Pflege der Zugangswege und Infektionen

4.1 Wund- und Sondenversorgung bei HEE

Empfehlung 31

Die PEG-Ausgangsstelle sollte täglich überprüft und durch eine aseptische Wundversorgung sauber und trocken gehalten werden, bis sich der Stomakanal gebildet hat und die Wunde verheilt ist (durchschnittlich 5-7 Tage nach der Erstanlage).

Empfehlungsgrad B

66. National Nurses Nutrition Group (NNNG). Exit Site Management for Gastrostomy Tubes in Adults and Children. UK2013. [257]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Good practice guideline 4	**Countries:** n/a **Centers:** n/a **Setting: n/a** **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** In the first days following initial gastrostomy placement correct fixation of the gastrostomy tube is essential to promote the formation of a healthy stoma tract extending from the stomach to the outer abdominal wall. Apply a dressing impregnated with an antimicrobial agent directly onto tissue surrounding the gastrostomy tube, under the fixation device until further appropriate systemic treatment is identified and initiated.		
Relevant recommendations/statements	Until granulation of the stoma tract has taken place it is advisable to change the sterile dressing on a daily basis and provide local disinfection (usually up to day 7 post procedure). If the gastrostomy tube has a flat internal disc or flange the gastrostomy tube should be gently advanced / inserted into the stomach and returned to its initial position: - As per manufacturers guidance and local policy - As a minimum, by 2-3cm from day 10 onwards - At least once a week but not more frequently than once a day regardless of whether the distal tip of the tube sits in the stomach or small intestine. Rotating of the gastrostomy tube should be undertaken if the tube's distal tip sits in the stomach. Where appropriate rotation of the tube should be commenced 7-10 days after tube insertion, as per local guidance, and be undertaken on at least a weekly basis but not more frequently than once a day. This action should be undertaken where the tube has an internal flange, disc, basket or balloon. If overgranulation is observed:		

	- Apply a barrier film to protect surrounding skin - If overgranulation tissue is exuding ensure the affected skin is cleaned as a minimum, once a day (see above) - Consider swabbing the site for bacterial and fungal infection - Apply foam dressing impregnated with an antimicrobial agent under the fixation device/ main body of the tube - Change as clinically indicated (dressings commonly need changing initially after 48-72 hours). Ensure care is taken not to put undue pressure on the internal bumper whilst changing dressings - If overgranulation tissue is extensive apply a double layer of foam dressing over the affected area - Review effectiveness of treatment after 1 week (or as per local guidelines) In addition: - Protect surrounding skin with barrier cream - Cleanse skin daily with antimicrobial cleanser - The use of a silver dressing directly onto overgranulating tissue - Cover site with a single layer foam - Secure external fixator directly on top of both dressings. Ensure no undue pressure is placed on the internal bumper when changing these dressings. - Monitor stoma site daily to ensure no adverse reactions are developing from silver dressing. Change dressing only if there is evidence of significant exudate or patient discomfort. Otherwise change on a weekly basis. If infection is suspected and inflammation due to poor tube positioning has been eliminated, consider the following actions: - Apply a dressing impregnated with an antimicrobial agent directly onto tissue surrounding the gastrostomy tube, under the fixation device until further appropriate systemic treatment is identified and initiated. - If bacterial or fungal infection is confirmed administer systemic antibiotics or antifungal agents as prescribed. - In some persistent cases following treatment for a fungal infection it may be advisable to replace the gastrostomy tube (particularly if a silicone tube is in situ)

67. Roveron G, Antonini M, Barbierato M, Calandrino V, Canese G, Chiurazzi LF, et al. Clinical Practice Guidelines for the Nursing Management of Percutaneous Endoscopic Gastrostomy and Jejunostomy (PEG/PEJ) in Adult Patients: An Executive Summary. Journal of Wound Ostomy & Continence Nursing. 2018;45:326-34. [228]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Clinical practice guideline 1++	**Countries:** n/a **Centers:** n/a **Setting:** PEG and PEJ (enteral feeding) **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a

Notes	**Author's Conclusion:** The guidelines presented in this article describe care of adults with PEG, PEJ, PEGJ, or surgically implanted gastrostomies and jejunostomies. They are intended to be used by nurses caring for patients with EN in all care settings, including acute and critical care facilities, operating rooms, digestive endoscopy services, artificial nutrition outpatient units, gastroenterology units, and home care.
Relevant recommendations/statements	Management of the Stoma and Tube: Cleanse the stoma and peristomal skin of the gastric or jejunal EN tube with sterile saline and gauze 24 hours after placement to remove any discharge or material around the tube. If necessary, cover the stoma with a sterile gauze in order to absorb exudate or other fluids. Cleanse the stoma and peristomal skin with sterile solution every day for the first week. After 7 to 10 days, the output point of the tube can be cleansed (after loosening the external fixer, if necessary) with running water and non-perfumed soap using a clean cloth. Rotate the position of the gastrostomy tube 360° after the first 24 hours to prevent adhesion and repeat this maneuver at least once weekly, but no more than once daily, to prevent BBS. We recommend against rotating jejunal tubes in order to avoid perforation. We also recommend avoiding rotation of a PEGJ because the jejunal extension lacks a retaining disc and rotation could displace the tube. In addition to rotation of the PEG tube described earlier, the risk of BBS may be reduced by gently pushing the EN tube into the stomach 2 to 3 cm after loosening the exterior fixer, and then gently pulling it back until it reaches the area of minimal resistance (the internal gastric wall). The maneuver should be repeated at least once weekly, and no more than once daily. This push/pull maneuver should not be initiated until 7 to 10 days after initial insertion of a PEG tube, when the gastrocutaneous tract has healed. A gastric tube with a retention balloon should be inflated with distilled water to prevent precipitation of salt or encrustations with subsequent failure of balloon deflation. Check the volume of fluid in the balloon (to prevent accidental dislocations of the tube), and the clarity of the solution (to highlight possible losses) once weekly. Tube replacement and methods to assess tube position: We recommend performing the first planned tube change in a clinic or hospital environment (strength of recommendation D). After initial healing of the stoma (at least 1 month from the first tube placement), replacement may be completed in the home care setting by patients themselves or by a nurse if patients are not able to perform it.

Empfehlung 32

Als Alternative zur klassischen aseptischen Wundversorgung sollte während den ersten 2 Wochen ein Glyzerin-Hydrogel oder Glykogel-Verband über eine Woche ohne Inspektion verwendet werden.

Empfehlungsgrad B

68. Blumenstein I, Borger D, Loitsch S, Bott C, Tessmer A, Hartmann F, et al. A glycerin hydrogel-based wound dressing prevents peristomal infections after percutaneous endoscopic gastrostomy (PEG): a prospective, randomized study. Nutr Clin Pract. 2012;27:422-5. [260]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** Germany **Centers:** 1 university, 2 general hospitals	**Total no. Patients:** n=68 **Inclusion criteria:** cancer patients undergoing PEG	1. Group 1: received glycerin hydrogel (GHG); n=34 → changes of dressing: day 1, weeks 1,2,4

	Setting: GHG as antimicrobial property **Funding Sources:** ZAFES (Frankfurt am Main), Medi-Globe GmbH (Schweinfurt) **Dropout rates:** n/a **Study limitations:** study´s open design, no blinding possible, low number of patients	**Exclusion criteria:** no need of enteral nutrition, patients without cancer	2. Group 2: traditional wound dressing; n=34 → daily changes during week 1,2,4
Notes	- Study period: January 2007 to December 2008; 30-day post procedure follow-up; randomization - Assessment of PEG site: different infection sites - Enteral feeding was started within 4-6 hours of the procedure; leakage or soiling prompted immediate dressing change **Author's Conclusion:** The GHG wound dressing significantly reduces peristomal wound infections and is a convenient, cost-effective alternative for wound management following PEG.		
Outcome measures/results	- Validated scoring system for wound reactions →peristomal infection score was calculated by summing up individual scores for local erythema, induration, and exudation - Another infection score: to stratify infections into 5 grades of wound reaction - Wound reaction grade III, or purulent secretions → culture swabs		- At the end of the first and second weeks, a statistically significant reduction of the mean infection scores was seen in patients with GHG wound dressings (first week: 1.64 ± 1.6 vs 3.12 ± 2.69, P < .008; second week: 1.37 ± 1.11 vs 2.53 ± 2.37, P < .02) - After 7 days, wound reactions occurred in 14.7% in the GHG group vs 47.05% in the traditional group (p<0.005) - GHG n=29 and n=18 traditional group revealed grade 0 and I wound reactions (p>0.02) - GHG wound dressing required 5 times less frequent dressing changes - Procedure-related mortality was zero for both treatment groups - wound dressing of 4 patients in the GHG group had to be removed ahead of time: in 3 cases due to excessive wound secretion and in 1 case due to a mild local allergic reaction that seemed to be caused by the gel - total costs, including costs for dressing material, wound cleaning, and labor, are considered, cost-effectiveness analysis for the first month reveals a net cost saving of about €310/$425 per patient in favor of the GHG dressing

69. Aschl G, Kirchgatterer A, Fleischer M, Hinterreiter M, Hubner D, Kranewitter W, et al. [The frequency of wound infections after PEG-placement and utilization of glycogel wound dressing: a randomized controlled trial]. Wien Klin Wochenschr. 2008;120:224-7. [229]66.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Austria **Centers:** clinic Wels-Greiskirchen, Wels **Setting:** PEG wound infections **Funding Sources:** no funding **Dropout rates:** 2% (n=2; 98 patients had successful PEG procedure) **Study limitations:** n/a	**Total no. Patients:** n=100 **Inclusion criteria:** consecutive patients in need of PEG **Exclusion criteria:** no PEG	Comparison of wound infections: 1. standard wound management: daily dressing changes as well as cleaning and disinfection (day 1 to day 7); n=48 2. glygogel dressing; n=50 → routine antibiotic prophylaxis in both groups
Notes	- study period: August 2004 to January 2006 - specific wound scoring system: daily; 30-day follow-up by phone calls - Only with heavy contamination the glycogel dressing was changed, otherwise no routine change was intended. **Author's Conclusion:** Regarding wound infection rates after PEG placement, glycogel wound dressing was found to be as effective as standard wound dressing. Thus, omitting daily changes of regular wound dressings by using glycogel dressing instead may be advantageous for patients and generally help to decrease overall cost.		

Outcome measures/results	primary outcome: wound infections
	→ scoring system: erythema, induration, secretion
	secondary outcomes:
	- indication for PEG placement
	- complications
	  - major: perforation, infections with peritonitis, abscess, sepsis, need for premature removal of probe as well as bleeding and hematoma requiring transfusion or intervention
	  - minor: wound infections requiring local therapy or systemic antibiotic therapy, small hematomas
	- mortality
			- The indications for PEG placement were not significantly different between the two groups
			- standard wound care: a total of 88% of patients (n = 42) had no relevant infection (50%,n=24 with score 0 or 1; 38%,n=18 had score 2); 10% (n = 5) presented with serious local infection (score 3); one patient (2%) had severe infection necessitating PEG removal (score 4)
			- group using glycogel dressing: 88% of the patients (n = 44) did not show any relevant sign of infection (54%, n = 27 with score 0 or 1; 34%,n=17 had score 2); 8%(n=4)had serious local infection (score 3), 2% (n = 1) had severe infection (score 4); 2% (n = 1) were lost to follow up
			- 31% of both groups had a therapy with antibiotics due to other indications
			- Mortality: standard wound care 4% (n=2) during first 7 days and 15% (n=7) after 30 days → consequences of their disease
			- Group with glycogel dressing: 8% (n=4) during first 7 days; 14% (n=7) after 30 days → consequences of their disease

70. Pars H, Çavusoglu H. Effects of 3 Different Methods of Care on the Peristomal Skin Integrity of Children with Percutaneous Endoscopic Gastrostomy Tubes: A Prospective Randomized Controlled Trial. Adv Skin Wound Care. 2018;31:172-81.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** Turkey **Centers:** n=3 in Ankara **Setting:** PEG in children, different dressing methods **Funding Sources:** Scientific and Technological Research Council of Turkey (TUBITAK) **Dropout rates:** no dropout **Study limitations:** no valid reliable measurement tool for evaluating wound sites of children with PEG tube → create PSIOF, stoma monitoring only once a week, no blinding	**Total no. Patients:** n=60 **Inclusion criteria:** children (≤ 18 years), PEG insertion planned, agreement to participate **Exclusion criteria:** cancer	Comparison of effects of 3 different dressing methods on peristomal skin integrity with PEG tubes: 1. Hydrogel: n=20 2. Soap and water: n=20 3. Saline solution: n=20 → daily change of dressings during the first week; then weekly for group 1 and daily for groups 2 and 3
Notes	- 1 evaluation was performed at hospital and 4 during home visits in the first month after PEG insertion - Study was performed in accordance with good clinical practice guidelines (Declaration of Helsinki) **Author's Conclusion:** Because the dressing requires 6 times fewer changes per month, and wound site infection in the stoma site is minimized, the use of glycerin hydrogel should be considered for inclusion in pediatric stoma care procedures.		
Outcome measures/results	- Evaluations were performed using a PEG region peristomal skin integrity observation form - Devices measuring: stoma region (color, lesion, hemorrhage, pain, edema, maceration, buried bumper syndrome, drainage → PSiOF), pH, moisture, temperature - Data collection: age, gender, educational status of parents, diagnosis, PEG tube size, hospital that inserted PEG tube, PEG insertion environment - Patient Identification Information Form and Peristomal Skin Integrity Observation Form (PSIOF) → record od sociodemographic information	- Baseline characteristics were homogenously distributed (p>0.05) - majority of participants were 1 years or younger, male, with parents who graduated from high school, PEG insertion was primarily precipitated by a neurologic disorder - No major complications during the study - Moisture levels showed significant difference (p=0.000); moisture in the stoma region were normal in the saline solution group, high in the hydrogel group, and low in the soap and water group (P=0 .05) - Complications potentially affecting peristomal skin integrity in the stoma region (erythema, drainage, hemorrhage, hypergranulation tissue) were observed most frequently in the soap and water group (5%-45%) and least frequently in the hydrogel group (15%-25%)	

		- However, there was no statistically significant difference among the groups with respect to these complications (P=0 .05). - Problems at stoma site: 18.3% at first visit, 36.7% at final visit; wound site infection in 11.6% (Group 1: n=1, Group 2: n=4, Group 3: n=2) - Most common problem at stoma site: erythema (36.6%), drainage (36.6%), hypergranulation tissue (21.7%), and hemorrhage near the granulation tissue (18.3%) - No patients required oral antibiotics for increased erythema and drainage - no statistically significant relationship between pH, odor, turgor, hemorrhage, buried bumper syndrome, pain, edema, and maceration in any of the groups (P 9 .05) - significant relationship was observed among temperature, color, lesion, and drainage at the stoma sites between the visits - At visits after the first day, statistically significant increases were observed in the ratio of patients with stoma site temperatures greater than 35°C (P =0 .004, Q = 15.600), lesions at the stoma site (P =0.04, Q = 10.000), drainage at the stoma site (P =0.000, Q = 23.579) in the soap and water group, and abnormal stoma color (pale pink and reddish stoma) in all of the groups (P =0.000, Q = 46.706).

<u>Empfehlung 33</u>

Nach der Stomaheilung können die Verbandswechsel auf ein oder zwei2 Mal pro Woche reduziert und die Eintrittsstelle kann mit Seife und Wasser in Trinkwasserqualität gereinigt werden.

Empfehlungsgrad 0

71. National Nurses Nutrition Group (NNNG). Exit Site Management for Gastrostomy Tubes in Adults and Children. UK2013. [257]
→ see No. 66

Empfehlung 62

Nach der Mobilisierung sollte die Sonde in ihre Ausgangsposition zurückgebracht werden, wobei ein gewisser freier Abstand (0,5-1 cm) zwischen Haut und Außenpolster bestehen sollte.

Empfehlungsgrad 0

72. McClave SA, Jafri NS. Spectrum of morbidity related to bolster placement at time of percutaneous endoscopic gastrostomy: buried bumper syndrome to leakage and peritonitis. Gastrointest Endosc Clin N Am. 2007;17(4):731-46. [263]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case reports 3	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** In conclusion, endoscopists need to be aware of the spectrum of complications related to placement of the external bolster. Attention to detail at the time of placement and careful follow-up in the period immediately following should help prevent the development of more serious sequelae. At the first sign of an adverse event or injury to the PEG tract, urgent endoscopy and the initiation of multiple therapeutic strategies should be effective in preserving the PEG site and allowing continuation of enteral feeding.		
Relevant recommendations/statements	Ulceration due to bolster: replacement of jejunal tube → external clamping device was applied to fix the position of the PEG with the internal bolster away from the ulcer to allow healing. Buried bumper syndrome: The severity of buried bumper syndrome ranges from simple ulceration underneath the internal bolster to outward erosion of the PEG tube through the anterior abdominal wall. Typically, buried bumper syndrome is a more chronic complication occurring most often between 3 and 6 months after PEG placement. Clearly, excessive tension between the internal and external bolsters is the biggest factor in generating this complication. Excess tension between the bolsters reduces blood flow to the tissue and leads to pressure necrosis and mucosal ischemia → In general, studies in animal models and patients suggest that placing the bolster too tight probably causes more problems than leaving the bolster too loose. PEGs made of the stiffer polyurethane material may be more likely to injure the surrounding tissue than PEGs made from softer silicone. → The management of buried bumper syndrome depends on early recognition, endoscopy to evaluate the extent of injury, and a determination as to whether the PEG site is salvageable. With the development of any signs of buried bumper syndrome, endoscopy is required to view the gastric mucosal surface. At the time of endoscopy, the PEG should be pushed inward slightly to evaluate for ulceration underneath the internal bolster. Endoscopy also helps determine the extent of communication with the lumen of the stomach. The key issue at the time of endoscopy is to determine whether the PEG site is salvageable and whether it may be reused for placement of a new PEG.		

	→ If endoscopy determines that the site is salvageable, it should be determined which direction of PEG removal will cause the least damage to the PEG tract - pulling the old PEG out through the abdominal wall causes the least amount of damage to the PEG tract/ In other cases, pulling the PEG back into the stomach and out the mouth may cause less trauma to the PEG site. → the embedded PEG tube should be cut down short to within 3 to 5 cm of the anterior abdominal wall. → In more advanced buried bumper syndrome, the defect around the newly placed PEG may be significant enough that continued peristomal drainage may be anticipated. A number of steps may be required to allow complete healing of the site to occur → Proton pump inhibitor therapy should be initiated at two to three times the standard dosage to eliminate any acid content in the drainage around the PEG tube. → It is important to avoid the use of hydrogen peroxide or any scented cleansers on the skin around the PEG site because they have a drying, desiccating effect on the skin and can delay wound healing. Leakage and peritonitis: Immediately after PEG placement, there is greater likelihood of leakage and possible peritonitis. In the later periods, a shift in liability occurs toward greater risk of pressure necrosis and buried bumper syndrome. → The prevention of adverse sequelae from either extreme starts at the time of PEG placement: Leakage is minimized by the small size of the gastrostomy tube and the formation of a fibrous tract around the gastrostomy. Also, leakage is minimized by contraction of the thick gastric musculature around the PEG tube. The lack of such thick musculature in the small bowel may increase the chance for leakage around a DPEJ tube, as suggested by the fourth case presentation. → Removal or displacement of the PEG tube before maturation of the gastrocutaneous tract can result in peritonitis. Furthermore, mechanical failure of the internal bolster may result in displacement out into the peritoneal cavity → Repeat endoscopy following PEG placement, to set the external bolster under direct vision, is paramount. →Management of peritonitis depends on early recognition of is associated signs and symptoms A diagram or chart should be constructed delineating the external bolster settings to communicate the information to long-term caregivers. As an alternative, marking the appropriate depth on the feeding tube with an indelible marker communicates the same information For the first 4 days following PEG placement, the external bolster should be in opposition to the anterior abdominal wall, with a firm fit with little play in or out. It may be important during this time for caregivers not to change the dressing on the PEG site. The PEG patient should be re-evaluated at 4 days, at which time the external bolster is readjusted or moved back to allow 1 cm of play.

<u>Empfehlung 34</u>

Im Falle einer peristomalen Leckage des Mageninhalts an der Stomastelle kann die umgebende Haut mit Hautschutzmitteln auf Zinkoxidbasis oder anderen geeigneten Hautschutzmitteln angemessen geschützt werden.

Empfehlungsgrad 0

73. Itkin M, DeLegge MH, Fang JC, McClave SA, Kundu S, d'Othee BJ, et al. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the Society of Interventional Radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). Gastroenterology. 2011;141:742-65.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline 2+	**Countries:** n/a **Centers:** n/a **Setting:** Gastrointestinal access for Enteral Nutrition **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** Gastroenteric access is an integral part of the patient care provided by a variety of health care professionals. Transabdominal and natural orifice approaches have been proven to be successful and safe under endoscopic or image guidance.		
Relevant recommendations/statements	Contraindications to Enteral Access: Absolute contraindications to tube placement include mechanical obstruction of the GI tract (unless the procedure is indicated for decompression), active peritonitis, uncorrectable coagulopathy, or bowel ischemia. ASGE Recommendations: Warfarin should be stopped 5 days before the procedure. The INR should be checked on the day of the procedure and should be confirmed to be lower than 1.5. Warfarin may be started later on the night of the procedure, with the INR checked 1 week later. Recommendations for a high-risk procedure in a patient with a high-risk condition are as follows. A therapeutic dose of low molecular weight heparin should be substituted, with the dose withheld on the morning of the procedure. For clopidogrel therapy, the clinician should discuss the necessity of the procedure first with the primary care physician, as risk is significant. If the procedure is deemed to be essential, clopidogrel should be stopped 7 days before surgery and the patient given aspirin therapy in the interim. Clopidogrel therapy may be restarted on the morning after the procedure Technical Aspects - Nasoenteric and Oroenteric tubes: Many centers promote bedside auscultation for confirmation of an adequate position of the tube before use. However, this can be misleading, as inappropriate tube locations, such as in the lung, in the pleural cavity after perforation, or coiled in the esophagus may be misinterpreted as in proper position by bedside auscultatory techniques. For this reason, every patient should undergo radiography to confirm proper position of an NG or OG tube before feeding is initiated Continuous Care/Maintenance of GI Access – Tube Dressing and Positioning: The gastrostomy site should be cleaned with mild soap and water; hydrogen peroxide should not be used after the first week after placement as it can irritate the skin and contribute to stomal leaks. Daily cleaning of the tube with water and regular or antibacterial soap is adequate to keep the tube clean. Some institutions do not apply a dressing to the site. Peristomal leakage/irritation: Leakage of tube feeding formula and/or gastric contents around the gastrostomy site can be a significant management problem. Risk factors include infection of the site, increased gastric acid secretion, excessive cleansing with hydrogen peroxide, buried bumper syndrome, side torsion on the gastrostomy tube, and excessive tension between the internal and external bolsters. If the patient is not receiving acid suppression, proton pump inhibitor therapy should be started. Side torsion resulting in ulceration and enlargement of the tract may be corrected with a clamping device to stabilize the tube. The same result may also be accomplished by replacing the gastrostomy with a low-profile device. After the primary cause of the stomal leakage has been addressed, stoma adhesive powder or zinc oxide can be applied to the site to prevent local skin irritation.		

	Foam dressing rather than gauze can help to reduce local skin irritation caused by gastric contents. Another potential treatment option is conversion of the gastrostomy tube to a gastrojejunostomy Inadvertent tube removal: Gastrostomy tract maturation usually occurs within the first 7–10 days but may be delayed as long as 4 weeks in the presence of malnutrition, ascites, or corticosteroid treatment.

Empfehlung 35

Protonenpumpenhemmer können zur Verringerung der Leckage durch Minimierung der Magensäuresekretion eingesetzt werden, wobei mögliche Nebenwirkungen abzuwägen sind.

Empfehlungsgrad 0

74. Itkin M, DeLegge MH, Fang JC, McClave SA, Kundu S, d'Othee BJ, et al. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the Society of Interventional Radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). Gastroenterology. 2011;141(2):742-65. [226]
→ see No. 73

Empfehlung 36

Bei Verdacht oder Diagnose einer Infektion an der Eintrittsstelle kann ein antimikrobielles Mittel topisch auf die Eintrittsstelle der Sonde und das umgebende Gewebe aufgetragen und – falls die Infektion an der Eintrittsstelle durch diese Behandlung nicht behoben werden kann – mit systemischen Breitband-Antibiotika kombiniert werden.

Empfehlungsgrad 0

75. Boullata JI, Carrera AL, Harvey L, Escuro AA, Hudson L, Mays A, et al. ASPEN Safe Practices for Enteral Nutrition Therapy [Formula: see text]. JPEN J Parenter Enteral Nutr. 2017;41:15-103. [271]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline 1++	**Countries:** n/a **Centers:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a

	Setting: correct use of EN, risk of infections **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a		
Notes	**Author's Conclusion:** Enteral nutrition (EN) is a valuable clinical intervention for patients of all ages in a variety of care settings. Along with its many outcome benefits come the potential for adverse effects. These safety issues are the result of clinical complications and of process-related errors. The latter can occur at any step from patient assessment, prescribing, and order review, to product selection, labeling, and administration. To maximize the benefits of EN while minimizing adverse events requires that a systematic approach of care be in place. This includes open communication, standardization, and incorporation of best practices into the EN process.		
Relevant recommendations/statements	What is the best way to confirm accurate EAD placement in adult patients? - Obtain radiographic confirmation for any blindly placed short-term EAD to demonstrate that it is properly positioned in the GI tract prior to its initial use for administering feedings and medications in adult patients. - When attempting to insert a short-term feeding tube, obtain a tube aspirate for appearance and pH measurement. The appearance and pH are likely dependent on location. - Do not rely on the auscultatory method alone to differentiate between gastric and respiratory placement or between gastric and small bowel placement. - Mark the exit site of a feeding tube at the time of the initial placement and document either the incremental marking on the tube or the external length of the tube in the medical record. - Evaluate whether the incremental marking or external tube length changes, and, if a change is observed, use other bedside tests such as visualization and pH testing of tube aspirate to help determine if the tube has become dislocated. If in doubt, obtain a radiograph to determine tube location. How often should you replace long-term EADs? Consider tube replacement sooner than indicated in manufacturer guidelines if any of the following are identified: Stomal tract disruption, Peristomal infection that persists despite appropriate antimicrobial treatment, Skin excoriation. In patients with a PEG tube, most major complications have been reported to occur within the first few days of initial tube placement when the tube tract is not yet mature. The tract begins to mature approximately 7–10 days after PEG placement, and it takes a few weeks for fusion to take place between the stomach and peritoneum. If the gastrostomy tube dislodges in the first 7–10 days after insertion, the inserting provider needs to be contacted as soon as possible for further intervention. A dislodged PEG tube can become a medical emergency, as stomach contents are likely to leak into the peritoneum. The tube should not be reinserted blindly at this stage because it may be repositioned into the peritoneum. Possible approaches to management include immediate reinsertion under radiographic or endoscopic guidance, laparotomy, or conservative management (cessation of oral intake, nasogastric suction, and antibiotics) followed by reinsertion in 7–10 days. If displacement occurs after the tract is mature (>30 days), prompt replacement with a percutaneously balloon gastrostomy tube is recommended. Preventive maintenance of balloon gastrostomy tubes, which includes elective change at a fixed time interval (such as every 3–6 months), is the standard of practice in some facilities because of the potential for balloon failure. Can the EN feeding system be a source for contamination and infection and how can contamination in the EN feeding system be best prevented? - Use a closed EN delivery systems when possible.		

	- Follow the manufacturer's recommendations for duration of infusion through an intact delivery device (container and administration set). - Do not reuse the enteral delivery device for open or - If open systems are used, follow recommended hang times and avoid topping off remaining formula, which may result in a continuous culture for exponential: microbial growth, limit infusion time for open EN feeding systems to 4–8 hours maximum (12 hours in the home setting), limit infusion time for a reconstituted powder product or modular to 4 hours maximum, change the delivery device. - To limit the risk of microbial growth and biofilm formation, avoid unnecessary additions to the EN administration set. If additional equipment, such as 3-way stopcocks, are used, follow manufacturer recommendations or facility protocol for change and cleaning practices. - Establish and follow protocols for preparation: handling, storage of commercial and handmade EN, about hand hygiene (a critical point) and safe handling of EN preparation and administration; - extend education to patients and family members/ care givers who will continue this practice into the home setting. - Use effective hand hygiene in all aspects of EN preparation and administration. When gloves are used, they must be clean gloves, not having been involved in other nonrelated tasks. The importance of hand washing in minimizing transference of microbial growth and preventing hospital-acquired infections cannot be overstressed. - Store prepared or opened ready-to-feed solutions in an appropriate refrigerator, discarding any used solutions within 24 hours of preparation or opening. - Periodically survey and regularly monitor adherence. Document findings and take appropriate actions if protocols are not followed. - Keep all equipment, including syringes and containers for flush and medication administration, as clean and dry as possible. Store clean equipment away from potential sources of contamination. - Consider whether microbial growth related to EN might be implicated as part of the diagnosis when patients have adverse conditions such as diarrhea.

4.2 Beginn der EE nach Sondenplazierung

Empfehlung 37

Erwachsene mit einer unkomplizierten Platzierung der Gastrostomiesonde sollen innerhalb von 2 - -4 Stunden nach dem Eingriff mit der EE beginnen.

Empfehlungsgrad A

76. Toussaint E, Van Gossum A, Ballarin A, Arvanitakis M. Enteral access in adults. Clin Nutr. 2015;34:350-8. [204]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review	**Countries:** n/a	**Total no. Patients:** n/a	n/a

2+	**Centers:** n/a **Setting:** jejunal HEN feeding **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Inclusion criteria:** n/a **Exclusion criteria:** n/a	
Notes	**Author's Conclusion:** There are several techniques for providing enteral feeding access including nasogastric or nasojejunal tubes, and surgical or endoscopic percutaneous approaches. Despite the benefits and widespread use of enteral tube feeding, some patients may experience complications either due to the enteral access itself or to the enteral feeding. Prevention of complications is the major recommendation. The adherence to well-designed protocols by a multidisciplinary team is the best way for avoiding complications and taking care of potential side-effects.		
Relevant recommendations/statements	Jejunal feeding is an alternative in selected patients who do not tolerate gastric feeding or who have severe reflux and increased risk for aspiration pneumonia. Jejunal enteral feeding has been traditionally recommended for patients with severe acute pancreatitis to avoid pancreatic stimulation. Gastric or duodenal ulcers with active bleeding and a visible vessel is a relative contraindication for PG. In this case, because of the high risk of bleeding recurrence, it is advised that the procedure be delayed for 72 h. Gastrostomy tubes may be placed successfully after paracentesis if reaccumulation of ascitic fluid can be prevented for a period of 7-10 days following the procedure, to allow the tract maturation. Traditionally, after per oral PEG insertion, feeding was initiated after 12-24 h in order to allow better healing of the enteral opening and to prevent early leakage. Nevertheless, several prospective studies have shown that earlier initiation, at 3-4 h after PEG insertion, is safe. Guidelines recommend infusing saline 3-6 h after the procedure, and if this is well tolerated to continue with enteral nutrition. Routine water flushing after feedings can prevent tube occlusion. Complications related to NG or NJ tube insertion include patient discomfort, epistaxis, sinusitis, tube malposition, and esophageal injury including pressure ulcers. Complications related to jejunal tube placement are similar in nature and frequency to those observed with PG. In addition, direct PJ may lead to jejunal volvulus, small bowel perforation, and persistent enterocutaneous fistulas after tube removal. Jejunal volvulus can be avoided by not rotating the tube, but only moving it by forward and backward motions. Various strategies to reduce aspiration have been studied. These include backrest elevation, post-pyloric feeding (by NJ, PGJ, or PJ), and administration of motility agents to promote gastric emptying. it is advised for all patients receiving enteral nutrition to have their backrest elevated 45°. In cases of persistent reflux or delayed gastric emptying despite motility agents, postpyloric feeding can be provided		

<u>Empfehlung 38</u>

Die Einleitung der EE sollte einem Stufenplan folgend einschleichend über mehrere Tage erfolgen, um Komplikationen zu reduzieren.

Bei jejunaler Sondenlage sollte besonders langsam appliziert werden, um die Gefahr von osmotisch bedingten Unverträglichkeiten zu reduzieren.

Empfehlungsgrad B

77. Abu-Hilal M, Hemandas AK, McPhail M, Jain G, Panagiotopoulou I, Scibelli T, et al. A comparative analysis of safety and efficacy of different methods of tube placement for enteral feeding following major pancreatic resection. A non-randomized study. Jop. 2010;11:8-13. [278]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2-	**Countries:** UK **Centers:** Hepatobiliary and Pancreatic Surgical Unit, Southampton University Hospital **Setting:** Comparison of 3 routes of EN following pancreaticoduodenectomy **Funding Sources:** n/a **Dropout rates:** no dropout **Study limitations:** no randomization to different feeding tube techniques, different group number, choice of method was surgeon related→ bias?	**Total no. Patients:** n=100 **Inclusion criteria:** patients undergoing pancreatic resection **Exclusion criteria:** no enteral feeding	Comparison of: 1. percutaneous transperitoneal jejunostomy (PJ): n=25 2. percutaneous transperitoneal gastrojejunostomy (PTGJ): n=32 3. nasojejunal route (NJ): n=43 → enteral feeding started within 24h of operation and increased over 2-3 days to meet full nutrition requirement
Notes	- Normal saline was administered via the feeding tube at 10 mL/h post operatively. Enteral feeding with Nutrison standard (Nutricia, Trowbridge, United Kingdom) to provide 1 kcal/mL was started at 10 mL/h, 24 hours postoperatively. This was increased daily as tolerated by 20 mL to a maximum of 80 mL/h. Most patients were allowed to commence oral intake when enteral nutrition was in progress - PJ, PTGJ tubes: feeding catheter was removes in outpatients at 4-6 weeks; NJ group: feeding stopped when patients were able to tolerate full oral intake containing solid food **Author's Conclusion:** Enteral nutrition following pancreatic resection can be delivered in different ways. Nasojejunal feeding was associated with fewest and less serious complications. On current evidence surgeon preference is a reasonable way to decide enteral nutrition but a randomized controlled trial is needed to address this issue.		
Outcome measures/results	Primary outcome: - Tube related complications (ineffectual feeding, increase in morbidity/patients' discomfort Other information: - Efficiency - Safety		- N=7 had total pancreatectomies; n=93 had Whipple´s operations - Total of 188 complications in 64 patients - Complications: - PJ group: 16 of 25 patients (64.0%) had 30 complications - PTGJ group. 24 of 32 patients (75.0%) developed 50 complications NJ group: 24 of 43 patients (55.8%) developed 38 complications (P=0.231)

	- Demographic data - type of procedure/reconstruction - hospital stays - type of feeding tube - nasogastric aspirates - time to return of bowel function - time to stop enteral feeding - postoperative surgical and general complications	- The frequency of surgical complications was significantly different (P=0.003) among the three different feeding tubes→ Biliary leak/stricture was significantly higher (P=0.006) in patients with the PTGJ tube - The incidence of catheter-related complications was higher in percutaneous techniques: 24% in percutaneous transperitoneal jejunostomy and 34% in percutaneous transperitoneal gastrojejunostomy as compared to nasojejunal technique (12%) - Median time to complete establishment of oral intake was 14, 14 and 10 days in percutaneous transperitoneal jejunostomy, percutaneous transperitoneal gastrojejunostomy, and nasojejunal groups - Nasojejunal tubes were removed at median 11 days (mean 11.5 days) compared to 5-6 weeks for percutaneous transperitoneal jejunostomy and percutaneous transperitoneal gastrojejunostomy - Commonest catheter-related complication in the percutaneous transperitoneal jejunostomy and percutaneous transperitoneal gastrojejunostomy was blockage (n=6; 10.5%), followed by pain after removal of feeding tube at 5-6 weeks (n=5; 8.8%); in the nasojejunal group it was blockage (n=3; 7.0%), followed by displacement (n=2; 4.7%) - Two patients died postoperatively in this cohort→ no catheter-related mortalities

<u>Empfehlung 39</u>

Zur Vermeidung von Sondenkomplikationen sollte insbesondere vor und nach Applikation von Medikamenten gespült werden.

Empfehlungsgrad 0

78. Phillips NM, Endacott R. Medication administration via enteral tubes: a survey of nurses' practices. J Adv Nurs 2011; 67: 2586-2592. doi:10.1111/j.1365-2648.2011.05688.x [286]								
Study design	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
	Type	**Duration**		**n**	**age**	**Characteristics**		
Observation study IIb	Questionnaire for dealing with CVC	2006-2007	Hospital	181 (92 intensive care; 52 surgery; 30 medical departments; 7 medical-surgical departments)	n/a	nurses	96% flush tube after medication; 28% flush before medication; 12% flush between each medication	Nurse use different methods: possibly endangering of the patient

4.3 Wund- und Katheterversorgung bei HPE

Empfehlung 40

Zur Abdeckung der Katheteraustrittsstelle sollte entweder ein steriler Mull oder ein steriler, halbdurchlässiger Transparentverband verwendet werden.

Empfehlungsgrad B

79. Gillies D, O'Riordan E, Carr D, O'Brien I, Frost J, Gunning R. Central venous catheter dressings: a systematic review. Journal of advanced nursing. 2003;44:623-32. [295]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** Canada, USA, Sweden, England, The Netherlands **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** patients in an acute care setting with a CVC; studies should focus on gauze and tape compared with transparent polyurethane film **Exclusion criteria:** n/a	comparing the effects of gauze and tape and/or transparent polyurethane dressings on CVCs - two studies compared gauze and tape with Opsite IV3000 - two compared Opsite with Opsite IV3000 - one compared Tegaderm with Opsite IV3000 - one compared Tegaderm with Opsite

	Study limitations: small patient sample; no sufficient power to detect any differences between groups		
Notes	**Author's Conclusion:** Based on these findings, policy at The CHW has been changed to allow the decision to use gauze and tape or Opsite IV3000 to be based on the preferences of patients and carers.		
Outcome measures/results	Catheter-related sepsis, tunnel infection, exit site infection		- no evidence of any difference in the incidence of infectious complications between any of the dressing types compared

80. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline 2+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** Interventions to improve reliability of care should focus on making the implementation of best practice easier to achieve.		
Relevant recommendations/statements	- educate healthcare personnel regarding the indications for intravascular catheter use, proper procedures for the insertion and maintenance of intravascular catheters, and appropriate infection control measures to prevent intravascular catheter-related infections - weigh the risks and benefits of placing a central venous device at a recommended site to reduce infectious complications against the risk for mechanical complications - keep all components of the pressure monitoring system (including calibration devices and flush solution) sterile - minimize the number of manipulations of and entries into the pressure monitoring system. - periodically assess knowledge of and adherence to guidelines for all personnel involved in the insertion and maintenance of intravascular catheters - designate only trained personnel who demonstrate competence for the insertion and maintenance of peripheral and central intravascular catheters. - ensure appropriate nursing staff levels in ICUs		

81. Ullman AJ, Cooke ML, Mitchell M, Lin F, New K, Long DA, et al. Dressing and securement for central venous access devices (CVADs): A Cochrane systematic review. International journal of nursing studies. 2016;59:177-96. [294]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- to compare the available dressing and securement devices for central venous access devices (CVADs)
Notes	**Author's Conclusion:** More, high quality research is needed regarding the relative effects of dressing and securement products for CVADs.		
Outcome measures/results	CVAD-related bloodstream infection, CVAD tip colonization, entry and exit site infection, skin colonization, skin irritation, failed CVAD securement, dressing condition and mortality		- Unclear whether there is a difference in the rate of CVAD-related bloodstream infection between securement with gauze and tape and standard polyurethane (RR 0.64, 95 % CI 0.26 to 1.63, low quality evidence), or between chlorhexidine gluconate-impregnated dressings and standard polyurethane (RR 0.65, 95 % CI 0.40 to 1.05, moderate quality evidence) - High quality evidence that medication-impregnated dressings reduce the incidence of CVAD-related bloodstream infection relative to all other dressing types (RR 0.60, 95 % CI 0.39 to 0.93) - Moderate quality evidence that chlorhexidine gluconate-impregnated dressings reduce the frequency of CVAD-related bloodstream infection per 1000 patient days compared with standard polyurethane dressings (RR 0.51, 95 % CI 0.33 to 0.78) - Moderate quality evidence that catheter tip colonization is reduced with chlorhexidine gluconate-impregnated dressings compared with standard polyurethane dressings (RR 0.58, 95 % CI 0.47 to 0.73), but the relative effects of gauze and tape and standard polyurethane are unclear (RR 0.95, 95 % CI 0.51 to 1.77, very low-quality evidence)

<u>Empfehlung 41</u>

Bei gefährdeten Patienten sollten als Zusatzmaßnahme für die Austrittsstelle von ZVKs Verbände, die kontinuierlich desinfizierende Substanzen freisetzen, wie z. B. Chlorhexidin, verwendet werden.

Empfehlungsgrad B

82.	**Ullman AJ, Cooke ML, Mitchell M, Lin F, New K, Long DA, et al. Dressing and securement for central venous access devices (CVADs): A Cochrane systematic review. International journal of nursing studies. 2016;59:177-96. [294]**
→ see No. 81	

83.	**Kommission für Krankenhaushygiene und Infektionsprävention beim Robert Koch-Institut. Prävention von Infektionen, die von Gefäßkathetern ausgehen: Teil 1– Nichtgetunnelte zentralvenöse Katheter Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut. Bundesgesundheitsblatt-Gesundheitsforschung-Gesundheitsschutz 2018; 60: 171-206 [296]**
Guideline	Die Kommission empfiehlt: Verband an der Kathetereintrittsstelle: Antisepsis und Verbandswechselintervalle - Mittel der Wahl sind alkoholbasierte Formulierungen mit Zusatz von Chlorhexidin oder Octenidin (Kat. IB). Chlorhexidin-freisetzende Verbände am ZVK - CHX-freisetzende Katheterverbände für ZVK bei Erwachsenen und bei pädiatrischen Intensivpatienten sollen vorrangig eingesetzt werden, wenn die in der prospektiven Surveillance ermittelten CABSI-Raten trotz überprüfter Implementierung anderer evidenzbasierter Präventionsmaßnahmen anhaltend hoch sind (Kat. IA). - In besonders vulnerablen Patientenkollektiven (z. B. Patienten mit hochgradiger Immunsuppression, nach Stammzell- oder Organtransplantation) kann der Einsatz CHX-freisetzender Katheterverbände für ZVK als grundsätzlicher Bestandteil eines Bündels für die Erhaltungspflege nach Insertion erwogen werden. Hierüber entscheiden die behandelnden Ärzte nach einer entsprechenden Risikoanalyse (Kat. IA).
Relevant recommendations/ statements	- Die lokale Verträglichkeit der Verbände sollte vor allem bei langfristiger Anwendung (>14 Tage) sorgfältig beobachtet werden; schwere lokale oder systemische Unverträglichkeitsreaktionen sind zu dokumentieren und an den Hersteller zu melden (Kat. IV). - Zum Einsatz CHX-haltiger Pflasterverbände an der Eintrittsstelle anderer Gefäßkatheter (z. B. Hämodialyse) können bislang keine Empfehlungen ausgesprochen werden (Kat. III). - Die Relevanz der lokal und zeitlich begrenzten Applikation von CHX auf die Selektion von Bakterien mit verminderter CHX-Empfindlichkeit (z. B. Staphylokokken) ist nicht abschließend beurteilbar, dieses Problem sollte jedoch aufmerksam weiterverfolgt werden.

Empfehlung 42

Der Überleitungsschlauch zwischen Nährlösungsbeutel und ZVK zur Verabreichung der HPE sollte bei jeder neuen Infusion bzw. innerhalb von 24 Stunden nach Beginn der Infusion ersetzt werden.

Empfehlungsgrad B

84. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]
→ see No. 80

85. Austin PD, Hand KS, Elia M. Systematic review and meta-analyses of the effect of lipid emulsion on microbial growth in parenteral nutrition. The Journal of hospital infection. 2016;94:307-19. [300]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Meta-Analysis 1-	**Countries:** n/a **Center:** n/a **Setting:** n/a **Funding Sources:** the 2012 Galen Award from Pharmacy Research UK **Dropout rates:** n/a **Study limitations:** Study conditions and methodologies varied widely; small sample size	**Total no. Patients:** unmatched datasets (N=306); matched datasets (N=38 pairs) **Inclusion criteria:** laboratory-based microbial growth studies in lipid emulsion, lipid PN or lipid-free PN over a 48-h period **Exclusion criteria:** studies that did not define infusate composition; if they duplicated previous work or if cfu/mL were not reported at both time zero and at 48	systematic review with meta-analyses examined effects of nutrients on microbial growth in PN infusates over a 48-h period using the growth ratio {GR= log10[colony-forming units (cfu)/mL at 48 h/cfu/mL at time zero]}
Notes	**Author's Conclusion:** Any recommendations about the duration of PN infusion from a single container should account for all these factors, and should be weighted according to microbial species likely to contaminate PN.		
Outcome measures/results	the extent of microbial growth promotion or suppression over 48 h in lipid emulsion, lipid PN and lipid-free PN, expressed as a microbial growth ratio		- factors influencing GR in PN: glucose, microbial species, temperature, osmolarity, presence of vitamins, trace elements and lipid, and amino acid profile - unmatched datasets: a general linear model found that lipid inclusion in PN represented 3.3% of the variability, which was less than that due to glucose concentration (5.8%), microbial species (35.3%) and microbe -infusate interaction (4.4%) - matched datasets: lipid inclusion in PN represented 5.4% of the variability (P=0.076),which was less than that due to glucose concentration (8.5%;P=0.025), microbial species (75.5%;P<0.001) and microbe -infusate interaction (13.3%;P=0.382) - the presence of lipid in PN at fixed glucose concentrations did not significantly increase GR of Candida albicans, Escherichia coli or

		Staphylococcus epidermidis (P=0.352,P=0.025 and P=0.494, respectively; overall P=0.175)

Empfehlung 43

Beim Verbandwechsel und bei der Hautdesinfektion um den Katheter soll eine alkoholische 0,1%-ig Octenidin oder eine alkoholische 2 %-ige Chlorhexidinlösung verwendet werden.

Empfehlungsgrad A

86. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]
→ see No. 80

87. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Annals of internal medicine. 2002;136:792-801. [305]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Meta-Analysis 1-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** the authors did not state how any discrepancies were resolved; the authors did not state how the papers were selected	**Total no. Patients:** n/a **Inclusion criteria:** RCTs **Exclusion criteria:** n/a	- to evaluate the efficacy of skin disinfection with chlorhexidine gluconate, compared with povidone-iodine solution, in preventing vascular catheter-related bloodstream infection - all studies used a 10% povidone-iodine solution for the control group
Notes	**Author's Conclusion:** The incidence of bloodstream infections is significantly reduced in patients with central vascular lines who receive chlorhexidine gluconate versus povidone-iodine for insertion-site skin disinfection.		

Outcome measures/results	- primary outcome: catheter-related bloodstream infection - secondary outcomes: catheter colonization	- the RR of catheter colonization and catheter-related bloodstream infection was significantly lower with chlorhexidine gluconate than with povidone-iodine - the summary RR was 0.49 (95% CI: 0.31, 0.71) for catheter colonization and 0.49 (95% CI: 0.28, 0.88) for catheter-related bloodstream infection - absolute risk reduction was 7.1% for colonization and 1.1% for catheter-related blood-stream infection - the test for heterogeneity was significant for catheter colonization (P<0.001), but not for catheter-related bloodstream infection (P>0.2)

88. Mimoz O, Lucet JC, Kerforne T, Pascal J, Souweine B, Goudet V, et al. Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. Lancet (London, England). 2015;386:2069-77. [306]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** France **Centers:** 11 French intensive-care units **Setting:** **Funding Sources:** University Hospital of Poitiers, CareFusion **Dropout rates:** n/a **Study limitations:** masking was not feasible; the possible effect of differences in the antiseptic types and concentrations in the study solutions or application methods could not be assessed; adhesion to the study protocol was not regularly checked by formal audits	**Total no. Patients:** 2,349 **Inclusion criteria:** at least one of central-venous, hemodialysis, or arterial catheters **Exclusion criteria:** n/a	- comparison of two skin antisepsis - group 1 (n=1181): 2% chlorhexidine–70% isopropyl alcohol (594 patients with scrubbing, 587 without) - group 2 (n=1168): 5 % povidone iodine–69 % ethanol, (580 patients with scrubbing, 588 without)

Notes	**Author's Conclusion:** For skin antisepsis, chlorhexidine–alcohol provides greater protection against short-term catheter-related infections than does povidone iodine–alcohol and should be included in all bundles for prevention of intravascular catheter-related infections.	
Outcome measures/results	- Primary outcome: incidence of catheter-related infections - Secondary outcome: incidence of catheter colonization	- Chlorhexidine–alcohol was associated with lower incidence of catheter-related infections (0·28 vs 1·77 per 1000 catheter-days with povidone iodine–alcohol; hazard ratio 0·15, 95% CI 0·05–0·41; p=0·0002) - Scrubbing was not associated with a significant difference in catheter colonization (p=0·3877) - No systemic adverse events, but severe skin reactions occurred more frequently in those assigned to chlorhexidine–alcohol (27 [3%] patients vs seven [1%] with povidone iodine–alcohol; p=0·0017)

89. Lai NM, Lai NA, O'Riordan E, Chaiyakunapruk N, Taylor JE, Tan K. Skin antisepsis for reducing central venous catheter-related infections. The Cochrane database of systematic reviews. 2016;7:Cd010140. [307]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** RCTs that assessed any type of skin antiseptic agent used either alone or in combination compared with one or more other skin antiseptic agent(s), placebo or no skin antisepsis in patients with a CVC in place **Exclusion criteria:** n/a	- to assess the effects of skin antisepsis as part of CVC care for reducing catheter-related BSI
Notes	**Author's Conclusion:** Further RCTs are needed to assess the effectiveness and safety of different skin antisepsis regimens in CVC care; these should measure and report critical clinical outcomes such as sepsis, catheter-related BSI and mortality.		
Outcome measures/results	Catheter-related-bloodstream infections; catheter colonization		- 3 studies compared different antisepsis regimens with no antisepsis- no difference - the most frequent comparison was chlorhexidine solution versus povidone-iodine solution (any base)- very low-quality evidence that chlorhexidine may reduce catheter-related BSI compared with povidone-iodine (RR of 0.64, 95% CI 0.41 to 0.99; ARR 2.30%, 95% CI 0.06 to 3.70%) - very low-quality evidence that skin antisepsis with chlorhexidine may also reduce catheter colonization relative to povidone-iodine

90. Darouiche RO, Wall MJ, Jr., Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. The New England journal of medicine. 2010;362:18-26. [308]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** 4 % **Study limitations:** n/a	**Total no. Patients:** 849 **Inclusion criteria:** Patients 18 years of age or older who were undergoing clean-contaminated surgery (i.e., colorectal, small intestinal, gastroesophageal, biliary, thoracic operations performed under controlled conditions without substantial spillage or unusual contamination) **Exclusion criteria:** history of allergy to chlorhexidine, alcohol, or iodophors; evidence of infection at or adjacent to the operative site; and the perceived inability to follow the patient's course for 30 days after surgery	They randomly assigned adults undergoing clean-contaminated surgery in six hospitals to preoperative skin preparation with either chlorhexidine–alcohol (n=409) scrub or povidone–iodine scrub (n=440) and paint
Notes	**Author's Conclusion:** Preoperative cleansing of the patient's skin with chlorhexidine–alcohol is superior to cleansing with povidone –iodine for preventing surgical-site infection after clean-contaminated surgery.		
Outcome measures/results	- primary outcome: any surgical-site infection within 30 days after surgery - secondary outcome: individual types of surgical-site infections		- the overall rate of surgical-site infection was significantly lower in the chlorhexidine–alcohol group than in the povidone–iodine group (9.5% vs. 16.1%; P= 0.004; relative risk, 0.59; 95% confidence interval, 0.41 to 0.85) - chlorhexidine–alcohol was significantly more protective than povidone–iodine against both superficial incisional infections (4.2% vs. 8.6%, P= 0.008) and deep incisional infections (1% vs. 3%, P=0.05) but not against organ-space infections (4.4% vs. 4.5%) - Similar results were observed in the per-protocol analysis of the 813 patients who remained in the study during the 30-day follow-up period - Adverse events were similar in the two study groups

91. Yasuda H, Sanui M, Abe T, Shime N, Komuro T, Hatakeyama J, et al. Comparison of the efficacy of three topical antiseptic solutions for the prevention of catheter colonization: a multicenter randomized controlled study. Critical care (London, England). 2017;21:320.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Japan **Centers:** n/a **Setting:** 16 intensive care units **Funding Sources:** Maruishi Pharmaceutical and Yoshida Pharmaceutical Company **Dropout rates:** 30% **Study limitations**: primary outcome evaluated is catheter colonization, which is only a surrogate outcome for CRBSI; some of the catheter colonization data was missing after randomization; patient and physician blinding was not possible; randomization was performed at the catheter level and not at the patient level	**Total no. Patients:** 1132 **Inclusion criteria:** central venous catheters; arterial catheter; hemodynamic monitoring and frequent blood sampling **Exclusion criteria:** catheters inserted before ICU admission; catheters inserted for long-term total parenteral nutrition or chemotherapy for seven or more days; catheters changed using a guidewire	- three antiseptic solutions applied during catheter insertion and dressing changes: 0.5 % and 1.0 % alcohol/chlorhexidine gluconate (CHG) and 10 % aqueous povidone-iodine (PVI) - 796 catheters were included in the full analysis set
Notes	**Author's Conclusion:** Both 0.5 % and 1.0 % alcohol CHG are superior to 10 % aqueous PVI for the prevention of intravascular catheter colonization.		
Outcome measures/results	- Primary endpoint: incidence of catheter colonization - Secondary endpoint: incidence of catheter-related bloodstream infections (CRBSI); antiseptic solution-related adverse events		- Catheter-tip colonization incidence was 3.7, 3.9, and 10.5 events per 1000 catheter-days in 0.5 % CHG, 1% CHG, and PVI groups, respectively (p=0.03) - Pairwise comparisons of catheter colonization between groups showed a significantly higher catheter colonization risk in the PVI group (0.5% CHG vs. PVI: hazard ratio, HR 0.33 [95% confidence interval, CI 0.12–0.95], p= 0.04; 1.0% CHG vs. PVI: HR 0.35[95% CI 0.13–0.93], p= 0.04 - sensitivity analyses including all patients by multiple imputations showed consistent quantitative conclusions (0.5% CHG vs. PVI: HR 0.34, p= 0.03; 1.0% CHG vs. PVI: HR 0.35, p= 0.04)

		- no significant differences were observed in the incidence of CRBSI between groups - systemic and local unknown serious adverse events were not observed in any of the three groups

Empfehlung 44

Eine strikt aseptische Technik für die Pflege von ZVK im häuslichen Bereich soll sichergestellt werden.

Empfehlungsgrad A

92. Gavin NC, Button E, Keogh S, McMillan D, Rickard C. Does Parenteral Nutrition Increase the Risk of Catheter-Related Bloodstream Infection? A Systematic Literature Review. JPEN Journal of parenteral and enteral nutrition. 2017;41:918-28. [311]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1+	**Countries:** US, Brazil, France **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 2854 **Inclusion criteria:** Adult or pediatric patients with a CVAD for infusion therapy in any healthcare setting; studies that compared patients with a CVAD who did and did not have PN therapy **Exclusion criteria:** patients with PN infusing through a peripheral venous catheter	- comparative rates of catheter-related bloodstream infection (CRBSI) in patients with central venous access devices (CVADs) who received PN vs those who did not receive PN therapy
Notes	**Author's Conclusion:** The data presented in this systematic review are not sufficient to establish whether patients receiving PN are more at risk of developing CRBSI than those who do not.		
Outcome measures/results	- primary outcome: CRBSI - secondary outcomes: CVAD microbial colonization and identification of clinical isolates		- 11 studies: six studies produced significant results in favor of non-PN, 4 studies showed no evidence of a difference between PN and non-PN, and 1 study produced significant results in favor of PN when analyzed per patient with multiple CVADs - incidence ranged from 0 to 6.6 CRBSIs per 1000 CVAD days in the PN patients and 0.39 to 3.6 CRBSIs per 1000 CVAD days in the non-PN patients - patients receiving PN were statistically less likely to develop colonization compared with those who did not receive PN

		- Fungi and yeasts were reported to colonize the blood of patients receiving PN more frequently than patients receiving non-PN infusions

93. Santarpia L, Buonomo A, Pagano MC, Alfonsi L, Foggia M, Mottola M, et al. Central venous catheter related bloodstream infections in adult patients on home parenteral nutrition: Prevalence, predictive factors, therapeutic outcome. Clinical nutrition (Edinburgh, Scotland). 2016;35:1394-8. [312]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective observational study 2-	**Countries:** Italy **Centers:** Clinical Nutrition Outpatient Unit of Federico II University Hospital in Naples **Setting:** n/a **Funding Sources:** none **Dropout rates:** none **Study limitations:** n/a	**Total no. Patients:** 172 **Inclusion criteria:** n/a **Exclusion criteria:** HPN for less than 2 weeks and patients receiving PN through a peripheral vein	- Patients received HPN
Notes	**Author's Conclusion:** CRBSI and antibiotic resistance of infecting agents remain an important challenge in adult patients on HPN; an active research on strategies to counteract the phenomena is required.		
Outcome measures/results	central venous catheter related bloodstream infection		- 94 CRBSIs were diagnosed on 238 CVC - Coagulase negative (CoNs) Staphylococci were the most frequently infecting agents (52.8% as single agent) with17.1 % Staphylococcus epidermidis infection - Gram-negative bacteria represented 18.6% infections, fungi 7.1%, finally 15% infections were polymicrobial - previous catheterizations and the presence of an enterocutaneous stoma were significantly related with a higher infection risk ($p<0.0001$ in both cases)

94. Edakkanambeth Varayil J, Whitaker JA, Okano A, Carnell JJ, Davidson JB, Enzler MJ, et al. Catheter Salvage After Catheter-Related Bloodstream Infection During Home Parenteral Nutrition. JPEN Journal of parenteral and enteral nutrition. 2017;41:481-8.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective Cohort study 2+	**Countries:** USA **Centers:** n/a **Setting:** n/a	**Total no. Patients:** 1146	- n= 620 were men; n= 420 woman

	Funding Sources: grant UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS) **Dropout rates:** 9 % **Study limitations:** the management of CRBSI by the local providers; the data may not be generalizable to the overall population of the US; limited uniformity	**Inclusion criteria:** patients who were newly started on HPN during the study period **Exclusion criteria:** any patient who had hemodynamic instability, infective endocarditis that was accompanied by CRBSI, or for whom an antibiotic or ethanol lock was used during the course of HPN	- a retrospective search in the HPN program at Mayo Clinic, Rochester, Minnesota for the records of all patients who received HPN from January 1, 1990, to December 31, 2013
Notes	**Author's Conclusion:** Since most episodes of CRBSI are caused by skin commensals, effective treatment without removal of the central venous catheter is possible in most cases.		
Outcome measures/results	Primary outcome: incidence of CRBSI Secondary outcome: rates of catheter salvage		- median total duration on HPN was 124.5 days - Mean (SD) age at HPN initiation was 53.3 (15.3) years - 465 CRBSIs developed in 187 patients (18%) - 70% of catheters were salvaged: 78% of infections with coagulase-negative staphylococci; 87% with methicillin-sensitive Staphylococcus aureus, and 27% with methicillin-resistant S aureus

Empfehlung 45

Die Händedesinfektion sollte durch intensives Waschen der Hände mit Seife und Wasser und anschließend mit alkoholischen Handdesinfektionsmitteln, die reichlich auf die trockenen Hände appliziert werden, vor und zwischen dem Herrichten der Infusion, vor und nach dem Zugang zu einem ZVK oder dem Anlegen eines Verbandes durchgeführt werden.

Empfehlungsgrad B

95. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]
→ see No. 80

96. National Clinical Guideline Centre (UK). Infection: Prevention and Control of Healthcare-Associated Infections in Primary and Community Care: Partial Update of NICE Clinical Guideline 2. National Institute for Health and Clinical Excellence: Guidance. 2012. [316]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline 2+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** An effective handwashing technique involves three stages: preparation, washing and rinsing, and drying. Preparation requires wetting hands under tepid running water before applying liquid soap or an antimicrobial preparation. The handwash solution must come into contact with all of the surfaces of the hand.		
Relevant recommendations/statements	- Hands must be decontaminated in all of the following circumstances: immediately before every episode of direct patient contact or care, including aseptic procedures; immediately after every episode of direct patient contact or care; immediately after any exposure to body fluids; immediately after any other activity or contact with a patient's surroundings that could potentially result in hands becoming contaminated; immediately after removal of gloves - Decontaminate hands preferably with a hand rub, except in the following circumstances, when liquid soap and water must be used: when hands are visibly soiled or potentially contaminated with body fluids or; in clinical situations where there is potential for the spread of alcohol-resistant organisms (such as Clostridium difficile or other organisms that cause diarrheal illness) - An emollient hand cream should be applied regularly to protect skin from the drying effects of regular hand decontamination. If a particular soap, antimicrobial hand wash or alcohol product causes skin irritation an occupational health team should be consulted		

97. Picheansathian W. A systematic review on the effectiveness of alcohol-based solutions for hand hygiene. International journal of nursing practice. 2004;10:3-9.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** this study did not control the confounding factors of	**Total no. Patients:** n/a **Inclusion criteria:** effect of alcohol-based solutions in reducing microorganisms on the hands of health care workers or agar plates; skin problems on hands when using alcohol-based solutions and	- studies published between January 1992 and April 2002 in English and Thai - studies related to the effectiveness of alcohol-based solutions

	compliance with hand hygiene and alcohol dosage	time involved in using alcohol hand rubs **Exclusion criteria**: expert opinion, literature reviews	
Notes	**Author's Conclusion:** The availability of bedside alcohol-based solutions increases compliance with hand hygiene among health care workers.		
Outcome measures/results	effectiveness of alcohol-based solutions for hand hygiene		- alcohol-based hand rubbing removes microorganisms effectively, requires less time and irritates hands less often than does handwashing with soap or other antiseptic agents and water

98. Girou E, Loyeau S, Legrand P, Oppein F, Brun-Buisson C. Efficacy of handrubbing with alcohol based solution versus standard handwashing with antiseptic soap: randomised clinical trial. BMJ (Clinical research ed). 2002;325:362. [318]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** France **Centers:** n/a **Setting:** three intensive care units in a French university hospital **Funding Sources:** Bode SA, Hamburg, Germany **Dropout rates:** none **Study limitations:** no use of the glove juice technique, which may be more effective in recovering the whole bacterial burden on hands	**Total no. Patients:** 23 **Inclusion criteria:** permanent and temporary nurses and nursing assistants **Exclusion criteria:** n/a	- 23 healthcare workers - n= 12: handrubbing with alcohol-based solution - n= 11: handwashing with antiseptic soap - Imprints taken of fingertips and palm of dominant hand before and after hand hygiene procedure
Notes	**Author's Conclusion:** During routine patient care handrubbing with an alcohol-based solution is significantly more efficient in reducing hand contamination than handwashing with antiseptic soap.		
Outcome measures/results	main outcome: bacterial reduction of hand contamination		- with handrubbing the median percentage reduction in bacterial contamination was significantly higher than with handwashing (83 % v 58 %, P= 0.012), with a median difference in the percentage reduction of 26 % (95 % confidence interval 8 % to 44 %) - median duration of hand hygiene was 30 seconds in each group

99. Kac G, Podglajen I, Gueneret M, Vaupre S, Bissery A, Meyer G. Microbiological evaluation of two hand hygiene procedures achieved by healthcare workers during routine patient care: a randomized study. The Journal of hospital infection. 2005;60:32-9. [319]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** France **Centers:** n/a **Setting:** Hôpital Europeen Georges Pompidou **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** observational bias	**Total no. Patients:** 50 **Inclusion criteria:** health care workers **Exclusion criteria:** n/a	- group 1: handwashing with unmedicated soap - group 2: hand rubbing with an alcoholic solution - imprints of palms and fingertips were taken separately before and after each hand hygiene procedure
Notes	**Author's Conclusion:** Handrubbing is more efficacious than handwashing for the decontamination of healthcare workers' hands. Gloving may reduce microbiological hand contamination by transient pathogens.		
Outcome measures/results	microbiological efficacy		- hand rubbing produced a significantly greater reduction in microbiological load than handwashing (P< 0.0001 for palms and P=0.0003 for fingertips) - working in a medical ward rather than in an intensive care unit was significantly associated with increased hand contamination (P=0.03 for palms and P=0.02 for fingertips) - the only factor associated with hand contamination by transient pathogens was the absence of gloving during the healthcare procedure (odds ratio 4.8; 95% confidence interval 1.2–19; P=0.03)

Empfehlung 46

Für den intravenösen Zugang sollte ein nadelfreier Konnektor verwendet werden.

Empfehlungsgrad B

100. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]
→ see No. 80

101. Casey AL, Burnell S, Whinn H, Worthington T, Faroqui MH, Elliott TS. A prospective clinical trial to evaluate the microbial barrier of a needleless connector. The Journal of hospital infection. 2007;65:212-8.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** UK **Centers:** the University Hospital Birmingham **Setting:** Wellcome Building Critical Care Unit **Funding Sources:** n/a **Dropout rates:** none **Study limitations:** n/a	**Total no. Patients:** 60 **Inclusion criteria**: cardiothoracic surgery; central venous catheter as part of his or her peri- and postoperative management **Exclusion criteria:** n/a	- n= 25 in the control group: three-way stopcocks with caps - n= 35 in the test group: Clearlink Y-type extension sets - prior to, and following each manipulation of the three-way stopcock luers or Clearlink devices, a 70% (v/v) isopropyl alcohol swab was used for disinfection of the connections
Notes	**Author's Conclusion:** The use of such needle-free devices may therefore reduce the intraluminal risk of catheter-related bloodstream infection and thereby supplement current preventive guidelines.		
Outcome measures/results	Rate of catheter-related blood stream infection		- On average, the Clearlink device was activated significantly more times per patient than opening of the three-way stopcock luers (3.0 vs 2.3, ranges: 1-23 vs 0-16) (P= 0.004) - Forty out of 193 (21%) Clearlink devices were contaminated with microorganisms on the external silicone compression seal - significant reduction in the number of contaminated silicone compression seals after disinfection compared with non-disinfected devices (3.8 vs 21%, P=0.0004) - nine out of 25 (36%) patients had one or more luers contaminated with microorganisms in the control group compared to one out of 25 (4%) patients in the Clearlink group (P=0.01) - Of the intravenous connections activated once, there were significantly more luers contaminated in the three-way stopcock group than the Clearlink group (P=0.03)

102. Yebenes JC, Vidaur L, Serra-Prat M, Sirvent JM, Batlle J, Motje M, et al. Prevention of catheter-related bloodstream infection in critically ill patients using a disinfectable, needle-free connector: a randomized controlled trial. American journal of infection control. 2004;32:291-5. [321]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT	**Countries:** n/a	**Total no. Patients:** 243	

1+	**Centers:** n/a **Setting:** polyvalent intensive care unit **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations**: low sensitivity in detecting endoluminal colonization of the method of diagnosis; possibility of false-negative cases	**Inclusion criteria:** the need for a subclavian or jugular non-tunneled, noncoated, polyurethane central venous multilumen catheter **Exclusion criteria:** CVCs inserted outside the ICU, removed before 72 hours of insertion, or guide wire inserted	- Study group (N=139 catheters): catheters with disinfectable, needle-free connectors - Control group (N=139 catheters): catheters with 3-way stopcocks - n= 243 patients and 278 catheters
Notes	**Author's Conclusion:** To add a disinfectable, needle-free connector to the CDC recommendations reduces the incidence of catheter-related bloodstream infection in critically ill patients with central venous catheters.		
Outcome measures/results	- incidence rate of catheter-related bloodstream infection		- the catheters' mean insertion duration was 9.9 days - both groups were comparable regarding patient and catheter characteristics - incidence rate of catheter-related bloodstream infection was 0.7 per 1000 days of catheter use in the study group, compared with 5.0 per 1000 days of catheter use in the control group (P= .03)

103. Casey AL, Worthington T, Lambert PA, Quinn D, Faroqui MH, Elliott TS. A randomized, prospective clinical trial to assess the potential infection risk associated with the PosiFlow needleless connector. The Journal of hospital infection. 2003;54:288-93. [322]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** UK **Centers:** University Hospital Birmingham NHS Trust **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 77 **Inclusion criteria:** patients requiring a CVC as part of their clinical management **Exclusion criteria:** n/a	- the microbial contamination rate of luers of central venous catheters (CVCs) with either PosiFlow needleless connectors or standard caps attached was investigated - the efficacy of 70% (v/v) isopropyl alcohol, 0.5% (w/v) chlorhexidine in gluconate 70%(v/v) isopropyl alcohol and 10% (w/v) aqueous povidone–iodine to disinfect the intravenous connections was also assessed - after 72 h in situ the microbial contamination rate of 580 luers, 306 with standard caps and 274 with needleless connectors attached, was determined

			- the microbial contamination rate of the external compression seals of 274 needleless connectors was also assessed to compare the efficacy of the three disinfectants
Notes	**Author's Conclusion:** The use of needleless connectors may reduce the microbial contamination rate of CVC luers compared with the standard cap.		
Outcome measures/results	microbial contamination rate		- the internal surfaces of 55 out of 306 (18%) luers with standard caps were contaminated with microorganisms, whilst only 18 out of 274 (6.6%) luers with needleless connectors were contaminated (P<0,0001) - of those needleless connectors disinfected with isopropyl alcohol, 69.2% were externally contaminated with microorganisms compared with 30.8% disinfected with chlorhexidine/alcohol (P<0,0001) and 41.6% with povidone – iodine (P<0,0001)

104. Btaiche IF, Kovacevich DS, Khalidi N, Papke LF. The effects of needleless connectors on catheter-related bloodstream infections. American journal of infection control. 2011;39:277-83. [323]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review 2-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	use of needleless connectors, including the standard split septum and the luer-activated mechanical valve connectors
Notes	**Author's Conclusion:** Needleless connectors reduce needlestick injuries and facilitate nursing care and catheter management.		
Outcome measures/results	catheter-related bloodstream infections		- when a different PPV (Posiflow) (n5274) was compared with a standard cap (n5306) in critically ill patients, there was a lower percentage of contaminated hubs with the PPV as compared with the standard cap (6.6% vs 18%, respectively; P,.0001) - four clinical trials reported no significant difference on CRBSI rates between the mechanical valves and standard connectors - CRBSI rates significantly increased following the introduction of a negative displacement mechanical valve (CLAVE) and a PPV (CLC2000), as compared with the time when a split septum connector (Interlink)was used (5.8 vs 2.6 CRBSIs per 1,000 catheter-days, respectively; P= .031)

105. Williams A. Catheter Occlusion in Home Infusion: The Influence of Needleless Connector Design on Central Catheter Occlusion. Journal of infusion nursing : the official publication of the Infusion Nurses Society. 2018;41:52-7. [324]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective observational study 2+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** lack of standardized methods for defining occlusion; limited geographic distribution of the patient population; small sample size; study patient population did not include patients in hospitals and intensive care units	**Total no. Patients:** 720 **Inclusion criteria:** all adult and pediatric patients with 1 CVC **Exclusion criteria:** n/a	- this retrospective observational study compared occlusion rates associated with a split-septum neutral-displacement needleless connector versus those of a solid-surface neutral-reflux needleless connector in patients undergoing home infusion therapy
Notes	**Author's Conclusion:** Although challenging, it is important to select the best option among the available connectors, and the decision should be based on careful risk-benefit analysis.		
Outcome measures/results	Rate of catheter occlusion		- the neutral-reflux needleless connector was associated with a significant reduction in occlusion rate and thrombolytic use versus the neutral-displacement needleless connector - the rate of catheter occlusion was significantly greater with split-septum neutral-displacement needleless connectors than with solid-surface neutral-reflux needleless connectors (P= .001; 95% confidence interval [CI], 0.35-1.25) - after switching from a split-septum neutral-displacement needleless connector to a solid-surface neutral-reflux needleless connector, there was a 56.4 % reduction in the total number of doses of alteplase per 100 central-line days and the associated cost

Empfehlung 47

Nadellose Systeme mit einem geteilten Septumventil können mechanischen Ventilen aufgrund des erhöhten Infektionsrisikos vorgezogen werden. Empfehlungsgrad 0

106.	**O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]**
→ see No. 80	

107.	**Btaiche IF, Kovacevich DS, Khalidi N, Papke LF. The effects of needleless connectors on catheter-related bloodstream infections. American journal of infection control. 2011;39:277-83. [323]**
→ see No. 104	

108.	**Williams A. Catheter Occlusion in Home Infusion: The Influence of Needleless Connector Design on Central Catheter Occlusion. Journal of infusion nursing : the official publication of the Infusion Nurses Society. 2018;41:52-7. [324]**
→ see No. 105	

Empfehlung 48

Nabenkonnektoren (nadelfreie Konnektoren) sollten vor jeder Nutzung mit einem geeigneten Mittel (alkoholisches Chlorhexidinpräparat oder Povidon-Jod oder Alkohol 70 %) und ausreichend langer mechanischer Reibung gereinigt und desinfiziert werden, dürfen nur mit sterilen Gegenständen in Kontakt kommen und sollten nicht öfter als alle 3 Tage gewechselt werden.

Empfehlungsgrad B

109.	**O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]**
→ see No. 80	

110.	**Marschall J, Mermel LA, Fakih M et al. Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals: 2014 Update. Infect Control Hosp Epidemiol 2014; 35: 753-771. doi:10.1086/676533 [325]**
Guideline **Relevant recommendations/ statements**	- Require education of healthcare personnel involved in insertion, care, and maintenance of CVCs about CLABSI prevention (quality of evidence: II). Reeducate when an institution changes component of the infusion system that requires a change in practice (e.g., when an institution's change of the needleless connector requires a change in nursing practice). - Disinfect catheter hubs, needleless connectors, and injection ports before accessing the catheter (quality of evidence: II). Before accessing catheter hubs, needleless connectors, or injection ports, vigorously apply mechanical friction with an alcoholic chlorhexidine preparation, 70% alcohol, or povidone-iodine. Alcoholic chlorhexidine may have additional residual activity compared with alcohol for this purpose. Apply mechanical friction for no less than 5 seconds to reduce contamination. It is unclear whether this duration of disinfection can be generalized to needleless connectors not tested in these studies. - Use an antiseptic-containing hub/connector cap/port protector to cover connectors (quality of evidence: I)

111.	**Moureau NL, Flynn J. Disinfection of Needleless Connector Hubs: Clinical Evidence Systematic Review. Nurs Res Pract 2015; 2015: 796762. doi:10.1155/2015/796762 [326]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 1- AMSTAR 2 6/13	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: Critically low Risk of bias of single studies: n/a Inconsistency: n/a Indirectness: low Impreciseness: n/a Publication bias: n/a The evidence base for the effectiveness of various disinfection strategies is low level, resulting in	**Total no. Studies:** 140 publications + 34 abstracts/posters **Inclusion criteria:** any NC disinfection publications and abstracts that fit subcategories for disinfection, hub contamination/infection prevention, education/ compliance, surveys, and guidelines/ recommendations for disinfection **Exclusion criteria:** non research papers, studies of adult, pediatric, or neonatal increasingly important role patients not inclusive of intravascular device disinfection practices, primary populations outside acute care, publications not translated into English, studies prior to 1984	Evaluation of the supporting evidence for disinfection practices of NC, catheter hub, stopcock, and side ports that reduce the transfer of microorganisms through intravascular device access.

	recommendations compiled from the available publications, lack of high quality RCTs, risk of unintentional bias due to the lack of randomization and control groups/ strategies, in addition to small sample sizes and retrospective study designs		
Notes	**Author's Conclusion:** Aseptic technique is the foundation for safe delivery of intravenous medications and solutions. More and more studies reveal lack of compliance with disinfection of access ports prior to and after access, despite educational initiatives, and better disinfection agents. Rather than creating devices such as the ultraviolet C port to eradicate contamination within the hub, the goal should be to eliminate surface pathogens before entering the NC or catheter. Passive disinfection caps reduce guess work, provide clinicians with a point of use solution, and reduce contamination. It is critical for healthcare facilities and clinicians to take responsibility for compliance with aseptic technique for NC disinfection, to monitor compliance regularly, to involve frontline staff in solutions, and to facilitate education that promotes under- standing of the consequences of failure to comply with the standard of care for access site disinfection.		
Outcome measures/results	Risks for contamination, compliance with disinfection, optimal technique, disinfection time		- The greatest risk for contamination of the catheter after insertion is the NC with 33–45% contaminated, and compliance with disinfection as low as 10%. - The optimal technique or disinfection time has not been identified, although scrubbing with 70% alcohol for 5–60 seconds is recommended. - Studies have reported statistically significant results in infection reduction when passive alcohol disinfection caps are used (48–86% reduction).

Empfehlung 49

Zur passiven Desinfektion von Hub-Konnektoren (nadelfreie Konnektoren) können antiseptische Barrierekappen verwendet werden.

Empfehlungsgrad 0

112. Menyhay SZ, Maki DG. Disinfection of needleless catheter connectors and access ports with alcohol may not prevent microbial entry: the promise of a novel antiseptic-barrier cap. Infection control and hospital epidemiology. 2006;27:23-7. [327]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**

Simulation study no Level of evidence possible according to SIGN	**Countries:** US **Centers:** n/a **Setting:** n/a **Funding Sources:** Oscar Rennebohm Foundation of Madison, Wisconsin **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- 105 commercial, needleless luer-activated valved connectors, each accessible by a blunt male-connector luer-lock attachment were tested - the membranous septum of each test device was first heavily contaminated with ~10^5 colony-forming units of Enterococcus faecalis and then was allowed to dry for 24 hours - 15 of the contaminated devices were not disinfected (positive controls), 30 were conventionally disinfected with a commercial 70% alcohol pledget, and 60 had the antiseptic cap threaded onto the connector and then removed after 10 minutes - the test connectors were then accessed with a sterile syringe containing nutrient broth media, which was injected, captured on the downstream side of the intraluminal fluid pathway, and cultured quantitatively
Notes	**Author's Conclusion:** The antiseptic-barrier cap provided a high level of protection, even in the presence of very heavy contamination.		
Outcome measures/results	efficacy of conventional alcohol disinfection before access		- all 15 control connectors (100%) showed massive transmission of microorganisms across the membranous septum (4,500-10,000 colony-forming units) - of the 30 connectors accessed after conventional disinfection with 70% alcohol, 20 (67%) showed transmission of microorganisms (442-25,000 colony-forming units) - In contrast, of the 60 connectors cultured after application of the novel antiseptic cap, only 1 (1.6%) showed any transmission of microorganisms (P< .001)

113.	**Moureau NL, Flynn J. Disinfection of Needleless Connector Hubs: Clinical Evidence Systematic Review. Nurs Res Pract 2015; 2015: 796762. doi:10.1155/2015/796762 [326]**
→ see No. 111	

114.	**Merrill KC, Sumner S, Linford L et al. Impact of universal disinfectant cap implementation on central line–associated bloodstream infections. Am J Infect Control 2014; 42: 1274-1277. doi:10.1016/j.ajic.2014.09.008 [328]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
quasi-experimental short interrupted time	**Countries:** United States **Centers:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** all patients	In addition to an existing standard central line bundle, a new intervention consisting of a luer-lock disinfectant cap with 70% alcohol was implemented in all intravenous

series intervention study No suitable checklist available	**Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Ongoing education was implemented simultaneously by the hospital, which might have affected the CLABSI rates; use of the disinfectant cap may have resulted in an increased vigilance to compliance to the central line bundle, which was not measured as part of the study, cost estimates were based on projections reported in the literature, although costs were about 50% lower than other reports, they might not reflect true costs	(newborn to adults) with peripheral and central lines residing on 13 inpatient units at 1 hospital beginning in January 2012. **Exclusion criteria:** patients in the emergency department, ambulatory care, surgical services, labor and delivery, and well-baby nursery and patients who were postpartum.	(IV) needleless connectors on patients with peripheral and central lines. Compliance to the disinfectant cap was monitored weekly.
Notes	**Author's Conclusion:** Central line-associated bloodstream infections (CLABSI) is a serious, preventable, health care-acquired infection. This study found a relationship between implementation of a disinfectant cap and reduced rates of CLABSI, cost, length of stay, and mortality. As this increasing body of knowledge becomes available, infection preventionists might need to consider that some time-honored traditions (e.g., scrub the hub) should now be replaced with new product technology. Further, this study found success in implementation of a quality improvement feedback loop and found that compliance rates resulted in prevention of CLABSI. This improvement model might prove successful in other infection prevention campaigns.		
Outcome measures/results	rate of central line-associated bloodstream infections (CLABSI), incidence ratios, compliance, savings		- the rate of central line-associated bloodstream infections (CLABSI) decreased following implementation of the disinfectant cap. The incidence rate ratios (.577, P = .004) for implementing the disinfectant caps was statistically significant, indicating that the rate of patient infections decreased by >40%. - Increased compliance rates were associated with lower infection rates. - Disinfectant cap use was associated with an estimated savings of almost $300,000 per year in the hospital studied.

115.	O'Connell S, Dale M, Morgan H et al. Curos™ Disinfection Caps for the Prevention of Infection When Using Needleless Connectors: A NICE Medical Technologies Guidance. Applied Health Economics and Health Policy 2020; 19: 145-153. doi:10.1007/s40258-020-00602-8 [329]
Guideline **Relevant recommendations/ statements**	- CurosTM disinfection caps contain a sponge that is impregnated with 70% isopropyl alcohol, and it is claimed that use of the cap will disinfect the needleless connector after 1 min. The cap can also be used to protect against contamination between intravenous line accesses for up to 7 days if not removed. Once removed, the cap must be replaced with a new cap to maintain sterile conditions. - The main change made by Cedar includes a change to nurse time in the manual disinfection arm. The company submission assumed that manual disinfection would take 45 s of nurse time per disinfection compared with 15 s using Curos. The rationale for this was that nurses would need to wait for a 30-s drying time in the manual disinfection arm, whereas Curos does not have this requirement. - The model submitted by the company found Curos to be cost saving in both the hospital and ICU settings when compared with manual disinfection. - Infection prevention is a multifaceted process, of which dis- infection is only a part. As a result, there is a 'bundle' of processes and interventions that make up an infection management protocol for staff. This bundle approach can include numerous elements, such as hand hygiene, caps and gowns, disinfection of access ports with wipes or caps, and regular education and training for staff. - The committee assessed a number of possible scenarios where the inclusion of Curos disinfection caps as part of the disinfection bundle may lead to cost savings through a reduction in infection rates. The final guidance concluded that while it is possible that Curos could lead to cost savings through a reduction in bloodstream infections, further research is required to address uncertainties about the clinical benefits.

Empfehlung 50

Zur Vermeidung von Port-Komplikationen sollte der Portnadelwechsel bei täglicher PE alle 3–7 Tage erfolgen. Bei intermittierender Ernährung über ein Portsystem sollte die Kanüle für die infusionsfreie Zeit entfernt werden.

Empfehlungsgrad B

116.	Sitges-Serra A, Linares J, Perez JL, Jaurrieta E, Lorente L. A randomized trial on the effect of tubing changes on hub contamination and catheter sepsis during parenteral nutrition. JPEN Journal of parenteral and enteral nutrition. 1985;9:322-5. [331]		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Spain **Centers:** Hospital de Bellvitge "Princeps d'Espanya" **Setting**: Department of Surgery and Services of Microbiology and Pharmacy **Funding Sources:** n/a	**Total no. Patients:** 52 **Inclusion criteria:** adult surgical patients; TPN through a plastic (Cavafix) subclavian catheter **Exclusion criteria:** n/a **Exclusion criteria:** n/a	- Group A (n=20): frequency of tubing replacement: every 2 days - Group B (n=32): frequency of tubing replacement: every 4 days - TPN was administered over 24 hours using lipid containing mixtures in 3-liter plastic bags - group of 43 patients was used as an historic control series

	Dropout rates: none **Study limitations:** n/a		
Notes	**Author's Conclusion:** Delaying tubing changes does not increase catheter sepsis or hub contamination rates and, together with adequate hub protection, has proved to be a valuable factor in controlling an outbreak of catheter sepsis due to the coagulase negative staphylococci.		
Outcome measures/results	catheter-related sepsis; hub colonization		- Sterile, colonized, or infected hubs were equally distributed in both groups (A: 80,15, and 5% us B: 84, 6, and 10%) - significant ($p < 0.001$) differences between the trial and the historic series in respect to rates of hub colonization infection (19 vs 50%) and catheter sepsis (5.7 vs 40%)

117. Maki DG. Prospective Study of Replacing Administration Sets for Intravenous Therapy at 48- vs 72-Hour Intervals. JAMA 1987; 258: 1777. doi:10.1001/jama.1987.03400130091039 [332]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** United States **Centers:** University of Wisconsin Hospital and Clinics **Setting:** n/a **Funding Sources:** funds allocated for infection control research by the administration of University of Wisconsin Hospital and Clinics and by a gift for research support from Phyllis Lee of Madison, Wis **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 479 **Inclusion criteria:** Patients without granulocytopenia (<1000/(μL) who were scheduled to receive IV therapy and who were hospitalized on one general surgery nursing unit; on the unit for otolaryngology, plastic surgery, and vascular surgery patients; on a medical oncology or a surgical intensive care unit; and on the hospital's Center for Trauma and Life Support **Exclusion criteria:** n/a	Study of the safety of replacing intravenous delivery systems, including those used in total parenteral nutrition, at 72- compared with 48-hour intervals in 487 patients.
Notes	**Author's Conclusion:** These data indicate that extrinsic contamination of intravenous fluid is a rare cause of endemic nosocomial septicemia, and for most infusions it is unnecessary to routinely replace delivery systems more frequently than every 72 hours.		
Outcome measures/results	prevalence of contamination of intravenous fluid, type of contamination, extrinsic contamination of intravenous fluid		- Although the prevalence of contamination of intravenous fluid was higher in administration sets replaced at 72-hour intervals (10/664,1.5%) than in sets

		replaced every 48 hours (6/710,0.8%), the difference is not statistically significant. - Contamination in both groups was almost exclusively with small numbers of coagulase-negative staphylococci (range, 1 to 27 colony-forming units/mL) - no contaminated infusion was associated with clinical signs of sepsis or concordant bacteremia. - Contaminants were recovered less frequently from peripheral venous infusions (0.6%) than from infusions used for central venous access or hemodynamic monitoring (1.5%) or total parenteral nutrition (3.6%); - infusions in an intensive care unit were more frequently contaminated (2.5%) than infusions on medical and surgical wards (0.9%). - These data indicate that extrinsic contamination of intravenous fluid is a rare cause of endemic nosocomial septicemia, and for most infusions it is unnecessary to routinely replace delivery systems more frequently than every 72 hours.

118. Matlow AG, Kitai I, Kirpalani H et al. A Randomized Trial of 72- Versus 24-Hour Intravenous Tubing Set Changes in Newborns Receiving Lipid Therapy. Infect Control Hosp Epidemiol 1999; 20: 487-493. doi:10.1086/501657 [333]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** Canada **Centers:** a 35-bed, teaching, referral, neonatal intensive-care unit (NICU) **Setting:** n/a **Funding Sources:** Ministry of Health of Ontario. **Dropout rates:** n/a **Study limitations:** generalization to other populations may not be warranted	**Total no. Patients:** 1189 **Inclusion criteria:** all neonates admitted to the NICU between July 11, 1991, and October 31, 1994, for whom intravenous lipid was ordered **Exclusion criteria:** for sampling administration sets were applied: use for administration of blood or blood products, and disconnection of the set from the catheter hub for more than 4 hours, or without sterile gauze coverage	Infants requiring intravenous lipid therapy were randomly assigned to have intravenous sets changed on a 72- or a 24-hour schedule, in a 3:1 ratio, in order to compare the infusate contamination rates in an equivalent number of tubing sets. Patients were randomized in pharmacy, on receipt of the order for intravenous lipid therapy, to either 72- or 24- hour administration set changes and followed until 1 week after discontinuation of lipids or discharge from the NICU. Microbial contamination of the infusate was assessed in both groups at the time of administration set changes. Contamination rates were analyzed separately for the lipid and amino acid-glucose tubing sets.
Notes	**Author's Conclusion:** Microbial contamination of infusion sets is significantly more frequent with 72- than with 24-hour set changes in neonates receiving lipid solutions. This may be associated with an increased mortality rate.		

Outcome measures/results	contamination of lipid infusate, mortality rate, the total number of blood cultures ordered for "septic workup," and the number of positive blood cultures	- During the study period, 1,101 and 1,112 sets were sampled in the 72- and 24-hour groups, respectively. - Microbial contamination rates were higher in the 72-hour group than the 24-hour group for lipid infusions (39/1,101 [3.54%] vs 15/1,112 [1.35%]; P=.001) and for amino acid infusions (12/1,093 [1.10%] vs 4/1,103 [0.36%]; P=.076). - Logistic regression analysis controlling for birth weight, gestational age, and type of venous access showed that only the tubing change interval was significantly associated with lipid set contaminations (odds ratio, 2.69; P=.0013). - The rate of blood cultures ordered was higher in the 72- versus the 24-hour group (6.11 vs 4.99 per 100 patient days of total parenteral nutrition; P=.017), and a higher proportion of infants randomized to the 72-hour group died (8% vs 4%; P=.05), although the excess deaths could not clearly be attributed to bacteremia.

119. Raad I, Hanna HA, Awad A, Alrahwan A, Bivins C, Khan A, et al. Optimal frequency of changing intravenous administration sets: is it safe to prolong use beyond 72 hours? Infection control and hospital epidemiology. 2001;22:136-9. [334]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** n/a **Centers:** n/a **Setting:** tertiary university cancer center **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 512 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- randomized study of infusion-related contamination associated with changing IV tubing sets within 3 days versus within 4 to 7 days of placement - group 1 (n=280): IV tubing sets replaced within 3 days - group 2 (n=232): IV tubing sets replaced within 4 to 7 days of placement
Notes	**Author's Conclusion:** In patients at low risk for infection from infusion- or catheter-related infection who are not receiving TPN, blood transfusions, or interleukin-2, delaying the replacement of IV tubing up to 7 days may be safe, as well as cost-effective.		
Outcome measures/results	infusion- or catheter-related contamination or colonization of IV tubing		- higher level of tubing colonization in the 4- to 7-day group versus the 3-day group (median, 145 vs 50 colony-forming units; P=.02) - three episodes of possible infusion-related bloodstream infections, all of which occurred in the 4- to 7-day group (P=.09) - when the 84 patients who received TPN, blood transfusions, or interleukin-2 through the IV tubing were excluded, the two groups had a comparable rate of colonization (0.4% vs 0.5%), with no catheter- or infusion-related BSIs in either group

Empfehlung 51

Natriumchlorid 0,9 % soll in pulsierender Applikation zum Spülen (A) und sollte als Verriegelungslösung (B) verwendet werden.

Empfehlungsgrad A (Spülung) und B (Verriegelung)

120. Goossens GA. Jerome M. Janssens C. Peetermans WE. Fieuws S. Moons P. et al. Comparing normal saline versus diluted heparin to lock non-valved totally implantable venous access devices in cancer patients: a randomized. non-inferiority. open trial. Ann Oncol 2013; 24:1892e9. [341]										
Study design	**Intervention**				**Patients**		**Results**			
	Drug/tool	**Amount / day**	**Duration**	**Diagnostic tool**	**n. (studies n.)**	**Characteristics**	**CRBSI rate / 1000 days**		**CRBSI RR (95% CI)**	**CVC replacement RR (95% CI)**
RCT Ib	Saline 0.9% lock vs HL 100 U/mL	NR	180 days postop		802	Cancer patients with new totally implantable CVC	Saline 0.03 vs HL 0.10 (p = 0.18)	Central venous thrombosis: Saline 2.8% vs HL 3.3%		

121.	**Pittiruti M, Bertoglio S, Scoppettuolo G et al. Evidence-based criteria for the choice and the clinical use of the most appropriate lock solutions for central venous catheters (excluding dialysis catheters): a GAVeCeLT consensus. The journal of vascular access 2016; 17: 453-464. doi:10.5301/jva.5000576 [337]**
Expert consensus 4 **Relevant recommendations/ statements**	- A pulsatile positive “push and pause” (“start and stop”) technique is the most appropriate methodology of flushing. - Saline lock is as appropriate as anticoagulant lock in prevention of occlusion of non-dialysis central venous access.

Empfehlung 52

Heparin sollte als Verriegelungslösung nicht verwendet werden.

Empfehlungsgrad B

122. Fornaro C, Piubeni M, Tovazzi V et al. Eight-week interval in flushing and locking port-a-cath in cancer patients: A single-institution experience and systematic review. European Journal of Cancer Care 2018. doi:10.1111/ecc.12978: e12978. doi:10.1111/ecc.12978 [338]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1- retrospective cohort study 2- AMSTAR 2 1/13 NOS 6/9	**Countries:** Italy **Centers:** Medical Oncology Unit of Spedali Civili of Brescia **Setting:** n/a **Funding Sources:** donations of “gli Amici di Carlo” in memory of Carlo Ridon, “gli amici di Andrea” in memory of Andrea Gadeschi and “gli amici di Marco Treccani” in memory of Marco Treccani; Fondazione FIRM Onlus, Cremona, Italy **Dropout rates:** n/a **Study limitations:** **A) Systematic Review** Overall confidence in the results of the review: Critically low Risk of bias of single studies: n/a Inconsistency: n/a Indirectness: moderate Impreciseness: n/a Publication bias: n/a **B) Retrospective cohort study** Risk of bias: moderate Inconsistency: n/a Indirectness: moderate Impreciseness: moderate	**Total no. Studies:** 6 **Total no. Patients:** 390 **Inclusion criteria:** patients with a cancer diagnosis who underwent at least two consecutive flushing/locking procedures **Exclusion criteria:** n/a	This study retrospectively compares the frequency of complications occurred using standard versus delayed flushing schedules. We performed a systematic review of the published studies about PAC complications associated with longer flushing intervals. From 2005 to October 2009, the standard procedure of PAC flushing and locking every 4 weeks was employed, while from November 2009 to January 2014, the periodic flushing was performed every 8 weeks. Flushing and locking were performed using 10 cc of normal saline solution followed by 5 cc of heparin solution (4 ml heparin/100 ml of normal saline solution). Patients enrolled were followed up to December 2017. In this study, we retrospectively compared the frequency of complications occurred using the standard timing (every 4 weeks) versus the delayed schedule (every 8 weeks). We also performed a systematic review of published studies reporting the frequencies of PAC complications adopting a longer flushing interval than the standard 4 weeks.

	Publication bias: n/a		
Notes	**Author's Conclusion:** In conclusion, this study shows that PAC flushing and locking every 8 weeks is feasible and safe, with benefits for both patients and nursing staff. A prospective phase III study is warranted to provide a formal demonstration of efficacy.		
Outcome measures/results	number of occlusions, infections and mechanical dysfunctions, complications		- One hundred and six patients had their PAC flushed/locked every month, 347 patients performed the flushing/locking procedures every eight weeks, 63 patients switched from the four to the eight-week schedule. - No difference was seen in the number of occlusions, infections and mechanical dysfunctions between the two patient groups. - A total of 12 patients (11%) and 31 patients (8.9%) had complications in 4- and 8-week flushing group respectively (p = 0.54). - Mechanical complications , occurred in 18 patients (4.6%), 6 patients (5.7%) in the 4-week group and 12 patients (3.5%) in the 8-week group respectively (p = 0.31) - Infections, mainly caused by Staphylococcus Epidermidis and Saprophyticus, had a whole prevalence of 3.9% (10 patients). It was observed in 2 patients (1.9%) in the 4-week flushing group and 8 patients (2.3%) in the 8-week flushing group respectively (p = 0.80). - Occlusions were found in 15 patients (3.8%): 4 patients in the first group (3.8%) and 11 patients (3.2%) in the second one (p = 0.76). - The systematic literature review confirmed, in a total of 1,347 patients, the absence of an increased proportion of complications with delayed schedules. - PAC flushing and locking every eight weeks are feasible and safe.

123. Diaz JA, Rai SN, Wu X et al. Phase II Trial on Extending the Maintenance Flushing Interval of Implanted Ports. J Oncol Pract 2017; 13: e22-e28. doi:10.1200/jop.2016.010843 [339]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Prospective cohort Study 2- JBI 6/8	**Countries:** USA **Centers:** University of Louisville James Graham Brown Cancer Center **Setting:** Cancer center **Funding Sources:** Yes, source not mentioned	**Total no. Patients:** 87 **Inclusion criteria:** Patients age 18 years or older who decided to keep their port in place upon completion of systemic therapy were eligible for enrollment if their physician had no further plans for treating their	The port was flushed the day of enrollment regardless of the prior flush schedule. Thereafter, patients were scheduled for four additional port flushes in 3-month intervals. Each port flush was performed by following standard sterile precautions using 10 mL of normal saline followed by 5 mL of heparin flush (100 units/mL). If there was no blood return, tissue plasminogen activator (t-PA; 2 mg/2 mL) was used in an attempt to restore function. This procedure could be repeated three times if necessary at 20- to 30-minute intervals.

	Dropout rates: 44% **Study limitations:** Risk of bias: moderate Inconsistency: n/a Indirectness: high Impreciseness: high Publication bias: n/a	malignancy in the foreseeable future **Exclusion criteria:** We excluded patients who had their ports removed immediately after completion of therapy and patients with disease recurrence or history of port failure or port malfunction	
Notes	**Author's Conclusion:** We conclude that extending the maintenance flushes of ports in adult oncologic patients to once every 3 months is safe, effective, and likely to increase patient adherence and satisfaction while decreasing costs to the patient and to the health care system.		
Outcome measures/results	port related complications on a scale of 1 (mild difficulty drawing blood) to 5 (port failure)		The mean follow-up time was 283 days (median, 308 days), accounting for a total of 24,202 catheter-days. A total of 10 PRCs occurred in 10 patients (11.49%; 95% CI, 4.85% to 18.14%; 0.414/1,000 catheter-days), all of them related to port occlusions and all of them in patients younger than 60 years of age. No infections, symptomatic thrombosis, or port failures occurred during the study. The mean time to PRC was 184 days, with five of the 10 patients developing the PRC on the first 3-month-interval flush.

124. López-Briz E, Ruiz Garcia V, Cabello JB et al. Heparin versus 0.9% sodium chloride locking for prevention of occlusion in central venous catheters in adults. The Cochrane database of systematic reviews 2018; 7: CD008462-CD008462. doi:10.1002/14651858.CD008462.pub3 [340]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 1++ AMSTAR 2 15/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** NIHR, via Cochrane Incentive Award funding (17/62/08) to Cochrane Vascular **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: High	**Total no. Studies:** 11 **Inclusion criteria:** randomized controlled trials in adults ≥ 18 years of age with a CVC that compared intermittent locking with heparin at any concentration versus NS **Exclusion criteria:** letters, editorials, commentaries, reviews, and lectures that did not contain original research data	To assess the effectiveness and safety of intermittent locking of CVCs with heparin versus normal saline (NS) in adults to prevent occlusion.

	Risk of bias of single studies: high Inconsistency: low Indirectness: low Impreciseness: high Publication bias: moderate		
Notes	**Author's Conclusion:** Given the very low quality of the evidence, we are uncertain whether intermittent locking with heparin results in fewer occlusions than intermittent locking with NS. Low-quality evidence suggests that heparin may have little or no effect on catheter patency. Although we found no evidence of differences in safety (sepsis, mortality, or hemorrhage), the combined trials are not powered to detect rare adverse events such as heparin-induced thrombocytopenia.		
Outcome measures/results	Occlusion of CVCs, duration(in days)of catheter patency, Episodes of CVC-related sepsis and CVC-related colonization, mortality, hemorrhage from any site in the body, heparin-induced thrombocytopenia (HIT), CVC-related thrombosis, number of additional CVC insertions		- We noted differences in methods used by the included studies and variation in heparin concentrations (10 to 5000 IU/mL), time to follow-up (1 to 251.8 days), and the unit of analysis used (participant, catheter, line access). - Combined results from these studies showed fewer occlusions with heparin than with NS (risk ratio (RR) 0.70, 95% confidence interval (CI) 0.51 to 0.95; P = 0.02; 1672 participants; 1025 catheters from 10 studies; I2 = 14%) and provided very low-quality evidence. - We carried out subgroup analysis by unit of analysis (testing for subgroup differences (P = 0.23; I2 = 30.3%). When the unit of analysis was the participant, results show no clear differences in all occlusions between heparin and NS (RR 0.79, 95% CI 0.58 to 1.08; P = 0.15; 1672 participants; seven studies). - Subgroup analysis using the catheter as the unit of analysis shows fewer occlusions with heparin use (RR 0.53, 95% CI 0.29 to 0.95; P = 0.03; 1025 catheters; three studies). When the unit of analysis was line access, results show no clear differences in occlusions between heparin and NS (RR 1.08, 95% CI 0.84 to 1.40; 770 line accesses; one study). - We found no clear differences in the duration of catheter patency (mean difference (MD) 0.44 days, 95% CI -0.10 to 0.99; P = 0.11; 1036 participants; 752 catheters; six studies; low-quality evidence). - We found no clear evidence of a difference in the following: CVC-related sepsis (RR 0.74, 95% CI 0.03 to 19.54; P = 0.86; 1097 participants; two studies; low-quality evidence); mortality (RR 0.76, 95% CI 0.44 to 1.31; P = 0.33; 1100 participants; three studies; low-quality evidence); haemorrhage at any site (RR 1.32, 95% CI 0.57 to 3.07; P = 0.52; 1245 participants; four studies; moderate-quality evidence); or heparin- induced thrombocytopenia (RR 0.21, 95% CI 0.01 to 4.27; P = 0.31; 443 participants; three studies; low-quality evidence).

125. Dal Molin A, Allara E, Montani D, Milani S, Frassati C, Cossu S, et al. Flushing the central venous catheter: is heparin necessary? The journal of vascular access. 2014;15:241-8. [342]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** n/a **Study limitations**: no searching for gray literature	**Total no. Patients:** n/a **Inclusion criteria:** RCTs evaluating the use of heparin versus normal saline or other solution in the flushing of central catheter among adult patients **Exclusion criteria:** n/a	- to assess the efficacy of heparin flushing in the lock of central venous catheters - eight studies were included
Notes	**Author's Conclusion:** There is no evidence of a different effectiveness between heparin flushing and normal saline or other solutions in reducing catheter occlusions.		
Outcome measures/results	- primary outcome: occlusion - secondary outcomes: venous thromboembolism, catheter-related bloodstream infection and heparin-induced thrombocytopenia		- no evidence that heparin was more effective than normal saline in reducing occlusions - unclear whether urokinase and lepirudin were more effective than heparin in reducing occlusions - Vitamin C solution does not appear to prolong catheter patency

126. Bradford NK, Edwards RM, Chan RJ. Normal saline (0.9% sodium chloride) versus heparin intermittent flushing for the prevention of occlusion in long-term central venous catheters in infants and children. The Cochrane database of systematic reviews 2020; 4: CD010996-CD010996. doi:10.1002/14651858.CD010996.pub3 [345]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 1++ AMSTAR 2 14/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: moderate Risk of bias of single studies: high	**Total no. Studies:** 4 **Inclusion criteria:** randomized controlled trials (RCTs) that compared the efficacy of intermittent flushing with normal saline versus heparin to prevent occlusion of long-term CVCs in infants and children aged up to 18 years of age **Exclusion criteria:** temporary CVCs	To assess the clinical effects (benefits and harms) of intermittent flushing of normal saline versus heparin to prevent occlusion in long- term central venous catheters in infants and children.

	Inconsistency: high Indirectness: moderate Impreciseness: high Publication bias: n/a Methodological weaknesses in all studies, because of the nature of the outcomes (occlusion, infection, duration of catheter days), a lack of blinding may have impacted the outcome assessment	and peripherally inserted central catheters (PICC)	
Notes	**Author's Conclusion:** The review found that there was not enough evidence to determine the effects of intermittent flushing with normal saline versus heparin to prevent occlusion in long-term central venous catheters in infants and children. It remains unclear whether heparin is necessary to prevent occlusion, CVC-associated blood stream infection or effects duration of catheter placement. Lack of agreement between institutions around the world regarding the appropriate care and maintenance of these devices remains.		
Outcome measures/results	Occlusion of the CVC, CVC-associated blood stream infection or colonization of the catheter, duration in days of catheter placement		- The four trials directly compared the use of normal saline and heparin; the studies all used different protocols for the intervention and control arms, however, and all used different concentrations of heparin. Different frequencies of flushes were also reported between studies. In addition, not all studies reported on all outcomes. - The certainty of the evidence ranged from moderate to very low because there was no blinding; heterogeneity and inconsistency between studies was high; and the CIs were wide. - CVC occlusion was assessed in all four trials. We were able to pool the results of two trials for the outcomes of CVC occlusion and CVC-associated blood stream infection. The estimated RR for CVC occlusion per 1000 catheter days between the normal saline and heparin groups was 0.75 (95% CI 0.10 to 5.51; 2 studies, 229 participants; very low certainty evidence). - The estimated RR for CVC-associated blood stream infection was 1.48 (95% CI 0.24 to 9.37; 2 studies, 231 participants; low-certainty evidence). - The duration of catheter placement was reported to be similar for the two study arms in one study (203 participants; moderate-certainty evidence), and not reported in the remaining studies.

127.	**Tribler S, Brandt CF, Fuglsang KA, Staun M, Broebech P, Moser CE, et al. Catheter-related bloodstream infections in patients with intestinal failure receiving home parenteral support: risks related to a catheter-salvage strategy. The American Journal of Clinical Nutrition. 2018;107:743-53. [350]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2+ JBI 6/8	**Countries:** Denmark **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** n/a **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: high Impreciseness: low Publication bias: n/a **T**his study lacks information on the type and duration of the antimicrobial therapy to treat CRBSIs, severity of the infection, and occurrence of secondary complications	**Total no. Patients:** 715 **Inclusion criteria:** CRBSIs in tunneled single-lumen CVCs **Exclusion criteria:** all temporary short-term CVC	This was a retrospective observational database study evaluating all CRBSIs that occurred in our adult HPS population from 2002 to 2016. It was based on the Copenhagen IF database combined with the Clinical Microbiological Database from the Department of Clinical Microbiology, Rigshospitalet.
Notes	**Author's Conclusion:** In conclusion, successful catheter salvage is frequently seen in HPS patients over a broad spectrum of causative microorganisms. However, polyinfections and Enterobacteriaceae entail an increased risk of CRBSI recurrence, in which CVC replacement potentially could be the most beneficial solution. With the emergence of various catheter locks, further, and preferably prospective randomized, studies are needed to evaluate their long- term efficacy on CRBSI recurrence rates. Although CVC management should always be individualized according to the clinical presentation of the patient, the findings from this study on microbial risk factors may provide guidance on achieving better short- and long-term outcomes for HPS patients in relation to CRBSI management, which is the ultimate goal in these rare patients with IF.		
Outcome measures/results	Number of CVCs, CRBSI incidence rate, mortality rate, salvage rate, infection type, overall risk of CRBSI relapse, CRBSI recurrence, HR for subsequent CRBSI, HR for new CRBSI after catheter salvage	- There were 2006 tunneled CVCs inserted in 715 adult HPS patients covering 2014.3 CVC years, with a CRBSI incidence rate of 1.83/1000 (n = 1350) and a mortality rate of 0.007/1000 CVC days (n = 5). - The mean ± SD salvage rate was 55.3% ± 5.5%, varying according to infection type [monoinfections (62.9% ± 4.4%) and polyinfections (58.6% ± 17.3%)] and causative microorganism [coagulase-negative Staphylococci (CoNS) (68.1% ± 9.4%), Staphylococcus aureus (42.6% ± 17.5%), and Enterobacteriaceae (54.3% ± 16.7%)]. - The overall risk of CRBSI relapse was 7.5%, and the risk of CRBSI recurrence was 7.3%.	

		- HR for a subsequent CRBSI was 14% lower in a replaced than in a retained CVC (95% CI: 0.74, 0.99). - HR for a new CRBSI after catheter salvage was 36% higher after polyinfections than after monoinfections (95% CI: 1.03, 1.79). - Enterobacteriaceae entailed an increased risk of CRBSI recurrence compared with CoNS (2.26; 95% CI; 1.08, 4.75) and S. aureus (4.45; 95% CI: 1.28, 15.5).

128. Łyszkowska M, Kowalewski G, Szymczak M et al. Effects of prophylactic use of taurolidine-citrate lock on the number of catheter-related infections in children under 2 years of age undergoing surgery. J Hosp Infect 2019; 103: 223-226. doi:10.1016/j.jhin.2019.04.022 [349]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
randomized, prospective, observational cohort study 2+ NOS 7/9	**Countries:** Poland **Centers:** n/a **Setting:** Pediatrics **Funding Sources:** n/a **Dropout rates:** 0% **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: moderate Impreciseness: moderate Publication bias: n/a	**Total no. Patients:** 86 **Inclusion criteria:** written informed consent by parents / guardians for child's participation in the study, age of children under 2 years, surgical treatment within observation, central venous catheter(CVC) inserted in perioperative period **Exclusion criteria:** lack of parents' / guardians' consent to their child participation in the study, age of children over 2 years, no indications for surgical treatment and CVC implantation.	Group 1: without taurolidine (T(-)), n=49 CVCs Group 2: with taurolidine (T(+)), n=48 CVCs
Notes	**Author's Conclusion:** Taurolidine-citrate lock is a safe and both treatment and apparently cost-effective method of preventing CRI in the youngest children.		
Outcome measures/results	Primary objective: change in the number of catheter related infections Secondary objective: safety and tolerability assessment of taurolidine citrate lock		Overall, there were 15 cases of catheter-related bloodstream infection and 2 cases of catheter colonization. More than half of the infections occurred between 15 and 28 days after CVC implantation (n = 9; 60%). Fourteen CRI occurred in occurred in the T(-) group, compared with 1 in T(+) group (OR = 4.98, 95%CI 1.45 – 17.06, p = 0.011)

129. Vernon-Roberts A, Lopez RN, Frampton CM et al. Meta-analysis of the efficacy of taurolidine in reducing catheter-related bloodstream infections for patients receiving parenteral nutrition. JPEN J Parenter Enteral Nutr 2022; 46: 1535-1552. doi:10.1002/jpen.2363 [354]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Meta-analysis 1+ AMSTAR 2 9/16	**Countries:** n/a **Centers:** n/a **Setting:** parenteral nutrition via central venous catheter **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: Critically low Risk of bias of single studies: moderate Inconsistency: moderate Indirectness: moderate Impreciseness: moderate Publication bias: n/a The obvious limitation of this study is the inclusion of a range of study designs and control comparisons. The assessment of bias highlighted a number of shortcomings in the identified papers; however, when compared with the available literature and other meta-analyses the results do not seem overstated as a consequence of including observational nonrandomized studies. Although some studies were	**Total no. Patients:** **Inclusion criteria:** reporting data on patients receiving PN specifically (with exclusion of data relating to other CVC uses), and the inclusion of overall efficacy data of taurolidine vs a control group in the form of a rate of CRBSIs per 1000 days or contain data to make this calculable **Exclusion criteria:** n/a	Taurolidine vs. control

	missing data that would allow a comprehensive review of all results, every effort was made to retrieve this data from authors and the number of studies with insufficient data for inclusion in the meta-analysis was low.		
Notes	**Author's Conclusion:** The use of CVC locking is one method among a number of CRBSI prevention techniques. However, this analysis highlights the importance of using the locking solution with superior efficacy for reducing CRBSIs in patients receiving PN. The inclusion of observational studies in this synthesis adds to the evidence base elucidated in previous meta-analyses, while having recognized limitations relating to study methodologies. This study adds to the growing evidence base that taurolidine provides effective CRBSI reduction for people with IF receiving PN.		
Outcome measures/results	Primary outcome: taurolidine efficacy against comparators Secondary outcomes: CRBSI-free days, CVCs, adverse events or side effects, satisfaction, and the cost difference of taurolidine vs control treatment	The pooled RR for all studies included in the synthesis was 0.49 (95% CI, 0.46–0.53; P ≤ 0.0001). This indicates a 51% decrease in risk of CRBSIs through the use of taurolidine compared with controls. This result should also be interpreted in the context of four studies being excluded from the pooled RR due to the taurolidine group having zero CRBSIs, therefore, the result favoring taurolidine efficacy is likely to be underestimated. The comparison of CRBSI-free days was made in five papers, with all reporting superior outcomes for patients in the taurolidine group. Outcomes relating to the use of taurolidine compared with control on the CVC itself were reported in seven papers. The number of catheter removals due to CRBSI was significantly reduced in the taurolidine group compared with control in two studies. Fourteen papers reported on whether their study cohort experienced side effects or adverse events relating to the use of taurolidine. Ten papers reported that no side effects or adverse events were experienced, and 4 papers (all among the adult population), reported effects from among a total of 77 patients (5.2% of pooled study cohort). Only one study reported on patient satisfaction with their assigned treatment group, and no significant difference between the two groups was observed (P = 0.48). Seven studies reported on costs associated with treatment for CRBSIs for both control and taurolidine groups. All studies showed reduced costs associated with taurolidine treatment as relating to the cost of hospital admissions for CRBSIs, drug costs, or CVC removal.	

Empfehlung 53

Taurolidinhaltige Verriegelungslösungen sollen bei Patienten mit hohem Risiko zur Verminderung des Risikos für CRBSI eingesetzt werden; bei Patienten mit normalem Risiko sollten sie als eine zusätzliche Strategie zur Verhinderung von CRBSI genutzt werden.

Empfehlungsgrad A (Hochrisiko für CRBSI), Empfehlungsgrad B (normales Risiko)

Empfehlung 54

Ethanol-Lösungen sollten nicht als Katheterverriegelungslösung eingesetzt werden.

Empfehlungsgrad B

130. Bisseling TM, Willems MC, Versleijen MW et al. Taurolidine lock is highly effective in preventing catheter-related bloodstream infections in patients on home parenteral nutrition: a heparin-controlled prospective trial. Clin Nutr 2010; 29: 464–468 [346]									
level of evidence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
Ib	prospective, controlled, randomized	Catheter lock irrigation: IG taurolidine vs. CG heparin; diagnosis of CRBSI with typical symptoms.	2 years	at home	30 (CG 14, IG 16)	n/a	HPN	Risk of infection ↓: CG 10 CRBSI vs IG 1 CRBSI; Infection-free time ↑: CG 175 d vs. IG 641 d; no adverse events in either group.	

131. Touré A, Lauverjat M, Peraldi C et al. Taurolidine lock solution in the secondary prevention of central venous catheter-associated bloodstream infection in home parenteral nutrition patients. Clin Nutr 2012; 31: 567-570. doi:10.1016/j.clnu.2012.01.001 [347]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective Cohort Study	**Countries:** France **Centers:** n/a	**Total no. Patients:** 15 **Inclusion criteria:** patients on long-	

2+	**Setting:** n/a **Funding Sources:** Association Lyonnaise de Logistique Posthospitalière (ALLP) **Dropout rates:** n/a **Study limitations:** retrospective study with a small size, our CBSI rates were high but did not represent the rate of our general population. They may have been overestimated, because TLS was used only in patients with recurrent CBSIs	term HPN for at least 2 years and at high risk of CBSI and who received taurolidine 1.35%/ Sodium citrate 4% within the last 12 months as secondary prophylaxis of CBSI **Exclusion criteria:** n/a	Each patient acted as his or her own control over two periods in which central venous catheter-associated bloodstream infection (CBSI)episodes were recorded during the pre and the per-intervention period. In the first period, only standardized strategies such as appropriate choice of insertion site of catheter, maximal barrier precautions during insertion, proper education and specific training of the staff, adequate policy of hand washing, appropriate dressing of the exit site, disinfection of hubs, stopcocks and needle-free connectors, and regular change of administration sets were used to reduce the incidence of CBSI. At the end of parenteral nutrition infusion, catheters were locked with 10 ml of saline solution to avoid catheter obstruction. In the second period, TLS was used and replaced saline solution to reduce CBSI. TLS was injected as bolus into the catheter at the end of PN (just the catheter volume, approximately 3 ml) and aspirated before the next intravenous treatment. As these patients received only parenteral nutrition, TLS remained approximately 12 h in the catheter. Serum saline locks were stopped during this period.
Notes	**Author's Conclusion:** In conclusion, this 24-month retrospective cohort study showed that TLS associated with standardized precautions significantly reduces the CBSI rate. This lock is of interest in such patients in order to reduce infectious complications, improve the quality of life and decrease the cost of HPN. The use of this lock for primary prevention of CBSI in HPN patients and the frequency of instillations require further discussion.		
Outcome measures/results	CBSI rate		- During the 24 months, the CBSI rate was 6.58/1000 catheter-days in the first period and 1.09/1000 catheter-days in the second period ($p < 0.001$). - In patients with TLS once a week (n = 8), the CBSI rate decreased from 4.8/1000 catheter-days to 1.37/1000 catheter-days ($p = 0.02$) and in patients with TLS after each TPN (n = 7), the CBSI rate decreased from 8.61/1000 catheter-days to 0.78/1000 catheter-days ($p = 0.001$).

132. Wouters Y, Roosenboom B, Causevic E, Kievit W, Groenewoud H, Wanten GJA. Clinical outcomes of home parenteral nutrition patients using taurolidine as catheter lock: A long-term cohort study. Clinical nutrition (Edinburgh, Scotland). 2019;38:2210-8. [352]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort study 2+ JBI 8/8	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** Baxter International Inc. (Illinois,	**Total no. Patients:** 270 **Inclusion criteria:** patients with a benign underlying disease leading to intestinal failure	- retrospective analysis of complications (CLABSIs, CRVTs and CVAD occlusions) and adverse events in adult HPN patients while using taurolidine as lock solution - n=270 used taurolidine; n=10 discontinued taurolidine and started using saline

	USA) and Geistlich Pharma AG (Wolhusen, Switzerland **Dropout rates:** n/a **Study limitations:** Risk of Bias: low Inconsistency: n/a Indirectness: moderate Impreciseness: low Publication bias: n/a Complications still could have been missed; despite correction for possibly relevant baseline confounders, there may still be a difference between patients with and without adverse events	**Exclusion criteria:** patients who used arteriovenous fistulae to administer parenteral nutrition	
Notes	**Author's Conclusion:** Complication rates remained low in the long-term, and use of taurolidine was generally safe.		
Outcome measures/results	- Primary outcome: effectiveness of taurolidine, as described by complication incidence rates - Secondary outcome: adverse events of taurolidine, complication rates of patients who subsequently discontinued taurolidine and started using 0.9% saline alternatively, and risk factors associated with complications		- CLABSIs, CRVTs and CVAD occlusions occurred at a rate of 0.60 (CI 95 % 0.52-0.69), 0.28 (CI 95 % 0.23-0.34), and 0.12 (CI 95 % 0.08-0.16) events per 1000 catheter days, respectively - in 24 (9%) patients, mild to moderate adverse events resulted in discontinuation of 2% taurolidine - several risk factors were identified for CLABSIs (a lower age, non-tunneled catheters, infusion frequency), CRVTs (site of vein insertion), and CVAD occlusions (type of CVAD)

133. Wouters Y, Theilla M, Singer P, Tribler S, Jeppesen PB, Pironi L, et al. Randomised clinical trial: 2% taurolidine versus 0.9% saline locking in patients on home parenteral nutrition. Alimentary pharmacology & therapeutics. 2018;48:410-22. [351]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Denmark, Israel, Italy, the Netherlands and the United Kingdom **Centers:** multicenter	**Total no. Patients:** 102 **Inclusion criteria:** a benign underlying disease leading to	- new catheter group: n= 36 received taurolidine and n= 35 received saline for 1 year - pre-existing catheter group: n= 16 received taurolidine and n= 15 received saline for 1 year

	Setting: n/a **Funding Sources:** Geistlich Pharma AG **Dropout rates:** 16 % excluded from per-protocol analysis **Study limitations:** study was performed against the background of a certain infectious complication rate; inclusion of the pre-existing catheter group	intestinal failure; an estimated life expectancy ≥ 1 year **Exclusion criteria:** antibiotic therapy <2 months prior to trial inclusion; silver impregnated or antimicrobial cuff catheters; significant cardio-vascular disease; clinically significant abnormalities in coagulation requiring intervention; thrombolytic therapy 6 weeks prior to CVAD insertion	
Notes	**Author's Conclusion:** Given its favorable safety and cost profile, taurolidine locking should be considered as an additional strategy to prevent CRBSIs.		
Outcome measures/results	- primary outcome: rates of CRBSIs/ 1000 catheter days - secondary outcomes: cost; exit site infections; patient satisfaction with the assigned catheter lock solution		- in the new catheter group, rates of CRBSIs/1000 catheter days were 0.29 and 1.49 in the taurolidine and saline arm respectively (relative risk, 0.20; 95% CI, 0.04-0.71; P= 0.009) - in the pre-existing catheter group, rates of CRBSIs/1000 catheter days were 0.39 and 1.32 in the taurolidine and saline arm respectively (relative risk, 0.30; 95% CI, 0.03-1.82; P= 0.25) - mean costs per patient were $1865 for taurolidine and $4454 for saline (P= 0.03) - the secondary outcomes were non-significant between taurolidine and saline

134. Wouters Y, Causevic E, Klek S et al. Use of Catheter Lock Solutions in Patients Receiving Home Parenteral Nutrition: A Systematic Review and Individual-Patient Data Meta-Analysis. JPEN Journal of parenteral and enteral nutrition 2020; 44: 1198-1209. doi:10.1002/jpen.1761 [353]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 1++ AMSTAR 2 9/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:**	**Total no. Studies:** 3 studies with 162 HPN patients and 45,695 catheter days **Inclusion criteria:** individual-patient data from prospective randomized controlled trials published on CLS in	Use of catheter lock solutions (CLSs) as a strategy to prevent catheter-related bloodstream infections (CRBSIs) has been evaluated in recent clinical trials. Our aim was to identify the most effective CLS formulation in patients receiving home parenteral nutrition (HPN).

	Overall confidence in the results of the review: critically low Risk of bias of single studies: high Inconsistency: high Indirectness: low Impreciseness: moderate Publication bias: n/a The quality of the present study is largely based on the individual quality of included studies. Limitations of these clinical trials may apply to this study as well; only 3 studies were included in the IPDMA, which particularly hampered inclusion of patients using heparin from the 2 excluded studies, CLSs were characterized based on their active component	HPN patients. Studies had to report CRBSI rates as primary or secondary outcome. At patient level, only adult intestinal-failure patients who received HPN and/or fluids via CVADs, English language **Exclusion criteria:** patients with an active malignancy or an untreated CRBSI at trial inclusion	
Notes	**Author's Conclusion:** In conclusion, this study showed that the use of taurolidine as CLSs was most effective in HPN patients for the prevention of CRBSIs. Adverse events were reported to be relatively infrequent and only mild to moderate. Risk factors for CRBSIs included the type of CLS, the underlying disease, and the type of CVAD used. We suggest discussing with patients the benefits and risks when starting taurolidine, especially in those who are considered at a higher risk for CRBSIs.		
Outcome measures/results	Primary outcome: number of CRBSIs per 1000 catheter days for each catheter lock solutions (CLSs) secondary outcomes: time to CRBSI and identification of patients with a higher risk for CRBSIs		Primary outcome - CRBSI rates were significantly decreased in patients using taurolidine (rate 0.13; 95% confidence interval [CI], 0.05–0.32) when compared with saline (rate 0.74; 95% CI, 0.31–1.74; P = .002) or heparin (rate 2.01; 95% CI, 1.03–3.91; P < .001). Secondary outcomes: - The cumulative proportion of CRBSI-free patients using taurolidine, saline, and heparin after 1 year was 88%, 56%, and 14%, respectively. - Three risk factors for CRBSIs were identified: type of CLS, intestinal dysmotility as underlying condition, and use of central venous catheters.

135. Gundogan K, Dave NJ, Griffith DP et al. Ethanol Lock Therapy Markedly Reduces Catheter-Related Blood Stream Infections in Adults Requiring Home Parenteral Nutrition: A Retrospective Study From a Tertiary Medical Center. JPEN Journal of parenteral and enteral nutrition 2020; 44: 661-667. doi:10.1002/jpen.1698 [355]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2- NOS 7/9	**Countries:** United States **Centers:** 700-bed tertiary care academic teaching hospital in Atlanta, GA, USA **Setting:** n/a **Funding Sources:** Division of Medical Intensive Care, Erciyes University Hospital, Kayseri, Turkey (to KG), and National Institutes of Health grant K24 DK096574 (to TRZ). **Dropout rates:** 11.2% **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: low Impreciseness: moderate Publication bias: n/a Retrospective study design and the small sample size, no comprehensive data on whether any of the historical controls received ALT during their course of observation, matching was based upon similar demographics and primary indication for, no matching based upon frequency of infusion or format of the PN infused via Hickman catheter before vs after institution of ELT	**Total no. Patients:** 98 **Inclusion criteria:** adult (≥ 18 year old) study subject had been discharged from EUH or Wesley Woods Geriatric Center or EUH between a predefined period of February 1, 2012, through March 31, 2013; study subject's HPN was managed by the EUH Nutrition and Metabolic Support Service in conjunction with the primary care physician; and study subject was expected to receive HPN and ELT via a tunneled, cuffed, silicone CVC for ≥ 90 days. **Exclusion criteria:** patient has clear documentation of poor follow-up and/or poor compliance with the use of ELT; patient received <1 week of ELT during the study period.	EUH medical records of adult HPN patients discharged with a tunneled, silicone CVC on ELT were retrospectively studied during a pre-hoc determined 14-month observation period (n = 87; 13,386 catheter days) and compared with clinically similar HPN patients from the same institution before institution of the ELT protocol for all appropriate patients. The ELT protocol involved instilling 2 mL of 70% ethanol into each catheter lumen daily after the HPN cycle, following initial flushing with normal saline.

	therapy, not monitor use of tissue plasminogen activator therapy		
Notes	**Author's Conclusion:** Available studies, albeit largely retrospective, strongly suggest that ELT may be an effective approach to reduce CRB- SIs in both adults and children requiring HPN. Prospective, rigorous, carefully controlled, randomized clinical trials (RCTs) are clearly needed to document efficacy of this approach. In order to define optimal modes of ELT ad- ministration, such RCTs should ideally evaluate the volume and concentration of ethanol administered, as well as the number of days per week of HPN in which ELT may be optimally required to reduce CRBSIs.		
Outcome measures/results	Diagnosis of CRBSI, CRBSI rate		- Only 5 of 87 patients (5.7%) who received ELT were diagnosed with a CRBSI (0.45/1000 catheter days) during observation. - We compared these data with our previously published clinically matched patient population from EUH (n = 22) receiving HPN via a silicone CVC without ELT. Of these historical controls, 45.5% were diagnosed with 1 or more CRBSIs (8.7/1000 catheter days) during observation (P < .001 vs the current ELT cohort).

Empfehlung 55

Wird ein PICC bei HPE eingesetzt, sollte eine nahtfreie Fixierung verwendet werden, um das Infektionsrisiko zu verringern.

Empfehlungsgrad B

136.	**Pironi L, Boeykens K, Bozzetti F et al. ESPEN guideline on home parenteral nutrition. Clin Nutr 2020; 39: 1645-1666. doi:10.1016/j.clnu.2020.03.005 [5]**
Guideline **Relevant recommendations/ statements**	- Peripherally inserted central venous catheters (PICCs) can be used if the duration of HPN is estimated to be less than six months. Grade of Recommendation 0 - Strong consensus (100% agreement) - If a PICC is used for HPN, a sutureless device should be used to reduce the risk of infection. Grade of Recommendation B - Strong consensus (100% agreement) - For the securement of medium - to long-term PICCs (> 1 month) a subcutaneously anchored stabilization device can be used to prevent migration and save time during dressing change. Grade of Recommendation 0 - Strong consensus (100% agreement)

137.	**Luo X, Guo Y, Yu H et al. Effectiveness, safety and comfort of StatLock securement for peripherally-inserted central catheters: A systematic review and meta-analysis. Nurs Health Sci 2017; 19: 403-413. doi:10.1111/nhs.12361 [356]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review			

1++	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** publication bias might exist due to language restrictions; it was reported that the effectiveness and complications of PICC are not only influenced by catheter securement devices but are also affected by operation proficiency and catheter maintenance, which are not described in the included studies and might result in heterogeneity; differences in the baseline characteristics and vein used among various publications might also result in heterogeneity, included studies varied in methodological quality; Whether or not blinding was performed was not reported in any of the trials, which could lead to researcher expectation bias	**Total no. Studies:** 12 **Inclusion criteria:** participants: patients with PICC, including both adults and children; interventions: StatLock securing PICC; comparators: tape or suture securing PICC; outcomes: catheter migration, catheter dislodgement, unplanned removal, indwelling time, occlusion, catheter restarts, skin ulceration, skin hypersensitivity, CRBSI, thrombosis, phlebitis, leakage, and comfort; study design: RCT **Exclusion criteria:** patients with high risk of infections (e.g. arteriovenous (AV) fistula or graft for hemodialysis) and obvious coagulation dysfunction, and duplicate articles, studies concerning other catheters (e.g. central venous catheter (CVC)), studies comparing the effectiveness of different types of PICC (e.g. varying PICC gauge or lumens), and studies with incomplete data and no reply after contacting the corresponding author	Evaluation of the effectiveness, safety and comfort of StatLock for the securement of peripherally-inserted central catheters.
Notes	**Author's Conclusion:** This systematic review and meta-analysis evaluated the effectiveness, safety, and comfort of StatLock for PICC securement, indicating that the StatLock securement device could reduce catheter-related complications and improve patient comfort compared to the previous standard of tape and sutures. However, as considerable heterogeneity was found among the included studies and the quality of evidence was relatively low for the main outcomes, the results should be viewed with caution. High-quality RCT with multi-center and larger samples are needed to confirm the effects.		

Outcome measures/results	Catheter migration, catheter dislodgement, unplanned removal, catheter occlusion, catheter restarts, indwelling time, safety assessment	- no significant difference in the incidence of catheter migration between the StatLock group and control groups (RR = 0.47, 95% CI: 0.18– 1.22, P = 0.12). - In the random-effects model, it seemed that StatLock led to a significantly lower risk of catheter dislodgement when compared with the control intervention (RR = 0.44, 95% CI: 0.22–0.86, P = 0.02), which mainly resulted from the difference between the StatLock group and the tape group (RR = 0.25, 95% CI: 0.14–0.44, P < 0.001). There was no substantial difference between the StatLock group and suture group (RR = 0.92, 95% CI: 0.49–1.74, P = 0.79). - The pooled effect size showed that StatLock significantly reduced the incidence of unplanned removal compared with the control intervention (RR = 0.32, 95% CI: 0.13–0.77, P = 0.01), which mainly resulted from the difference between the StatLock group and the tape group (RR = 0.21, 95% CI: 0.10–0.46, P < 0.01). Difference in the incidence of unplanned removal was similar between the StatLock group and the suture group (RR = 0.65, 95% CI: 0.40–1.04, P = 0.07). - no significant difference in the incidence of catheter occlusion between two groups (RR = 0.54, 95% CI: 0.27–1.04, P = 0.07) - The difference in the incidence of catheter restarts between the StatLock group and the control groups was not significant (RR = 0.44, 95% CI: 0.11–1.85, P = 0.26) - The effect estimate did not show a significant difference in the indwelling time between the StatLock group and the suture group (SMD = −2.44, 95% CI: −10.56, 5.69, P = 0.56) - Moreover, patients in the StatLock group had lower incidence of skin ulceration, phlebitis, catheter-related bloodstream infection, and cellulitis, and felt more comfortable compared with those in the control group.

<u>Empfehlung 56</u>

Für die Sicherung mittel- bis langfristiger PICCs (> 1 Monat) kann eine subkutan verankerte Stabilisierungsvorrichtung verwendet werden, um Zeit beim Verbandwechsel zu sparen und eine Kathetermigration zu verhindern.

Empfehlungsgrad 0

138. Goossens GA, Grumiaux N, Janssens C, Jerome M, Fieuws S, Moons P, et al. SecurAstaP trial: securement with SecurAcath versus StatLock for peripherally inserted central catheters, a randomised open trial. BMJ open. 2018;8:e016058. [358]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+	**Countries:** Belgium **Centers:** single-center **Setting:** university hospital Leuven **Funding Sources:** none **Dropout rates:** 2 % **Study limitations:** full economic assessment of the use of both securement devices is lacking; no blinding	**Total no. Patients:** 105 **Inclusion criteria:** patients scheduled for a PICC insertion with a polyurethane catheter; had a planned follow-up in the study center **Exclusion criteria:** known allergy to nickel and/or ethylene oxide	- StatLock which has to be changed weekly versus SecurAcath which could remain in place for the complete catheter dwell time - randomized patients: 105 adults (StatLock, n=53; SecurAcath, n=52) - primary analysis was based on all patients (n=92) with time measurements (StatLock, n=43; SecurAcath, n=49)
Notes	**Author's Conclusion:** Use of SecurAcath saves time during dressing change compared with StatLock. Training on correct placement and removal of SecurAcath is critical to minimize pain.		
Outcome measures/results	- primary outcome: needed time for the dressing change at each dressing change (SecurAcath) or at each dressing change combined with the change of the securement device (StatLock) - secondary outcomes: catheter migration at dressing change; CRBSI; catheter dislodgement resulting in premature PICC removal		- median time needed for dressing change was 7.3min (95%CI 6.4min to 8.3min) in the StatLock group and in the SecurAcath group 4.3min (95%CI 3.8 min to 4.9min) (P<0.0001) - time in the SecurAcath group was reduced with 41% (95% CI 29% to 51%) - incidence of catheter-related bloodstream infection was comparable between the groups - Pain scores were higher with SecurAcath than with StatLock at insertion (P=0.02) and at removal (P<0.001) and comparable during dressing change (P=0.38) and during dwell time (P=0.995)

139. Macmillan T, Pennington M, Summers JA, Goddard K, Zala D, Herz N, et al. SecurAcath for Securing Peripherally Inserted Central Catheters: A NICE Medical Technology Guidance. Applied health economics and health policy. 2018;16:779-91. [357]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review	**Countries:** n/a	**Total no. Patients:** n/a	n/a

2-	**Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Inclusion criteria:** n/a **Exclusion criteria:** n/a	
Notes	**Author's Conclusion:** Despite a challenging evidence base, the EAC was able to deliver a cogent assessment report and this, combined with expert clinical opinion, was used by the MTAC to make a positive recommendation for SecurAcath to be used in the NHS.		
Outcome measures/results	Recommendation: - The case for adopting SecurAcath for securing PICCs is supported by the evidence. SecurAcath is easy to insert, well tolerated, associated with a low incidence of catheter-related complications and does not usually need replacing while the catheter is in place. - SecurAcath should be considered for any PICC inserted for an anticipated medium- to long-term indwell time (15 days or more).		- statistically significant reduction in the time taken to change dressings when SecurAcath was used [4.3 min (95% CI 3.8–4.9) compared with 7.3 min (95% CI 6.4–8.3) for StatLock ($p < 0.0001$) - The External Assessment Centre (EAC) concluded that there was insufficient evidence to draw firm conclusions about the superiority of SecurAcath with regard to effectiveness and adverse events compared to StatLock - For a PICC line, the manufacturer estimated a saving of £41 with the use of SecurAcath instead of StatLock for an indwell time of 25 days

Empfehlung 57

Um Komplikationen zu vermeiden, sollte der ZVK nicht ungeschützt unter Wasser getaucht werden.

Empfehlungsgrad B

140. Ivy DD, Calderbank M, Wagner BD, Dolan S, Nyquist AC, Wade M, et al. Closed-hub systems with protected connections and the reduction of risk of catheter-related bloodstream infection in pediatric patients receiving intravenous prostanoid therapy for pulmonary hypertension. Infection control and hospital epidemiology. 2009;30:823-9.			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Observational study 2+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** General Clinical Research Centers, National Center for Research	**Total no. Patients:** 50 **Inclusion criteria:** pediatric patients with pulmonary arterial hypertension **Exclusion criteria:** n/a	- CR-BSI preventive measures were implemented, including the use of a closed-hub system and the waterproofing of catheter hub connections during showering - Fifty patients received intravenous prostanoid therapy

	Resources, National Institutes of Health **Dropout rates:** n/a **Study limitations:** observational study design; Increased education and surveillance with regard to catheter-related infection; they did not measure patient compliance with respect to maintaining dry connections		
Notes	**Author's Conclusion:** The closed-hub system and the maintenance of dry catheter hub connections significantly reduced the incidence of CR-BSI (particularly infections caused by gram-negative pathogens) in patients receiving intravenous treprostinil.		
Outcome measures/results	Rates of CR-BSI before and after implementing preventive measures were compared with respect to medication administered and type of bacterial infection		- the rate of CR-BSI during the study period was 0.51 infections per 1,000 catheter-days for epoprostenol and 1.38 infections per 1,000 catheter-days for treprostinil, which differed significantly (P < .01) - CR-BSIs caused by gram-negative pathogens occurred more frequently with treprostinil than with epoprostenol (0.91 infections per 1,000 catheter-days vs 0.08 infections) per 1,000 catheter-days; P < .01) - Patients treated with treprostinil after the implemented changes had a significant decrease in CR-BSI rate (1.95 infections per 1,000 catheter-days vs 0.19 infections per 1,000 catheter-days; P < .01)

141. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52:e162-93. [107]
→ see No. 80

142. Kolacek S, Puntis JWL, Hojsak I. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Venous access. Clinical nutrition (Edinburgh, Scotland). 2018;37:2379-91. [298]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline	**Countries:** n/a	**Total no. Patients:** n/a	n/a

2+	**Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Inclusion criteria:** n/a **Exclusion criteria:** n/a	
Notes	**Author's Conclusion:** In newborns and children, PICC and tunneled CVC should be used for administration of prolonged PN during hospitalization. In children requiring long-term PN and home PN a tunneled CVC is recommended.		
Relevant recommendations/statements	- Children with well-healed tunneled catheters may be allowed to swim, if a water resistant dressing is used to cover the whole catheter. Immediately after swimming the catheter exit site should be cleaned and disinfected, and the dressing changed		

Empfehlung 58

Die routinemäßige Entnahme von Blutproben aus ZVKs sollte wegen eines erhöhten Komplikationsrisikos möglichst vermieden werden.

Empfehlungsgrad B

143. Buchman AL, Opilla M, Kwasny M, Diamantidis TG, Okamoto R. Risk factors for the development of catheter-related bloodstream infections in patients receiving home parenteral nutrition. JPEN Journal of parenteral and enteral nutrition. 2014;38:744-9. [369]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2+	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 143 **Inclusion criteria:** patients who received HPN infusion at least twice weekly for at least 2 years **Exclusion criteria:** n/a	- n=125 adults and n=18 children - patients received HPN infusion at least twice weekly
Notes	**Author's Conclusion:** Numerous risk factors for CRBSI were identified for which simple and current countermeasures already exist.		
Outcome measures/results	rate of catheter-related bloodstream infection		- in adults, 331 central venous catheters (CVCs) were placed. Total catheter years were 1157. Median CVC dwell time was 730 days - in children, there were 53 CVCs placed. Total catheter years were 113.1. Median CVC dwell time was 515 days

		- there were 147 CRBSIs (0.13/catheter year;0.35/1000 catheter days). In children there were 33 CRBSIs (0.29/catheter year;0.80/1000 days; P < .001 versus adults) - increased PN frequency was associated with increased risk of CRBSI (P = .001) in children, but not in adults

144. Munck A, Malbezin S, Bloch J, Gerardin M, Lebourgeois M, Derelle J, et al. Follow-up of 452 totally implantable vascular devices in cystic fibrosis patients. The European respiratory journal. 2004;23:430-4. [370]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective study 2+	**Countries:** n/a **Centers:** 36 cystic fibrosis centers **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 315 **Inclusion criteria:** patients with cystic fibrosis **Exclusion criteria:** n/a	- n=315 patients - n=452 totally implantable vascular access devices (TIVADs)
Notes	**Author's Conclusion:** TIVADs appear to be safe and reliable for long-term intermittent venous access.		
Outcome measures/results	rate of complications in cystic fibrosis patients with TIVADs		- Long-term complications occurred with 188 devices (42%); they consisted mainly of occlusion (21%, requiring removal in 77%), infection (9.3%, requiring removal in 85%; septicemia in 7.3%; rate 0.3 per 1,000 days, Candida in 66%), and vascular thrombosis (4.7%, removal in 58%) - the mean functional time per device was 32± 25months, and ranged from 0–165 months (1,205 catheter-years)

<u>Empfehlung 59</u>

Unter Beachtung der klinischen Situation sollte eine systemische und intraluminale Antibiotikatherapie möglichst nach Antibiogramm versucht werden.

Empfehlungsgrad B

145. Messing B, Man F, Colimon R et al. Antibiotic-lock technique is an effective treatment of bacterial catheter-related sepsis during parenteral nutrition. Clin Nutr 1990; 9: 220–225 [389]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
IIa	Case reports	In case of complications (except catheter-associated sepsis): Catheter removal; in case of infection: treatment with antibiotic saline: antibiotic lock therapy (confinement in catheter for 12 h/d for 15 d).	2 years	at home	19	52 years (average)	HPN	Annual incidence rate 1.27, of which 84% bacterial catheter infection; by antibiotic lock therapy: prevention of systemic antibiotic therapy and no catheter change; 93% of infections could be controlled	HPN duration: 16 months (average)

146. Gaillard JL, Merlino R, Pajot N et al. Conventional and nonconventional modes of vancomycin administration to decontaminate the internal surface of catheters colonized with coagulase-negative staphylococci. JPEN J Parenter Enteral Nutr 1990; 14: 593–597 [390]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
IIb	experimental trial	In vitro model: conventional and non-conventional 3-d therapies with vancomycin to treat inner surface of catheters with S. epidermis mucus vs. with CG (PN solution only).	3 d/ treatment	n/a	5 catheters each	n/a	n/a	Vancomycin with conc. 7.5 mg/liter: low rate of early killing of S. epidermis; Vancomycin with high conc (450 or 5000 mg/liter): 100% kill in 2 h; bactericidal activity of vancomycin was increased by combinations with netilmicin/fosfomycin/rifampin: 2.56 ± 0.69 colonies/catheter vs. 0.77 ± 1.05/0.83 ±1.09/0.92 ±	

								1.10 colonies/catheter; vancomycin in antibiotic lock therapy: 0.0 colonies/catheter.	

147. Schwartz C, Henrickson KJ, Roghmann K et al. Prevention of bacteremia attributed to luminal colonization of tunneled central venous catheters with vancomycin-susceptible organisms. J Clin Oncol 1990; 8: 1591–1597 [391]									
level of evidence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
IIb	randomized, controlled	Immunosuppressive therapy; 10 U/mL heparin (H) vs. 10 U/mL heparin + 25 µg/mL vancomycin (HV) for catheter lock irrigation.	247±150 d/treatment, 11,095 d in total	hospital	45 (H 24, HV 21)	46 Monate (MW)	Children with oncologic or hematologic diseases; tunneled CVC.	Infection with vancomycin-susceptible bacteria (luminal colonization): H 5 patients vs. HV 0 patients	5 patients: 2 tunneled CVC; 1 patient: 3 tunneled CVC

148. Capdevila JA, Segarra A, Planes AM et al. Successful treatment of haemodialysis catheter-related sepsis without catheter removal. Nephrol Dial Transplant 1993; 8: 231–234 [388]									
level of evidence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
III	prospective, case reports	if sepsis is suspected: quantitative blood culture determination (catheter+ peripheral vein); if bacteria in catheter 4x ↑ than vein, then antibiotics (vancomycin or ciprofloxacin).	12 months	hospital	36	n/a	Renal insufficiency, double lumen catheter	13 sepsis episodes in 11 patients (each successfully treated); 25 fever episodes in 19 patients; fever onset: 73.5 d (MW) after catheter insertion.	

Empfehlung 60

Bei ausgeprägten lokalen oder systemischen Zeichen eines Infekts (beginnendes Organversagen) und/oder bei Nachweis von Katheter-induzierter Bakteriämie mit Problemkeimen (z. B. Candida albicans, Pseudomonas-Stämmen oder Staphilococcus aureus) sollte der ZVK entfernt werden.

Empfehlungsgrad B

149. Pironi L, Arends J, Bozzetti F, Cuerda C, Gillanders L, Jeppesen PB, et al. ESPEN guidelines on chronic intestinal failure in adults. Clinical nutrition (Edinburgh, Scotland). 2016;35:247-307. [528]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline 2++	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a
Notes	**Author's Conclusion:** CIF management requires complex technologies, multidisciplinary and multiprofessional activity, and expertise to care for both the underlying gastrointestinal disease and to provide HPN support. Two-thirds of the recommendations are considered strong. Specialized management and organization underpin these recommendations.		
Relevant recommendations/statements	- We recommend that HPN patients have access to infusion pumps or devices with specified safety features together with ancillary products, safe compounding and delivery systems - We recommend that the protein and energy requirements for CIF patients be based on individual patient characteristics (e.g. intestinal absorptive capacity as estimated by gastrointestinal anatomy and/or underlying disease) and specific needs (e.g. acute illness, protein malnutrition), and that the adequacy of the regimen is regularly evaluated through clinical, anthropometric, and biochemical parameters. - We recommend regular monitoring of signs and symptoms of dehydration, fluid balance, laboratory tests, and 24-h urine output as well as a timely adjustment of fluid supplementation to prevent chronic renal failure in patients on HPN. - We recommend that the aims of an HPN program include provision of evidence-based therapy, prevention of HPN- related complications such as catheter-related infections and metabolic complications and ensure quality of life is maximized.		

5 Nahrungsprodukte zur HEE und deren Anwendung

5.1 Standardsondenkost

Empfehlung 61

Bei Patienten mit Diarrhoe sollen ballaststoffreiche Sondennahrungen bevorzugt werden.

Empfehlungsgrad A

Empfehlung 62

Auch bei Patienten mit Obstipation kann ballaststoffhaltige Sondennahrung verwendet werden.

Empfehlungsgrad 0

150. Elia M, Engfer MB, Green CJ, Silk DB. Systematic review and meta-analysis: the clinical and physiological effects of fibre-containing enteral formulae. Aliment Pharmacol Ther. 2008;27(2):120-45. [401]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic review 1-	**Countries:** n/a **Centers:** n/a **Setting:** Enteral nutrition in community setting **Funding Sources:** funded in part by Numico **Dropout rates:** n/a **Study limitations:** lack of data from nonhospital settings, lack of data for evaluating the effect of fiber supplementation, often lack of sample size calculation, studies often didn´t specify a	**Total no. Studies:** n=51 (n=1762 subjects) **Inclusion criteria:** adults and children, non-RCT, observational cohort, controlled studies, RCT, patients and healthy volunteers, > 1 year of age, any nutritional status, based in any setting, studies including a self-selected diet arm with Comparison fiber-free/fiber-containing enteral feeds **Exclusion criteria:** studies with no oral or tube-feeding as their main source of nutrition, studies involving	Comparison: 1. Fiber-supplemented formula 2. Fiber-free formula → given as a sole source of nutrition for at least 3 days

	clear primary end point, different definitions of diarrhea and constipation and use of clinically relevant markers of gastrointestinal function, variability between the studies in the amount of fiber administered daily, heterogeneity between the studies	infant formulae and studies that did not involve a fiber-free period, epidemiological / dietary intake studies, animal or in vitro studies, literature reviews, observational case studies and acute studies (<3 days)	
Notes	**Author's Conclusion:** The review indicates that the fiber-supplemented enteral formulae have important physiological effects and clinical benefits. There is a need to use a consistent approach to undertake more studies on this issue in the community setting. - Represents the most comprehensive examination of the role of fibers in enteral formulae to date - Demonstrates that fiber-containing enteral formulae are well tolerated, especially when given as fiber mixtures - Demonstrates significant clinical benefits of fiber-supplemented enteral feeds in patients suffering from diarrhea, with a positive trend also observed for patients with constipation. The findings were relevant in both acute and chronic healthcare settings and across all age ranges - Reports a moderating effect of fiber supplementation on bowel function, which is most pronounced in patients at either end of the bowel function spectrum - Has highlighted the need for both consistent reporting of clinical end points in future studies and further studies in the community setting; - Concludes that first-line treatment with fiber-containing feeds should be considered as an important modality of clinical care	
Outcome measures/results	- Objective measures of gastrointestinal function: transit time, stool weight and bowel frequency - subjective measures of gastrointestinal function: incidence of diarrhea/constipation, stool consistency and gastrointestinal symptoms	- n=51 studies; of them n=43 were RCTs; of n=1762 subjects n=1591 were patients (n=38 studies) and n=171 were healthy volunteers (n=13 studies) - 47% of the studies feeding was administered via nasogastric tube; in 8% feeding via nasojejunal tube/needle catheter jejunostomy tube; in 8% variety of tube feeding routes were used; in 37% route was not explicitly stated - Over 15 different fiber sources in the different studies: soy, polysaccharide were most frequently studied followed by a mixture of 6 different fibers - In 65% of the studies a single fiber source was used, in 8% a mixture of 2 sources and in 4% a mixture of 5 sources; 6% of the studies were insufficient details - Fiber supplementation was generally well tolerated - In the hospital setting, the incidence of diarrhea was reduced as a result of fiber administration (OR 0.68, 95% CI: 0.48–0.96; 13 RCTs; high heterogeneity: I^2 = 38%, P = 0.05 → from ICU studies → incidence of diarrhea in the ICU studies was variable, ranging from 9–92% in the fiber-free groups. Subgroup analyses revealed a significant reduction in the incidence of diarrhea in the	

		non-ICU studies (OR 0.42, 95% CI: 0.25–0.72; P = 0.001; eight data sets from seven RCTs, n = 185 in fiber group and n = 183 in fiber-free group) and in the surgical studies alone - level of fiber intake was reported in six studies, ranging from 14.0 to 34.9 g／day → no significant relationship was observed between the level of fiber intake during feeding and incidence of diarrhea [intercept (log OR))0.33; slope 0.0009; z =)0.24; P = 0.81; n = 135 in fiber group and n = 135 in fiber-free group] - Meta-regression showed a more pronounced effect when the baseline incidence of diarrhea was high - nonsignificant trend for fiber to reduce the percentage of patients reporting constipation (test of overall effect, OR 0.57, 95% CI: 0.30–1.10; P = 0.09; test of heterogeneity, I^2 = 0%; P = 0.51); no analysis possible in patients with chronic conditions - fiber-containing feed significantly increased mean bowel frequency [test of overall effect, 0.14 (S.E. 0.05) times／day, z = 2.8, P = 0.005; test of heterogeneity, I^2 = 26%, P = 0.17] - In both patients and healthy subjects, fiber significantly reduced bowel frequency when baseline frequency was high and increased it when it was low, revealing a significant moderating effect of fiber - Whole gut transit time: - Patients: no significant effect (test of overall effect, 1.7 (S.E. 6.4) h, z = 0.26, P = 0.79; test of heterogeneity, I^2 = 52%; P = 0.12) - Healthy volunteers: fiber-supplemented enteral feed resulted in significantly faster gastrointestinal transit (Figure 6: test of overall effect, -9.3 (S.E. 2.29) h, z = -4.0, P < 0.001] - Fecal mass: - Healthy volunteers: mean fecal mass was significantly increased following treatment with a fiber-containing feed compared with fiber-free feed: 109 (S.E. 26) g vs. 74 (S.E. 21) g; test of overall effect, 35 g, z = 6.2, P < 0.001; test of heterogeneity, I^2 = 4% (P = 0.41)) - Patients: A meta-analysis of all studies showed a significant increase in fecal mass following fiber supplementation of the feed [test of overall effect, 21.2 (S.E. 6.4) g／day, z = 4.7, P < 0.001; test of heterogeneity, I^2 = 0%, P = 0.50]

5.2 Modifizierte Sondennahrungen

Empfehlung 63

Bei Patienten mit ausgeprägter Malassimilation kann bei Unverträglichkeit von Standardsondennahrung eine niedermolekulare Sondennahrung verwendet werden.

Empfehlungsgrad 0

151. Mundi MS, Velapati S, Kuchkuntla AR et al. Reduction in Healthcare Utilization With Transition to Peptide-Based Diets in Intolerant Home Enteral Nutrition Patients. Nutr Clin Pract 2020; 35: 487-494. doi:10.1002/ncp.10477			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cohort Study 2- JBI 6/8	**Countries:** United States **Centers:** n/a **Setting:** n/a **Funding Sources:** research grant from Nestlé. **Dropout rates:** n/a **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: low Impreciseness: moderate Publication bias: n/a Major limitation is that we were able to capture only data that were present in our EMRs, use of PBDs vs other therapeutic approaches at managing diarrhea was also at the discretion of the clinician, overall baseline primary diagnoses were statistically different when	**Total no. Patients:** 95 **Inclusion criteria:** n/a **Exclusion criteria:** n/a	Retrospective review of our prospectively maintained HEN database was conducted to assess tolerance, efficacy, and impact on healthcare utilization in patients on PBDs. The sample was subdivided into 2 groups: (1) HEN-naïve patients who were started on PBDs directly and (2) patients who were transitioned to PBDs because of intolerance of SPFs.

	compared with the switch group, with the top 2 diagnoses being pancreatic adenocarcinoma and pancreatitis, which could have led to this decision		
Notes	**Author's Conclusion:** The current study showed that PBDs were well tolerated as the initial formula in patients at risk for malabsorption, such as those with pancreatitis. Additionally, we noted that switching to PBDs in SPF-intolerant patients resulted in improved tolerance, as well as a reduction in healthcare utilization. Although PBDs may have increased cost compared with SPFs, these costs can be significantly outweighed by the cost of healthcare utilization, such as clinic visits, ER visits, or hospitalization. Additionally, prospective studies are necessary to confirm these findings in the HEN population and compare with other approaches, such as BTF. However, if confirmed, consideration should be made to transition patients to PBDs sooner if they are at high risk for malabsorption or intolerant to SPFs.		
Outcome measures/results	Symptoms, health care utilization (number of phone calls, emergency room visits, provider visits)	- 53 patients being started directly and 42 patients being transitioned from SPFs. - In patients transitioned to PBDs, symptoms of nausea and vomiting, diarrhea, abdominal pain, and distention improved significantly. - Healthcare utilization also declined significantly, including mean number of phone calls (1.8 ± 1.6 to 1.1 ± 0.9, P = 0.006), mean number of emergency room visits (0.3 ± 0.6 to 0.09 ± 0.3, P = 0.015), and mean number of provider visits (1.3 ± 1.3 to 0.3 ± 0.5, P < 0.0001).	

Empfehlung 64

Eine modifizierte enterale Sondennahrung mit reduziertem Gehalt an schnell resorbierbaren Kohlenhydraten sowie einem Fettanteil aus v. a. ungesättigten Fettsäuren, insbesondere einfach ungesättigten Fettsäuren, sollte bei Patienten mit Diabetes mellitus verwendet werden.

Empfehlungsgrad B

152. Hise ME, Fuhrman MP. The effect of diabetes-specific enteral formulae on clinical and glycemic indicators. Pract Gastroenterol. 2009:20. [413]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Review 2-	**Countries:** n/a **Centers:** n/a **Setting:** Diabetes specific enteral formulae	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	n/a

	Funding Sources: n/a **Dropout rates:** n/a **Study limitations:** n/a		
Notes	**Author's Conclusion:** It is evident from the studies described that the use of a high-fat, lower-CHO DSEF, whether used in tube- or orally-fed patients, are well tolerated and appear to lower postprandial blood glucose levels relative to a higher-CHO, lower-fat diet in patients with DM. Importantly, the use of such high-fat DSEF preparations in these patients did not lead to negative consequences. It is certainly clear from many studies that if glycemic control is improved, either through diet or through insulin delivery, untoward physiological changes can be averted. One would like to assume that if DSEF can lower the postprandial glucose response without altering lipid metabolism, that better patient outcomes will result. Unfortunately, none of the studies to date were able to show statistical evidence for improvement of patient outcomes, nor have most of the studies considered such outcomes as hospital-length-of-stay.		
Relevant recommendations/statements	With respect to available nitrogen and total energy, all of the currently available DSEF differ only marginally from the average standard enteral formula (SEF), and usually provide values ranging from approximately 18%–20% total kcal as protein (approximately 40–60 g/L) and approximately 1,000– 1,500 kcal/L total energy. The major differences between DSEF and SEF involve the relative amounts and percentages of total energy provided in the form of CHO and fat, and, differences in the amount and source of fiber. For DSEF relatively high fat, low CHO formulations yield values that range from approximately 80–120 g/L CHO (35%–50% of total kcal) and approximately 30–60 g/L (35%–50% of total kcal) as fat. The source of CHO in DSEF often includes increased amounts of fructose relative to SEF and can approach 15% of total calories. In addition, the fat in DSEF is usually provided in the form of higher amounts of mono-unsaturated fatty acids (MUFA) relative to SEF, and these fatty acids can represent >60% of the total fat provided. The amount of fiber is typically increased in DSEF relative to SEF and the sources of this fiber are usually fruits, vegetables or soy polysaccharide.		

	Primary endpoint	**Results**
	Fasting blood glucose, HbA_1C, capillary glucose, serum lipids, infection	- DSEF vs SEF demonstrated no difference: fasting blood glucose, HbA1C; - DSEF significantly lower than SEF for capillary glucose at week 1, 5 and 7 - No changes in lipid profile between groups - No difference in adverse events - Non-significant difference in infection rates
	Mean weekly values for: capillary glucose, triglyceride, insulin dose, mean daily insulin dose, GI symptoms	- DSEF vs SEF significantly different for capillary glucose at 1 week, no differences at week 2 - No differences in TG or daily and weekly insulin - No changes in lipid profile between groups - Diarrhea significantly higher in SEF vs DSEF - Nausea was lower in SEF vs DSEF
	Total insulin requirements, fasting blood glucose, HbA1C, GI tolerance and any adverse events	- DSEF vs SEF significantly different for the following: total insulin, fasting blood glucose, HbA1C - Feeding tolerance and adverse events were comparable between groups
	Total insulin requirements, fasting or afternoon blood glucose, HbA1C and safety criteria	- DSEF vs SEF significantly different for the following: - total insulin requirements, fasting blood glucose

		- No difference for HbA1C - Feeding tolerance and adverse events were comparable between groups
	Plasma glucose level, capillary blood glucose, Insulin/day requirements, Secondary endpoints: lipid GI tolerance, any adverse events, days of mechanical ventilation, ICU stay and mortality	- DSEF vs SEF significantly different for the following: plasma glucose levels, capillary blood glucose, insulin/day, insulin/g CHO received, insulin/g CHO received/kg - No differences in lipid profiles or clinical outcomes between groups

153. Craig LD, Nicholson S, Silverstone FA, Kennedy RD, Voss AC, Allison S. Use of a reduced-carbohydrate, modified-fat enteral formula for improving metabolic control and clinical outcomes in long-term care residents with type 2 diabetes: results of a pilot trial. Nutrition. 1998;14(6):529-34. [415]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1-	**Countries:** USA **Centers:** 2 long-term care facilities in New York **Setting:** long-term care residents, enteral nutrition, diabetes type 2 **Funding Sources:** Ross Products Division, Abbott Laboratories, Columbus, Ohio **Dropout rates:** 11.8% (n=4) for evaluation of 4 weeks and 20.6% (n=6) evaluation after 12 weeks **Study limitations:** low number of patients	**Total no. Patients:** n=34 (n=30 evaluable) **Inclusion criteria:** residents at least 50 years, history of type 2 diabetes, documented hyperglycemia (plasma glucose >200 mg/dl or fasting plasma glucose >140 mg/dl on 2 occasions), requiring total enteral nutrition support by tube, were able to tolerate a volume of formula that maintained body weight **Exclusion criteria:** n/a	Comparison: 1. Standard high-carbohydrate formula: n=14 2. Disease specific (DS): n=16 a. reduced-carbohydrate formula b. modified-fat enteral feeding → total nutrition support for 3 months
Notes	- Both formulas contain at least 100% of the US Recommended Daily Intakes for vitamins and minerals in their nutrient bases of about 1400 kcal → Volume of feeding administered to subjects was based on individual requirements and established by standard procedures of the dietary and medical personnel at the institutions - subjects were monitored weekly for changes in weight and formula volume was adjusted to maintain stable body weight **Author's Conclusion:** Overall, subjects randomized to the disease-specific formula experienced better numerical biochemical control and better clinical outcomes when expressed on a numerical and percentage basis. These included surrogate markers of diabetes control such as serum glucose and glycohemoglobin, as well as clinical outcomes such as incidence of infections and pressure ulcers. These findings confirm that the disease-specific formula provides better glycemic control, poses no risk to lipoprotein metabolism, and provides for better clinical outcomes.		

Outcome measures/results	- Metabolic response: glycemic control, lipids - Clinical outcomes: fevers, dehydration, pneumonia, urinary tract infections, skin infections, number and severity of pressure ulcers, hypo- and hyperglycemic events, vomiting diarrhea - Assessments: metabolic response, gastrointestinal tolerance, morbidity, medication usage, time spent by staff on resident care and status regarding clinical safety were made daily, weekly, or every 4 wk. - Daily assessments included gastrointestinal tolerance, morbidity, medication usage, and time spent by staff on resident care - Weekly assessments included preprandial blood glucose obtained via fingerstick three times per week at different times of the day, and weight - Fasting blood samples: baseline, every 4 weeks (serum glucose, HbA1c, serum lipids, routine serum - Use of insulin, oral hypoglycemic agents/medications were recorded daily	- N= 14 DS and n=13 standard formula completed e tire 12-week study - Groups were well-matched for physiologic and demographic parameters at baseline - Age: standard group 80±2 (range 52-100) vs. DS-group 82±3 (range 52-94) - Glycemic control: Fasting serum glucose and capillary (fingerstick) glucose values demonstrated better control in the disease-specific formula-fed group (no statistical differences) - average fasting glucose over study period: standard groupn7.8±0.8 mmol/L and DS group 7.1 ±0.4 mmol/L - HbA1c: numerically better for DS group → 7.0±0.4% standard group vs. 6.5±0.4% DS group - Capillary glucose (fingerstick): consistently higher for standard group → significant differences between groups at week 1 (p=0.05), week 5 (p=0.02) and week 7 (p=0.01) - Serum lipid profiles of this group were similar to or better than those of the standard formula-fed group; HDL 3-month concentration higher for DS group than standard group (p=0.038) - Glucose-lowering medications: amount of insulin administered to insulin-using subjects in the disease-specific formula-fed group was consistently less than before initiation of the formula, whereas the amount administered was consistently higher in the group fed the standard formula (each p=0.09 at weeks 2,5,6,7,8) - Clinical outcomes: for each outcome parameter subjects treated with DS formula were better off clinically than those administered standard formula: - fever → 23.5% of DS group vs. 46.7% of standard group - pneumonia → 6% of DS vs. 13.3% of standard group - overall infections: 58.8% DS vs. 73.3% standard group - no difference in adverse events

6 Nahrungsprodukte zur HPE und deren Anwendung

6.1 „All-in-one-Lösungen“ (AiO)

Empfehlung 65

Mehrflaschensysteme sollen für die HPE wegen höherer Risiken und aufwändigerer Handhabung durch das Personal und den Patienten nicht verwendet werden.

Empfehlungsgrad A

154. Didier ME, Fischer S, Maki DG. Total nutrient admixtures appear safer than lipid emulsion alone as regards microbial contamination: growth properties of microbial pathogens at room temperature. JPEN J Parenter Enteral Nutr 1998;22:291-296. [417]									
level of evidence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
III	prospective, comparative study	Investigation of microorganism growth at 4°C, 25°C & 35°C.	control after: 0, 12, 24, 48, 72 h and 5 d	Laboratory	35	n/a	representative TNA (17.6%, glucose, 5% amino acids, 4% lipids; pH 5.6, osmolarity 1778) & control solution (5% dextrose in water).	25°C/35°C: C. albicans and S. saprophyticus after 24-48 h; Dextrose solution: 2 Gram-negative species: S. marcescens and B. cepacia; TNA: poor culture medium for most MO; 4°C (refrigerator temperature): no growth.	

155. Durand-Zaleski I, Delaunay L, Langeron O, et al. Infection risk and cost-effectiveness of commercial bags or glass bottles for total parenteral nutrition. Infect Control Hosp Epidemiol 1997;18:183-188. [418]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	comparative study	Comparison of costs and medical benefits between conventional plastic bags (change 1x/d) and glass bottles (change 3x/d).	Length of the respective hospital stay	clinic	3	n/a	All TPN, One patient with Crohn's disease (IG1), one ICU patient (IG2), one other risk of nosocomial infection (CG)	Risk reduction of nosocomial bacteremia by TPN in pouch when threshold reaches 0.3%: in KG, not in IG1, slightly in IG2; Absolute reduction in infections: from 10% to 3%; Cost of bags: IG2 $90000 to $7000/life saved, (with 2/3 reduction in infections) or $180000 to $14000 (with 1/3 reduction in infections)	

156. Frei A, Dinkel R, Kemen M, et al. A new model for economic studies of therapies exemplified by postoperative parenteral nutrition. Zentralbl Chir 1997;122:358-65; discussion 366. [419]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	Comparative study	Two-chamber bag system in PN (KH+AS as fixed combination, fat separately) (IG) vs. comparative system: combi-nation of building block/multi-bottle system in PN (individual substrates	10 d (4 d in intensive care unit, 6 d in normal	ICU, normal ward	n/a	n/a	Individuals with the same duration of PN, comparable energy	Total cost: IG 2324.41 DM vs. CG 2728.99 DM → -14.82%; Nursing costs: IG 417.41 DM vs. CG 616.92 DM; material costs: IG 72.93 DM vs. CG 195.68 DM;	

		amino acids, carbohydrates, fats supplied separately) (CG).	care unit)				levels, nutrient ratios, electrolytes, trace elements, vitamins, PN in postoperative situation after major upper abdominal surgery.	total services nursing staff: IG 78 vs. CG 172; Total services physicians: IG 28 vs. CG 28; daily costs in intensive care unit: IG 337.71 DM vs. CG 382.64 DM; daily costs in normal care unit: IG 205.90 DM vs. CG 267.87 DM; substrate costs in KG 25.29 DM more expensive	

157. Pichard C, Schwarz G, Frei A, et al. Economic investigation of the use of three-compartment total parenteral nutrition bag: prospective randomized unblinded controlled study. Clin Nutr 2000;19:245-251. [420]

level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	prospective, randomized, controlled	Cost comparison (working time, nutrient solution, medical supplies): 1. separate nutrition bags (SB) 2. nutrient mixtures manufactured in the hospital (HCB) 3.3 Three-chamber bags (TCB)	6 months	ICU or gastrointestinal surgery	60	n/a	TPN	Cost: TCB < SB (120%) < HCB (150%); SB more labor time required.	HCB: more expensive, because of mixture production

Empfehlung 66

Das Zuspritzen von Elektrolyten (Elektrolytkorrekturen) und Supplementen (z. B. Glutamin, Omega-3-Fettsäuren, Vitamin B1, Zink u. a.) in industriell hergestellten Mehrkammerbeuteln sollte nach den Vorgaben der Hersteller bzgl. Stabilität und Kompatibilität bzw. nach Prüfung durch einen Pharmazeuten erfolgen.

Empfehlungsgrad B

158. Watrobska-Swietlikowska D. Compatibility of Maximum Inorganic and Organic Calcium and Phosphate Content in Neonatal Parenteral Solutions. Sci Rep 2019; 9: 10525-10525. doi:10.1038/s41598-019-46987-y [443]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Pharmacological study n/a	**Countries:** Poland **Centers:** n/a **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	Twelve basic (without calcium and phosphate salts) PN solutions were prepared aseptically following international recommendations under a laminar airflow hood in a class A horizontal laminar-airflow hood. Single-chamber, monolayer ethylene vinyl acetate bags, Exacta-Mix Eva Bag Parenteral, constituting the packaging of PN solutions was used. For this purpose, a Baxa 24 computer-controlled mixer was applied, allowing for precise transfusion following base fluids, i.e., 40% dextrose solution (B. Braun Melsungen, Germany), amino acids solution (Aminoven Infant 10% or Vaminolact, Fresenius Kabi, Uppsala, Sweden or Primene 10%, Baxter Deutschland GMBH, Germany), water for injections, sodium chloride (Natrium chloratum 10%, Polpharma, Starogard Gdański, Poland), potassium chloride solution (Kalium chloratum 15%, WZF Polfa, Warsaw, Poland), magnesium sulfate solution (Inj. Magnesii sulfurici 20%, Polpharma, Starogard Gdański, Poland) and trace elements (Peditrace, Fresenius Kabi, Uppsala, Sweden). No lipids were added because they would obscure the presence of a precipitate. Each of the twelve of PN solutions was prepared triplicate and was tested for compatibility using various concentrations of amino acid solutions and glucose.
Notes	**Author's Conclusion:** The maximum safe combination of calcium and phosphate for each investigated composition of PN solution, even in the worst-case situations, was proposed. This work is valuable in daily practice as it allows an increase in the limits of calcium and phosphate in PN solutions for infants. This study provides valuable data on the compatibility of inorganic and organic calcium salts with inorganic and organic phosphate salts in various combinations in PN solutions compounded for neonates. This data adds to the literature information which may be used to evaluate different options for administering calcium and phosphate in neonatal PN solutions. This may be valuable information when there is a shortage of PN organic additives of calcium and phosphate. It should be pointed out that any change in the composition of PN solutions needs a new analysis.		

Outcome measures/results	Visual inspection, microscopic observation, pH measurement, absorbance measurement, risk curves	Organic calcium and phosphate doses that did not cause opalescence were determined. Depending on the PN solution, they ranged from 50 mmol/L – 90 mmol/L after 24 hr. at 37°C. An amorphous, spongy precipitate, forming larger agglomerates was present in PN solutions with organic calcium and phosphate ions at concentrations above the therapeutic range. The pH of the PN solutions ranged from 5.23 to 7.18 Higher concentrations of organic calcium and phosphate ions were characterized by the highest pH values. There was no relationship between the presence of precipitation and a change in pH values. PN solutions with calcium and phosphate with no visual changes as well as with turbidity were examined in the visible light range. Absorbance at 600 nm was in the range of 0.0001–0.0120 for most of the samples. Absorbance above 0.1000 was measured for turbidity samples with precipitate. Using spectrophotometric measurement as well as visual and microscopic observation, maximum, safe for therapeutic use, calcium and phosphate ions concentrations were determined to ensure no precipitation at t = 24 hr. (37 °C).

159. Aeberhard C, Steuer C, Saxer C, Huber A, Stanga Z, Muhlebach S. Physicochemical stability and compatibility testing of levetiracetam in all-in-one parenteral nutrition admixtures in daily practice. European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences. 2017;96:449-55. [444]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Pharmaceutical trial no Level of evidence possible according to SIGN	**Countries:** n/a **Centers:** n/a **Setting:** laboratory medicine unit of the Cantonal Hospital **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** these results are related to PN regimen without vitamins or trace elements and the need for (home)PN; only one specialty of LEV and only two different PN were checked	**Total no. Patients:** n/a **Inclusion criteria:** n/a **Exclusion criteria:** n/a	- different concentrations of LEV were injected into two different all-in-one (AiO) PN admixture - stability and compatibility tests for the drug and the PN admixtures were performed over seven days at +4 °C, +23 ± 1 °C and +37 °C without light protection

Notes	**Author's Conclusion:** LEV showed compatibility and stability over seven days in the selected PN admixtures, and the described methods represented a valuable and timely approach to determine the stability and compatibility of the highly hydrophilic, not dissociated LEV in AiO admixtures under conditions of use.	
Outcome measures/results	compatibility and stability of LE	- the stability controls of LEV at different temperatures were within absolute ±20% of the theoretical value in a concentration range of 98.91–117.84% of the initial value - no changes in pH occurred (5.55 ± 0.04) and no microscopic out of specification data or visual changes were observed - the mean value of the largest lipid droplet in each visual field over seven days was 2.4 ± 0.08µm, comparable to that of the drug-free AiO admixture

6.2 Anwendung von AiO-Lösungen

<u>Empfehlung 124</u>

Die Glukosezufuhr unter HPE sollte beim Erwachsenen 2–4 g/kg/d betragen.

Empfehlungsgrad B

160. Lakananurak N, Tienchai K. Incidence and risk factors of parenteral nutrition-associated liver disease in hospitalized adults: A prospective cohort study. Clin Nutr ESPEN. 2019;34:81-86. [462]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Prospective observational study 2+	**Countries:** Thailand **Centers:** King Chulalongkorn Memorial Hospital **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** First, some causes of liver injuries such as infection are very difficult to exclude. Nevertheless, PNALD is recognized as liver	**Total no. Patients:** 44 **Inclusion criteria:** Patients aged 18 years or more who were expected to receive PN for at least 14 days **Exclusion criteria:** patients who had a history of liver diseases, abnormal liver tests and PN termination before 14 days without having any abnormalities of liver tests	Parenteral nutrition

	dysfunction in patients receiving PN that results from a complex set of risk factors. Additionally, infection is considered as one of the risk factors for PNALD rather than a distinctive cause of liver diseases. Second, liver biopsy was not done in this study because of its potential complications and no pathognomonic finding for the diagnosis of PNALD		
Notes	**Author's Conclusion:** PNALD was very common and occurred in around two-thirds of the adults receiving PN in acute care setting. In contrast to previous studies, cholestasis was more common than steatosis, and the median onset was not different between each subtype. In severely malnourished patients, physicians need to exercise caution and monitor for PNALD, intensively. Excess amount of carbohydrate should be avoided and administration of carbohydrates less than 4 g/kg/day should be considered.		
Outcome measures/results	AST, ALT, ALP, onset of PNALD, SGA, amount of energy, amount of carbohydrate, amount and type of fat, incidence and type of infection		Overall, 26 patients developed abnormal liver tests during the monitoring period. The possible causes of liver diseases, including viral hepatitis, drugs and toxins, ischemic hepatitis, and biliary obstruction, were evaluated and 25 patients had negative results. Overall, the incidence of PNALD in patients who received PN was 59.1% (26/44 patients). 22.7% (10/44 patients) had steatosis subtype, 34.1% (15/44 patients) had cholestasis subtype, and 2.3% (1/44 patients) had mixed subtype. The median onset of abnormal liver tests after receiving PN was 12.5 days (range: 4-42). The risk factor for developing PNALD was severe malnutrition assessed by SGA (SGA C). Severe malnutrition was significantly higher in patients with PNALD than patients without PNALD (p ¼ 0.001). Other risk factors such as mean energy (34.2 kcal/kg/day vs. 25.9 kcal/kg/day, p ¼ 0.006), mean carbohydrate (3.1 g/kg/day vs. 5 g/kg/day, p ¼ 0.001), and mean fat (0.9 g/kg/day vs. 1.3 g/kg/day, p ¼ 0.001) were also significantly higher in patients with PNALD

161. Wu G, Jiang Y, Zhu X, Jin D, Han Y, Han J, Wu Z, Wu Z. Prevalence and risk factors for complications in adult patients with short bowel syndrome receiving long-term home parenteral nutrition. Asia Pac J Clin Nutr. 2017;26:591-597. [55]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective observational study 2+	**Countries:** China **Centers:** n/a **Setting**: Clinical nutrition center **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Due to the limited number of patients, the results of this study should be interpreted with caution.	**Total no. Patients:** 47 **Inclusion criteria:** 1) patients diagnosed as SBS at the ages >18 years, 2) patients received HPN for more than 2 years. **Exclusion criteria:** 1) patients diagnosed as SBS at the ages <18 years, 2) patients with evolving primary malignancies either present at the time of short bowel occurrence or recurring during follow-up, 3) patients with liver/biliary abnormalities diagnosed before the initiation of HPN or identified as unrelated to HPN (i.e. inborn liver disease, acquired toxic or viral liver disease), and 4) patients that have discontinued HPN within 2 years	Parenteral nutrition
Notes	**Author's Conclusion:** In conclusion, our study described a series of adult patients with SBS receiving long-term HPN for more than 2 years over a period of 30 years and focused on the prevalence and risk factors of catheter-related sepsis and HPN associated liver/biliary disorders. However, due to the limited number of patients, the results of this study should be interpreted with caution. Further research is recommended in other clinical nutrition centers to further elucidate the prevalence and risk factors of HPN-associated complications in adult patients with the SBS receiving long-term HPN. Furthermore, the best treatment methods of these complications should be assessed in further studies.		
Outcome measures/results	Data related to the current program of HPN, venous catheter, biochemical and imaging examination, hospital stays, and cause of death, average value of HPN characteristics regarding the composition, volume, frequency, and duration time of the infusions		Most of the patients (32/47) applied traditional central venous catheter (CVC) to receive HPN while only 15 patients (15/47) applied peripherally inserted central venous catheter (PICC). The overall duration mean HPN was 8.13±4.81 years with HPN onset at ages of 45.1±14.8 years. In particular, 16 patients (34.0%) had HPN duration longer than 10 years, and the longest HPN duration was 30 years. The mean daily infusion time was 12.6 hours, and the mean HPN infusion time was 5.42 days per week. All patients received oral/enteral nutrition in our study. The delay between HPN onset and the first catheter infection was 1.02±0.46 years. The mean parenteral

		energy intake was 20.1 kcal/kg/d and the mean volume was 33.6 mL/kg/d. The composition of the parenteral nutrition varied with a mean glucose 3.01 g/kg/d (accounting for 59.1% non-protein calories) and 0.91 g/kg/d lipid (accounting for 38.8% non-protein calories), respectively. The entire study population was divided into two groups according to whether the HPN-associated liver/biliary disorders were present or not. Risk factors for biochemical liver/biliary disorders included a higher rate of catheter-related infections (p=0.009), shorter delay between HPN onset and the first infection (p=0.017), higher energy content of HPN (p=0.014), higher glucose rate of HPN (p=0.009), and lower lipid rate of HPN (p=0.022).

Empfehlung 67

Die zyklische Applikationsform sollte gegenüber der kontinuierlichen Applikationsform bevorzugt werden, weil dadurch die Gefahr von Infektionen und hepatischen Komplikationen reduziert werden kann.

Empfehlungsgrad B

162. Arenas Villafranca JJ, Nieto Guindo M, Álvaro Sanz E et al. Effects of cyclic parenteral nutrition on parenteral-associated liver dysfunction parameters. Nutr J 2017; 16: 66-66. doi:10.1186/s12937-017-0289-7			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective observational study 2+ JBI 6/8	**Countries:** Spain **Centers:** Costa del Sol Hospital **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of bias: moderate Inconsistency: n/a Indirectness: low Impreciseness: moderate	**Total no. Patients:** 37 **Inclusion criteria:** inpatients ≥18 years who initially received continuous parenteral nutrition and were subsequently prescribed with cPN following a decision of the team of artificial nutrition based on the local PN management protocol **Exclusion criteria:** severe liver disease evidenced by abnormal biochemical hepatic parameters, a	cyclic parenteral nutrition (cPN)

	Publication bias: n/a	history of renal failure, death during treatment or a duration of cPN ≤ 4 days	
Notes	**Author's Conclusion:** The administration of cPN was effective in reducing significantly abnormal hepatic biochemical values to normal levels, including AST, GGT, and total bilirubin, and in reducing almost significantly ALT levels. However, no changes were observed in ASP. The results obtained suggest that the administration of cPN is effective in reverting parental-associated liver dysfunction.		
Outcome measures/results	Qualitative parameters: sex, diagnosis at admission, indication of PN, hepatic comorbidities, start date of cPN, presence of insulin in cPN, infection during cPN and management of liver dysfunction prior to the administration of cPN (addition of taurine to the amino acid solution, reversal of the dietary carbohydrate/lipid ratio of PN composition, and reduction of carbohydrate and/or lipid supply). Quantitative parameters: age and biochemical parameters including AST, ALT, GGT, ALP, and total bilirubin that were measured at baseline and at completion of cNP using validated techniques		In all, 43.2% of patients received some treatment to manage LD prior to cPN. The lipid and carbohydrate supply was reduced in 8% of patients, and taurine was added to the amino acid emulsion in 38%. However, no significant improvements were achieved in any hepatic parameter through these interventions. Following cPN, an improvement in all hepatic function parameters except ALP was observed, as shown in, with statistically significant differences in AST ($p < 0.05$), GGT ($p < 0.05$) and total bilirubin ($p < 0.05$). No correlation was observed between improvements in hepatic function parameters and any demographic variable (age, sex, weight and BMI), neither with cPN duration. In total, 35% of patients had a hepatic comorbidity. Improvements in hepatic parameters were not found to be correlated with any previous comorbidity. The only exception was total bilirubin, which reduction was significantly greater in patients with high baseline total bilirubin levels. No correlation was observed either between the development of infection (54%), insulin supply through cPN (43%), enteral stimulus (54%) and the reduction in hepatic parameter values.

<u>Empfehlung 68</u>

Zur Prävention und Therapie hepatischer Komplikationen unter HPE sollten alternative Fettemulsionen, die neben Sojaöl weitere Öle wie MCT-, Oliven- oder Fischöl enthalten, verwendet werden.

Empfehlungsgrad B

163.	**Pradelli L, Mayer K, Klek S et al. omega-3 Fatty-Acid Enriched Parenteral Nutrition in Hospitalized Patients: Systematic Review With Meta-Analysis and Trial Sequential Analysis. JPEN J Parenter Enteral Nutr 2020; 44: 44-57. doi:10.1002/jpen.1672 [475]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review and Meta-Analysis 1++ AMSTAR2 12/16	**Countries:** n/a **Centers:** n/a **Setting:** n/a **Funding Sources:** Fresenius Kabi GmbH. **Dropout rates:** n/a **Study limitations:** Overall confidence in the results of the review: Critically Low Risk of bias of single studies: moderate Inconsistency: low Indirectness: high Impreciseness: moderate Publication bias: n/a	**Total no. Studies:** 49 (3641 patients) **Inclusion criteria:** human studies of adult hospitalized patients who were eligible to receive PN covering at least 70% of their total energy provision; Intervention with omega-3 enriched PN, RCT containing at least 1 predefined outcome **Exclusion criteria:** enteral nutrition, "off-label" interventions, studies where EN provided >30% of daily calories	Investigation of ω-3 fatty-acid enriched parenteral nutrition (PN) vs standard (non-ω-3 fatty- acid enriched) PN in adult hospitalized patients
Notes	**Author's Conclusion:** Study provides clear evidence that omega-3 fatty-acid enriched PN provides significant clinical and nonclinical benefits over standard non-ω-3 fatty-acid enriched PN in adult hospitalized patients		
Outcome measures/results	**Primary outcome**: Infection rate **Co-primary outcomes**: mortality rate length of hospital stay, length of intensive care unit stay, sepsis rate, hospital readmissions, intensive care unit-free days until day 30 or day 60, and ventilation-free days until day 30	- relative risk of infection was 40% lower with ω-3 fatty- acid enriched PN than standard PN (RR 0.60, 95% confidence interval [CI] 0.49-0.72; P < 0.00001) - Patients given ω-3 fatty-acid enriched PN had reduced mean length of intensive care unit stay (10 RCTs; 1.95 days, 95% CI 0.42-3.49; P = 0.01) and reduced length of hospital stay (26 RCTs; 2.14 days, 95% CI 1.36-2.93; P < 0.00001) - Risk of sepsis (9 RCTs) was reduced by 56% in those given ω-3 fatty-acid enriched PN (RR 0.44, 95% CI 0.28-0.70; P = 0.0004) - Mortality rate (co-primary outcome; 20 RCTs) showed a nonsignificant 16% reduction (RR 0.84, 95% CI 0.65-1.07; P = 0.15) for the ω-3 fatty-acid enriched group	

164. Mundi MS, Kuchkuntla AR, Salonen BR et al. Long-Term Use of Mixed-Oil Lipid Emulsion in Soybean Oil–Intolerant Home Parenteral Nutrition Patients. Journal of Parenteral and Enteral Nutrition 2019; 44: 301-307. doi:10.1002/jpen.1526 [477]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case series 3	**Countries:** USA **Centers:** Mayo Clinic **Setting:** patients on HPN **Funding Sources:** n/a **Dropout rates:** **Study limitations:** no RCT, no blinding	**Total no. Patients:** 17 **Inclusion criteria:** Intolerance to soybean oil intravenous lipid emulsion (SO ILE) defined as individuals with abnormal liver studies, hyperglycemia, or hypertriglyceridemia or individuals who experienced reported side effects during SO ILE infusion (examples include complaints of nausea or headache during lipid infusion), willingness to transition to mixed-oil intravenous lipid emulsion (MO ILE) **Exclusion criteria:** hypersensitivity to egg, soybean proteins, fish, or peanut proteins	Use of MO ILE for longer than 12 months
Notes	**Author's Conclusion:** ILE remains an integral part of PN as a major source of nonprotein energy and essential fatty acids. However, with long-term use of SO ILE–containing PN, some patients can develop complications such as IFALD. Our case series revealed that transition to MO ILE in these patients is a viable long-term option that allows for reduction in dextrose energy while leading to stability in some metabolic and liver parameters and producing an improvement in others. Long-term prospective RCTs in HPN patients are needed to assess the impact of MO in terms of liver function, inflammation, and lipid and glucose metabolism.		
Outcome measures/results	laboratory tests, liver function tests,		All 17 patients tolerated MO ILE well and maintained their BMI as well as total energy provided per day. There was an improvement in aspartate aminotransferase (AST; 56 [20–289] to 39 [16–140], P-value of 0.02), alanine aminotransferase (ALT; 66 [20–401] to 52 [17–79], P-value of 0.04), and total bilirubin (1.1 [0.2–4.2] to 0.6 [0.2–2.5], P-value of 0.02).

165.	**Klek S, Szczepanek K, Scislo L, Walewska E, Pietka M, Pisarska M, et al. Intravenous lipid emulsions and liver function in adult chronic intestinal failure patients: Results after 5 y of home parenteral nutrition. Nutrition. 2021;82:111029. [478]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1- ROB 5/7	**Countries:** Poland **Centers:** Intestinal Failure Center in Skawina, Poland **Setting:** n/a **Funding Sources:** Fresenius Kabi Deutschland GmbH **Dropout rates:** 3% **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: low Impreciseness: moderate Publication bias: n/a Lack of an intention-to-treat analysis and incomplete assessment of laboratory parameters.	**Total no. Patients:** 67 **Inclusion criteria:** adults (≥ 18 y of age) with CIF who were receiving PN including lipids and were metabolically stable (the absence of pathologic laboratory resulting in the change of PN regime for ≥ 1 mo.) and able to tolerate ≥ 1 g lipids/kg body weight daily as a part of PN **Exclusion criteria:** preexisting liver dysfunction; history of cancer and anti-cancer treatment with in the previous 5y; severe hyperlipidemia; severe coagulopathy; severe renal insufficiency; acute thromboembolic events; positive test for HIV, hepatitis B, or hepatitis C; known or suspected drug or alcohol abuse; participation in another interventional clinical trial in parallel or within 3 mo. before the start of the present study; women of childbearing potential (i.e., women who were not chemically or surgically sterile or who were not postmenopausal) or women of childbearing potential with a positive result on a standard pregnancy test and/or lactation	Study treatment was administered as part of HPN for a period of 60 mo. ILEs were mixed with other PN components in the compounding unit of Skawina Hospital Pharmacy and delivered via a central venous catheter in an all-in-one admixture that included amino acids, glucose, electrolytes, vitamins, and trace elements. For each patient, the required nutritional supply was calculated per day (protein: 1-1.2 g/kg; energy: 25-35 kcal/kg). The target daily lipid dose was 0.6 to 0.8 g/kg. All patients were allowed to consume provided food orally but oral intake of nutrients did not exceed 10% of the whole energy and protein intake, as assessed by a dietitian. Eligible patients were randomly assigned to receive HPN with one the following ILEs: MCT/LCT 50:50 (Lipofundin MCT/LCT, B Braun, MCT/LCT group), OO/SO 80:20 (ClinOleic, Baxter Healthcare, OO/SO group); SO/MCT/OO/FO 30:30:25:15 (SMOFlipid, Fresenius Kabi, SMOF group).
Notes	**Author's Conclusion:** Comprehensive evaluation of outcomes during an observation period of 5 y showed that mixed ILEs are safe and effective in patients with CIF requiring HPN. TBIL concentrations at 5 y were significantly lower among patients receiving a FO-containing ILE than in those receiving mixed ILEs		

	without FO, suggesting that FO- containing ILEs might be more advantageous with regard to preservation of liver function than mixed ILEs without FO during long- term PN in patients with CIF.	
Outcome measures/results	clinical and biochemical measures of liver function at 24 and 60 mo. after initiating study treatment; safety	- The most common etiology for CIF was vascular, followed by Crohn's disease, surgical complications, and radiation enteritis. - HPN was effective in improving nutritional status and was associated with low rates of catheter infections and clinical complications. - No significant differences were observed between groups in median concentrations serum glutamyl oxalate transaminase, serum glutamyl pyruvate transaminase, g-glutamyl transpeptidase, or alkaline phosphatase at 24 or 60 mo. - A significant reduction in median bilirubin concentration was observed in the SMOFlipid group at 60 mo. compared with baseline (6.8 µmol/L; interquartile range, 5.2-8.5 versus 7.7 µmol/L; interquartile range, 4.9-12.4; P = 0.0138).

Empfehlung 128

Zur Prophylaxe und Therapie einer Osteomalazie, Osteopenie bzw. Osteoporose unter HPE sollte eine optimierte Kalzium-, Phosphat-, Magnesium- und Vitamin-D-Zufuhr erfolgen.

Empfehlungsgrad B

166. Rondaij T, Kozjek NR, Popovič P et al. Vitamin D deficiency in patients with chronic intestinal failure on home parenteral nutrition. Clinical nutrition ESPEN 2021; 42: 258-261. doi:10.1016/j.clnesp.2021.01.026 [486]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Cross-sectional study JBI 8/8	**Countries:** Slovenia **Centers:** n/a **Setting:** long-term HPN program **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of bias: low Inconsistency: n/a Indirectness: moderate	**Total no. Patients:** 63 **Inclusion criteria:** adult patients, diagnosed with CIF, who were enrolled in a long term HPN program in Slovenia's single approved HPN center between January 2017 and December 2018. **Exclusion criteria:** n/a	

	Impreciseness: moderate Publication bias: n/a small sample size, vitamin D3 supplementation was not equal between all patients, exact data on this could not be attained		
Notes	**Author's Conclusion:** In summary, this study, performed on 63 patients with CIF enrolled in a home parenteral nutrition program, showed a high prevalence of vitamin D deficiency among these patients. Compared to research on healthy adult Slovene population, no significant difference regarding the prevalence of vitamin D deficiency can be observed. To our knowledge, this has been the largest study observing serum vitamin D levels in patients with CIF on HPN therapy. Even though our patients showed a high prevalence of vitamin D deficiency, this study failed to demonstrate an association between serum vitamin D levels and the prevalence of liver steatosis. Additional research is warranted to further explore these findings.		
Outcome measures/results	serum levels of 25-hydroxyvitamin D [25(OH)D], presence and degree of liver steatosis		Liver steatosis was present in 18 (28.6%) patients, of which 1 patient was diagnosed with severe steatosis, 3 patients with moderate steatosis and 14 patients with mild liver steatosis. The average serum concentration of 25-hydroxyvitamin D was 41.3 nmol/l. Severe vitamin D deficiency (<30 nmol/l) was diagnosed in 15 patients (24%) and insufficient vitamin D levels (30e50 nmol/l) were found in 30 patients (48%). Sufficient serum levels of vitamin D were found in 16 patients (26%) and only 1 patient had optimal serum levels (>75 nmol/l). No statistically significant association between absolute serum vitamin D levels and liver steatosis in the study population was found.

167. Napartivaumnuay N, Gramlich L. The Prevalence of Vitamin D Insufficiency and Deficiency and Their Relationship with Bone Mineral Density and Fracture Risk in Adults Receiving Long-Term Home Parenteral Nutrition. Nutrients 2017; 9: 481. doi:10.3390/nu9050481 [482]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective chart review 2+ JBI 8/8	**Countries:** Canada **Centers:** Northern Alberta Home Parenteral Nutrition Program **Setting:** Home parenteral nutrition **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:**	**Total no. Patients:** 186 **Inclusion criteria:** All adult patients followed by the Northern Alberta Home Parenteral Nutrition Program between 2002 and 2014 who required HPN for >6 months were included. **Exclusion criteria:** Patients with underlying malignancy were	All patients routinely received one standard parenteral multivitamin (without vitamin K) which contained 200 IU of vitamin D3 (cholecalciferol) per day. This is less than the Osteoporosis Canada recommendation of 400–2000 IU/day for all adult year round.

	Risk of bias: low Inconsistency: n/a Indirectness: moderate Impreciseness: moderate Publication bias: n/a evaluation of only a single bone mineral density result which may not be an adequate representation of the patient's bone health, different methodologies for vitamin D measurement	excluded from the study as were patients whom serum vitamin D levels and BMD were not recorded in the HPN Registry.	
Notes	**Author's Conclusion:** It is important to monitor vitamin D levels at least at six-month intervals, and adequately supplement with appropriate vitamin D route, such as intramuscular or separate vitamin D parenteral infusion and higher dosages given that the prevalence of vitamin D insufficiency and deficiency in HPN patients is common. In patients on long-term HPN, bone mineral density should be monitored annually and osteoporosis should be treated. Further studies need to be undertaken to establish the appropriate method of delivery, dose and duration of oral vitamin D supplementation in intestinal failure patients Factors such as vitamin K supplementation should also be taken into consideration as it may have potential benefit to bone mineral density.		
Outcome measures/results	Primary outcome: Prevalence of vitamin D sufficiency, insufficiency and deficiency Secondary outcomes: correlation of vitamin D status with bone mineral density and 10-year fracture risk		64.5% had abnormal bone mineral density and the majority of these patients were over 50 years of age. 6.5% had history of fragility fractures. When comparing the patients with fragility fracture to those without fracture, the BMD of all patients with fragility fracture was significantly lower than the no fracture group ($p < 0.001$). The HPN duration and oral vitamin D supplement dosage were not statically significantly different amongst those with fragility fracture compared to those without fracture. However, the vitamin D level was significantly higher in those patients with fragility fractures, 35.5 ± 9.45 ng/mL (88.78 ± 23.63 nmol/L) compared to those 24.92 ± 9.12 ng/mL (62.3 ± 22.8 nmol/L) without fracture group ($p = 0.029$). All patients with fragility fracture had received parenteral bisphosphonate infusion. HPN patients age <50 years old had similar vitamin D levels in the normal BMD group compared to the abnormal BMD group ($p = 0.45$). In HPN patients >50 years old, the vitamin D level was higher in those with osteopenia and osteoporosis compared to the normal BMD group but this was not statistically significant ($p = 0.31$). The mean vitamin D levels were considered suboptimal in all groups and were the lowest in the low fracture risk group, 23.9 ± 9.92 ng/mL (59.73 ± 24.80 nmol/L). Those patients with highest fracture risk did not have a lower mean vitamin D level than those with lowest fracture risk. The ten-year fracture risk did not correlate with vitamin D level.

Empfehlung 129

Bisphosphonate sollten zur Therapie einer verminderten Knochendichte unter HPE eingesetzt werden.

Empfehlungsgrad B

168. Cauley JA, Black D, Boonen S et al. Once-yearly zoledronic acid and days of disability, bed rest, and back pain: randomized, controlled HORIZON Pivotal Fracture Trial. J Bone Miner Res 2011; 26: 984–992 [490]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
Ib	randomized, controlled	15-minute intravenous administration of 5 mg zoledronic acid (IG), placebo (CG). Telephone interviews and clinic visits every 6,12,24 & 36 months.	3 years	At home / hospital	7736	65-89 years	Postmenopausal women	Back pain: IG -18 d vs. CG; decreased activity: IG -11 d vs. KG.	All: daily oral calcium intake of 1000-1500 mg & 400-1200 IU vitamin D.

169. Haderslev KV, Tjellesen L, Sorensen HA et al. Effect of cyclical intravenous clodronate therapy on bone mineral density and markers of bone turnover in patients receiving home parenteral nutrition. Am J Clin Nutr 2002; 76: 482–488 [491]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
Ib	randomized, controlled	Intravenously 1500 mg clodronate in 1500 mL isotonic NaCl solution every 3 months (IG), placebo (CG)	12 months	At home	20 (IG 10, CG 10)	CG 43±12, IG 41±12	HPN patients, BMD T score of lumbar spine or hip < -1; exclusion criteria: Renal insufficiency	BMD of the lumbar spine ↑: IG +0.8 ± 2.0% vs. KG -1.6 ± 2.0%, BMD of the hip↑: IG +1.6 ±3.0% vs. KG -1.8 ± 2.2%, Biochemical markers of bone resorption ↓	Clondronate infusion was well tolerated; all: vitamin D supplements.

							, bone metabolism affected by disease or medication, ≥ 3 alcohol. Drinks/d, pregnancy, lactating		

170. Cummings SR, San Martin J, McClung MR et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med 2009; 361: 756–765 [494]									
level of evi-dence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
Ib	randomized, controlled	all: 1000 mg calcium/day; 800 IU Vit. D/d , 400 IU Vit. D/d; subcutaneously 60 mg denosumab (IG) or placebo (CG) every 6 months.	36 months	n/a	7,868 women (IG 3,933, CG 3,935)	60-90 years	BMD T score of lumbar spine or hip < -2.5 but > -4.0 → osteoporosis , exclusion criteria: Affected bone metabolism, oral intake of bisphosphat e for > 3 years, serum 25-	Risk of new radiographic vertebral fracture ↓: IG 2.3% vs. KG 7.2% → reduction of 68%, Risk of new hip fracture ↓: IG 0.7% vs. KG 1.2% → decrease by 40%, Risk of new non-vertebral fracture ↓: IG 6.5% vs. KG 8.0% → reduction of 20%.	No increase in the risk of cancer, infections, cardiovascular disease, delayed healing of fractures, hypocalcemia; no osteonecrosis of the jaw, no adverse reactions to injection of denosumab.

							hydroxyvitamin D level < 12 ng/mL.		

171. Smith MR, Egerdie B, Hernandez Toriz N et al. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Engl J Med 2009; 361: 745–755 [493]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	randomized, multicenter study, controlled	60 mg subcutaneous denosumab every 6 months (IG) or placebo (CG) + ≥ 1 g Ca/day, ≥ 400 IU Vit. D/day.	36 months	n/a	1468 (CG 734, IG 734) → at the end of the study 912	75 (48-97)	Prostate cancer patients, BMI 15-45, androgen-deprivation therapy for at least 12 months.	After 24 mon: BMD in the lumbar region ↑: IG +5.6% vs. CG -1.0%, After 36 mon: new vertebral fractures ↓: IG 1.5% vs. CG 3.9%, > 1 fracture ↓: IG 0.7% vs. CG 2.5%	Serum values =, Hematology values =.

172. Hernandez MV, Peris P, Monegal A et al. Effects of intravenous pamidronate on renal function, bone mineral metabolism and bone mass in patients with severe osteoporosis. Am J Med Sci 2010; 339: 225–229 [492]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
III	prospective, non-controlled	30 mg APD in 500 mL 0.9% saline for 4 h every 3 months for 1 year; recommendation: 500-1000mg Ca/day, 400-800 IU Vit. D/day.	1 year	n/a	17	66,8 ± 9,4	Osteoporosis patients, intolerance or contraindication of oral biphosphate, 82% vertebral	After 1 week: type I collagen ↓: 32% and parathyroid hormone levels↑: 72%, no further change thereafter; BMD development =, new bone fractures in 46%, flu-like symptoms in 41% after APD infusion.	Despite symptoms after APD infusion, overall good tolerance

							fracture, BMI 25.95 ± 6.41.		

173. Szczepanek K, Pedziwiatr M, Klek S. Denosumab Improves Bone Mineral Density in Patients With Intestinal Failure Receiving Home Parenteral Nutrition: Results From a Randomized, Controlled Clinical Trial. JPEN J Parenter Enteral Nutr. 2018;42:652-657. [495]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+ ROB 5/7	**Countries:** Poland **Centers:** n/a **Setting:** n/a **Funding Sources:** none **Dropout rates:** 34.7% **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: low Impreciseness: moderate Publication bias: n/a	**Total no. Patients:** 49 **Inclusion criteria:** type III IF, benign underlying disease, HPN for a period not shorter than 12 months, age >18 years, and full DXA scanning at baseline **Exclusion criteria:** cancer as an underlying disease for type III IF and type I or II IF	Patients were randomly assigned to either the denosumab or control group. Intervention group: patients receiving a single dose of 60 mg denosumab (1 mL = 60 mg) injected subcutaneously in the thigh, abdomen, or arm and repeated after 12 months in all patients Control group: patients subjected to observation only The study period involved 12 months of intervention and 12 more months of observation, during which all patients were supposed to undergo DXA scanning of the lumbar part of the spine and femur.
Notes	**Author's Conclusion:** To our knowledge, this is the first randomized trial on the clinical efficacy of denosumab in HPN patients. The results suggest that it may be used as a successful anti-MBD treatment. However, several issues must be considered: for example, the need for more clinical studies in various patient groups and the question of reimbursement for denosumab.		
Outcome measures/results	primary outcome: T score and z score in select locations and bone mass density of L1–L4 and the femur secondary outcome: assessment of the tolerance of the treatment		- At baseline and after 12 months, the absorptiometry revealed T scores of −3.439 standard deviations (SD) vs −2.33 SD at lumbar segment 2 (L2) and −2.957 SD vs −2.067 SD at lumbar segment 3 (L3), z scores of −2.24 SD vs −1.36 SD at L2 and −1.995 vs −1.067 SD at L3, and BMD of 0.801 vs 0.946 at L2 and 0.857 vs 0.979 at L3, respectively. - The treatment tolerance was satisfactory: only 1 person (56-year-old woman) in the intervention group complained of sciatica and withdrew her consent. There were no other complaints or adverse events in the remaining patients. - Two serious outcomes were reported, without any correlation to the intervention. Two patients were weaned off HPN and hence discontinued. One patient experienced sciatica, resulting in discontinuation of the intervention.

Empfehlung 130

Wenn eine bedarfsdeckende HPE unvermeidlich zu einer Hyperglykämie führt, kann eine gleichzeitige Therapie mit Insulin, z. B. im HPE-Beutel supplementiert, durchgeführt werden.

Empfehlungsgrad 0

174. McCulloch A, Bansiya V, Woodward JM. Addition of Insulin to Parenteral Nutrition for Control of Hyperglycemia. JPEN J Parenter Enteral Nutr 2018; 42: 846-854. doi:10.1177/0148607117722750 [498]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review 2- AMSTAR2 2/16	**Countries:** n/a **Centers:** n/a **Setting:** parenteral nutrition **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of bias of single studies: n/a Inconsistency: low Indirectness: high Impreciseness: high Publication bias: n/a	**Total no. Patients:** n/a **Inclusion criteria:** Studies that evaluated any aspect of the addition of insulin into PN **Exclusion criteria:** no relevance to the topic, general review articles on hyperglycemia management in PN, studies involving neonates, and conference abstracts	addition of insulin into PN
Notes	**Author's Conclusion:** In conclusion, the few available studies support the use of insulin in PN for hospitalized patients on stable regimens, demonstrating good glycemic control and safety profile. There is no information available on the safety or efficacy of insulin in PN for patients at home, with only 1 report suggesting that this approach may be safe for patients without preexisting diabetes who experience feed-related hyperglycemia. However, given that this practice is relatively common and may significantly benefit such patients, there is a need for the efficacy and safety of this technique to be fully established via larger studies using standard protocols that will allow clear guidance to be formulated.		
Outcome measures/results	n/a		Insulin availability from PN ranges from 44% to 95%. This wide difference is most likely accounted for by the differing PN compositions, PN container material, assay methods, and type of insulin used in the analyses. Another finding to emerge from some of the studies is the differences in insulin availability with the addition or removal of certain constituents in the PN. insulin availability was significantly reduced if it contained the amino acid preparation HepatAmine as compared with FreAmine. The addition of electrolytes and vitamins improved insulin availability.

		Furthermore, the availability of insulin in PN decreases during the infusion: this same study demonstrated that in complete PN, the recovery of insulin was initially 96% 1 hour into the infusion but only 87.3% 1 hour prior to its completion. Various studies demonstrate the effectiveness and safety of insulin addition to PN in different dosages and delivery schemes. As well as efficacy, a key concern about adding insulin directly to PN is the danger of inducing hypoglycemia. The available data, although sparse, suggest that insulin can be delivered safely to inpatients who are being carefully monitored. There are no other reports in the literature of the use of insulin added to PN in the home environment or for longer periods.

175. McCulloch A, Bansiya V, Woodward JM. The addition of insulin to home parenteral nutrition for the control of hyperglycaemia: A case series. Clinical nutrition ESPEN 2019; 30: 204-207. doi:10.1016/j.clnesp.2018.11.014 [499]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Case series 3	**Countries:** UK **Centers:** n/a **Setting:** long-term HPN **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** n/a	**Total no. Patients:** 4 **Inclusion criteria:** receiving insulin by addition to HPN for three years or more **Exclusion criteria:** n/a	- commencement of insulin therapy in an inpatient setting - Insulin added to PN when BG values have stabilized for at least 24 h on variable rate intravenous insulin infusion - two thirds of the insulin required in the subsequent 24 h period is added to PN - the remaining insulin requirements are provided by once daily injection of long-acting subcutaneous insulin - If the patient is able to eat, then additional rapid acting subcutaneous insulin may be administered prior to food - Dosing changes are reviewed on a daily basis by the hospital's diabetes team. - PN is mixed by specialist pharmacists and only short acting human insulin is added to the PN solution - prior to discharge the patient or carer must be able to inject the required dosage of insulin directly into the bag of PN prior to starting each infusion using aseptic technique
Notes	**Author's Conclusion:** This report demonstrates that this route of insulin administration in PN-related hyperglycemia can be safe and effective in the homecare setting. Further studies are needed in the HPN cohort to make safe recommendations for the application of this technique in clinical practice.		
Outcome measures/results	HbA1c level		Case 1: Glycemic control was notably better with the addition of insulin to the PN and deteriorated significantly after the reversion to subcutaneous insulin administration.

		Case 2: Excellent glycemic control was maintained for 17 years until his death. He had no recorded admissions for hypoglycemia. Case 3: No hospital admissions with hypoglycemia were recorded during this time and she was able to maintain a good quality of life, undergoing teacher training and enjoying foreign holidays. Case 4: Blood glucose readings remained well controlled while on PN (4e9 mmol/l) and background insulin was progressively titrated to reduce inter-feed hyperglycemia. She continued this practice until her death at age 56 liver disease.

176. Olveira G, Abuín J, López R et al. Regular insulin added to total parenteral nutrition vs subcutaneous glargine in non-critically ill diabetic inpatients, a multicenter randomized clinical trial: INSUPAR trial. Clin Nutr 2020; 39: 388-394. doi:10.1016/j.clnu.2019.02.036 [500]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1+ ROB1 4/7	**Countries:** Spain **Centers:** 26 centers **Setting:** n/a **Funding Sources:** Instituto de Salud Carlos III (ISCIII, co-funded by FEDER, EU, "Una manera de hacer Europa"), Ministerio de Ciencia, Innovación y Universidades, Gobierno de Espa~na (PI15/01034), and SAEDYN 2016 research project. **Dropout rates:** 8.6% **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: high Impreciseness: moderate Publication bias: n/a Inequally distributed recruitement rate, probably	**Total no. Patients:** 163 **Inclusion criteria:** adult (>18 years) hospitalized non-critically ill (i.e., patients in non-intensive care unit setting) type 2 diabetes patients who planned to start with TPN (considering it provides more than 70% of the estimated total energy expenditure using Harris-Benedict equation taking into account stress factor) for any cause for at least 5 days **Exclusion criteria:** they were in intensive care units, were type 1 diabetes mellitus or post-total pancreatectomy diabetes, <18 years of age, pregnant, renal failure stage 3b o superior (glomerular filtration rate below 45 mL/min), or with intradialytic parenteral nutrition	<u>Regular insulin group (RI):</u> 100% of insulin requirements administered as Regular insulin (Actrapid HM; Novo Nordisk A/ S, Bagsværd, Denmark) added to the bag of TPN as basal and nutritional component. <u>Glargine insulin group (GI):</u> 50% of insulin requirements administered as Regular insulin (Actrapid HM; Novo Nordisk A/S, Bagsværd, Denmark) as nutritional component added to the bag of TPN þ 50% of insulin administered as subcutaneous Glargine insulin U100 as basal component (Lantus SoloStar; Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany or Abasaglar KwikPen; Eli Lilly Nederland B.V, Utrecht, Netherlands).

	underpowered for detection of complications		
Notes	**Author's Conclusion:** In conclusion, we have observed that both regimens (50% subcutaneous Glargine as basal component þ 50% Regular insulin as nutritional component versus 100% Regular insulin added to total parenteral nutrition bag (basal and nutritional component)) are similar in relation to its effectiveness to achieve an adequate metabolic control during PN infusion in non-critically ill patients with diabetes so both regimens could be used. Nevertheless, GI group achieved better metabolic control after TPN interruption and non-severe hypoglycemia rate was higher in the GI group. These data indicate that in patients with 100% Regular insulin added to TPN bag, Glargine may improve the transition and control after ist interruption if it is prescribed previously. This study opens the way for other clinical trials that might evaluate other insulin regimens and in other group of patients with hyperglycemia and PN.		
Outcome measures/results	Primary endpoint: mean capillary glucose during TPN infusion up to 15 days maximum. Secondary endpoint: 1) Percentage of capillary glucose above 180 mg/dL. 2) Mean capillary glucose 48 h after TPN interruption. 3) Glycemic variability (standard deviation and variation coefficient of capillary glucose) 4) Rate of hypoglycemia, percentage of patients with hypoglycemia and percentage of capillary glucose below or equal to 70 mg/dL. 5) Complications during hospitalization: a) Non-catheter and catheter related bloodstream infections: they were identified as an elevated white blood cell count in addition to one or more of the following: positive blood cultures, chest x-ray suggestive of pneumonia, positive urine culture, postoperative wound infection and use of antibiotics. b) Length of stay c) In-hospital mortality	No statistically significant differences were observed comparing mean values of different glycemic parameters neither during TPN infusion nor on each day of the study. We found significant differences in relation to time (a linear decrease) in both groups. No differences were observed between groups neither in mean capillary glucose nor in the descent of capillary glucose with respect to the first day. There were statistically significant differences in the rate of capillary glucose 70 mg/dL, the number of hypoglycemic episodes per 100 days of TPN and in the percentage of patients with non-severe hypoglycemia (higher on GI). However, none of the groups had any severe hypoglycemia episodes. Two days after the interruption of TPN, we observed significantly lower mean capillary glucose levels on GI group vs RI. No other statistically significant differences were observed between the two groups regarding complications. When data were analyzed per-protocol (excluding 12 patients that did not reach 5 days of TPN) the variables were still statistically significant.

7 Medikamentengabe und Zusätze bei HEN und HPE

7.1 Medikamentengabe über enterale Sonde

Empfehlung 136

Um bei der Verabreichung von Medikamenten durch enterale Sonden Komplexbildung und Ausfällungen und damit ein Verstopfen der Sonde zu vermeiden, sollen geeignete Hilfsmittel wie Mörser und Spritzen, ggf. unter Verwendung von Konnektoren, gemäß anerkannten Standards eingesetzt werden.

Empfehlungsgrad A

This recommendation is based on ISO 80369-3:2016 “Small-bore connectors for liquids and gases in healthcare applications — Part 3: Connectors for enteral applications” (https://www.iso.org/standard/50731.html)

7.2 Pharmakologisch wirksame Zusätze in der HPE

Empfehlung 138

Im Einzelfall können in der HPE ausgewählte, pharmakologisch wirksame Supplemente (z. B. Glutamin, Omega-3-Fettsäuren) verwendet werden.

Empfehlungsgrad 0

177. Burns DL, Gill BM. Reversal of parenteral nutrition-associated liver disease with a fish oil-based lipid emulsion (Omegaven) in an adult dependent on home parenteral nutrition. JPEN J Parenter Enteral Nutr 2013; 37: 274 – 280 [512]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
IIb	case report	omega-3 fish oil infusion	29 weeks	n/a	1	50	Female, midgut volvulus; 10	c-reactive protein (CRP) ↓	-

							cm jejunum; gallbladder removed; PN postoperativ ely (>5 years stable formula); formula/d: 2 L, 1280 kcal/d or 25.5 kcal/kg; PN-associated liver disease.		

178. Culkin A, Gabe SM, Bjarnason I et al. A double-blind, randomized, controlled crossover trial of glutamine supplementation in home parenteral nutrition. Eur J Clin Nutr 2008; 62: 575 – 583 [513]									
level of evi-dence	**Study design**	**Intervention**		**Setting**	**Participants**			**Results**	**Notes**
		Type	**Period**		**n**	**age (years)**	**characteristics**		
Ib	randomized, controlled, crossover study	IG: standard HPN with 10 g glutamine CG: standard HPN without glutamine; after 3 and 6 months swap and evaluation	6 months	clinic	20	n/a	HPN	plasma amino acids = intestinal permeability = intestinal absorption = oral intake = parenteral intake = quality of life =	6 months of 10 g/d glutamine has no adverse effects on the patient

179. Goulet O, Antebi H, Wolf C et al. A new intravenous fat emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil: a single-center, double-blind randomized study on efficacy and safety in pediatric patients receiving home parenteral nutrition. JPEN J Parenter Enteral Nutr 2010; 34: 485 – 495 [514]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
Ib	randomized, controlled	SMOFlipid 20% (IG), standard soy oil emulsion (Intralipid 20%) (CG)	4 weeks	n/a	28 (IG 15, CG 13)	5 months – 11 years	HPN for at least 4 weeks	Liver enzymes = bilirubin: IG -1.5 ± 2.4 µmol/L vs. CG 2.3 ± 3.5 µmol/L plasma α-tocopherol: 15.7 ± 15.9 µmol/L vs. 5.4 ± 15.2 µmol/L	

180. Wu GH, Wu ZH, Wu ZG. Effects of bowel rehabilitation and combined trophic therapy on intestinal adaptation in short bowel patients. World J Gastroenterol 2003; 9: 2601 – 2604 [516]									
level of evidence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
II	not randomized, not controlled	TPN treatment with target: positive nitrogen balance & prevention of weight loss.	5.9±4.3 years post-examination	clinic	38	38,0± 16,0	Short bowel syndrome (SBS): Jejenum + Ileum 35.8±21.2 cm; parenteral nutrition; no cancer	33 patients maintained good weight and serum albumin concentration; 2 patients died of malnutrition 2 years after treatment; 2 died of accident; 1 died of liver failure 5 years after treatment.	

181. Lloyd DA, Paynton SE, Bassett P et al. Assessment of long chain n-3 polyunsaturated fatty acid status and clinical outcome in adults receiving home parenteral nutrition. Clin Nutr 2008; 27: 822 – 831 [518]									
level of evi-dence	Study design	Intervention		Setting	Participants			Results	Notes
		Type	Period		n	age (years)	characteristics		
IIb	not randomized, controlled	Determination of n-3 polyunsaturated fatty acid status; HPN (IG).	n/a	at home	118 (IG 64, CG 54)	n/a	HPN patients (>3 months); CG and IG similar BMI and same sex, respectively.	Plasma phospholipid content EPA, DPA & DHA ↓ in IG	

8 Überwachung der medizinischen Ernährung im ambulanten Bereich und in Pflegeheimen

8.1 Wie soll überwacht werden?

Empfehlung 144

Patienten bzw. häusliches Pflegepersonal können geschult werden, um den Ernährungszustand, den Flüssigkeitshaushalt und den Zugangsweg (Ernährungssonde bzw. Infusionskatheter) zu überwachen.

Empfehlungsgrad 0

182. Konrad D, Roberts S, Corrigan ML, Hamilton C, Steiger E, Kirby DF. Treating Dehydration at Home Avoids Healthcare Costs Associated With Emergency Department Visits and Hospital Readmissions for Adult Patients Receiving Home Parenteral Support. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition. 2017;32:385-91. [527]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective analysis 2-	***Countries:*** n/a ***Centers:*** n/a ***Setting:*** n/a ***Funding Sources:*** none ***Dropout rates:*** n/a ***Study limitations***: several costs not accounted for in this study; retrospective study design	**Total no. Patients:** n/a **Inclusion criteria:** objective signs of dehydration **Exclusion criteria:**	- all home parenteral support patients received education on the signs and symptoms of dehydration from a nutrition support nurse and HPS clinician prior to hospital discharge
Notes	**Author's Conclusion:** By reducing emergency department visits and hospital readmissions, healthcare costs were avoided by a factor of 29 when home treatment was successful.		
Outcome measures/results	potential cost avoidance; number of dehydration		- in 2009, 64 episodes (77%) of dehydration were successfully treated at home versus 6 emergency department (ED) visits (7.5%) and 13 readmissions (15.5%) - in 2010, we successfully treated 170 episodes (84.5%) at home, with 9 episodes (4.5%) requiring ED visits and 22 hospital readmissions (11%) - the number of dehydration episodes per patient was significantly higher in 2010 ($P < .001$) and may be attributed to a shift in the patient population,

		with more patients having malabsorption as the indication for therapy in 2010 (P = .003)

8.3 Vorgehen beim Beenden von HEE / HPE

Empfehlung 152

HEE sollte beendet werden, wenn die Ernährungsziele erreicht sind und die orale Energieaufnahme des Patienten seinem Energie- und Nährstoffbedarf entspricht.

Empfehlungsgrad B

183.	**Bozzetti F, Arends J, Lundholm K et al. ESPEN Guidelines on Parenteral Nutrition: non-surgical oncology. Clin Nutr 2009; 28: 445-454. doi:10.1016/j.clnu.2009.04.011 [10]**
Guideline **Relevant recommendations/ statements**	- Nutritional support should be started if patient is undernourished or if it is anticipated that the patient will be unable to eat for more than seven days. It should also be started if an inadequate food intake (<60% of estimated energy expenditure) is anticipated for more than 10 days (Grade C). In such cases if nutritional support for any reason cannot be given through the enteral route, it has to be delivered by vein. A ‘‘supplemental’’ PN should substitute the difference between the actual oral/enteral intake and the estimated requirements (Grade C). - There is no rationale for giving PN if the nutrients intake by oral or enteral route is adequate, and for these reasons PN should not be administered in such conditions (Grade A).

9 Komplikationen

9.1 Refeeding-Syndrom

Empfehlung 155

Um einem Refeeding Syndrom (RFS) vorzubeugen oder ein Refeeding Syndrom zu behandeln, sollen die Nahrungszufuhr und die Flüssigkeitsgabe via HEE langsam (z. B. innerhalb von 7 Tagen) aufgebaut werden sowie ein rascher Ausgleich der Elektrolyte angestrebt werden.

Empfehlungsgrad A

184. Doig GS, Simpson F, Heighes PT, Bellomo R, Chesher D, Caterson ID, et al. Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial. Lancet Respir Med. 2015;3(12):943-52. [548]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
RCT 1++	**Countries:** Australia, New Zealand **Centers:** 13 tertiary care and community hospitals across Australia (11 sites) and New Zealand (two sites) **Setting:** ICU **Funding Sources:** National Health and Medical Research Council of Australia **Dropout rates:** 2.1% **Study limitations:** the self-reported difference in general health did not exceed the minimum threshold (questionable clinical importance), this effect on general health was not supported by differences	**Total no. Patients:** 339 **Inclusion criteria:** critically ill adults (aged ≥18 years) with serum phosphate concentration decreased to below 0·65 mmol/L within 72 h after starting nutritional support in a participating ICU; serum phosphate concentrations change greater than a 0·16 mmol/L decrease from any concentration previously recorded during the patient's ICU stay **Exclusion criteria:** patients with other major causes of hypophosphatemia—such as ongoing dialysis, recent parathyroidectomy, or treatment for hyperphosphatasemia	Nutritional support directed by a study caloric management protocol, which reduced energy intake to 20 kcal/h for at least 2 days. After 2 days on the study caloric management protocol, if serum phosphate concentrations did not need to be supplemented as determined by the study phosphate replacement protocol, energy intake was returned to normal during 2–3 days by clinicians adhering to the study gradual return to normal intake protocol. The study gradual return to normal intake protocol set energy goals to 40 kcal/h for 24 h, then increased goals to 60 kcal/h for 24 h, followed by 80% of calculated energy goals for another 24 h, with 100% of goals achieved by day 4. If a patient's serum phosphate concentrations dropped below 0·71 mmol/L at any time during management on the study gradual return to normal intake protocol, energy intake was reduced to 20 kcal/h and the patient was returned to day 2 of the study caloric management protocol.

	in physical function or performance status, larger studies with longer follow-up might be needed to fully explore these effects on quality of life.		
Notes	**Author's Conclusion:** Protocolized caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolized caloric restriction.		
Outcome measures/results	- Primary Outcome: number of days alive after discharge from the ICU, at the 60 day follow-up - Secondary Outcomes: major infectious complications (defined as an attributable case-mortality rate >15%),receipt of systemic antibiotic treatment, insulin infusion requirements, daily blood glucose concentrations, daily dose of phosphate replacement, lowest daily serum potassium and phosphate concentrations, days of organ dysfunction by individual organ system, days of multiple organ dysfunction syndrome, and other concomitant ICU treatments.	Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolized caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolized caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 vs 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days vs 53·65 [0·97] days, log-rank p=0·002).	

Empfehlung 156

Um einem RFS vorzubeugen oder es zu behandeln, kann insbesondere bei mangelernährten, katabolen Patienten vor Beginn der medizinischen Ernährungstherapie und initial engmaschig Kalium, Magnesium und Phosphat bestimmt und bei Bedarf substituiert werden.

Empfehlungsgrad 0

185. Boateng AA, Sriram K, Meguid MM et al. Refeeding syndrome: Treatment considerations based on collective analysis of literature case reports. Nutrition 2010; 26: 156-167. doi:10.1016/j.nut.2009.11.017 [553]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Systematic Review of case reports 2-	**Countries:** n/a **Centers:** n/a **Setting:** n/a	**Total no. Patients:** 54 **Inclusion criteria:** n/a	Management of the refeeding syndrome in 1. "earlier experience" group: 1969-1989 2. "modern experience" group: 1989-2008

AMSTAR2 2/16	**Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of bias of single studies: n/a Inconsistency: n/a Indirectness: low Impreciseness: high Publication bias: n/a	**Exclusion criteria:** Cases that did not clearly demonstrate complications as a result of nutritional supplementation were excluded.	
Notes	**Author's Conclusion:** Based on our review, the most effective means of preventing or treating RFS were the following: recognizing the patients at risk; providing adequate electrolyte, vitamin, and micronutrient supplementation; careful luid resuscitation; cautious and gradual energy restoration; and monitoring of critical laboratory indices.		
Outcome measures/results	Body mass index, onset of symptoms and signs, differences in nutrition supplementation		

186.	**Hamilton A. CNSG East Cheshire NHS Trust Guidelines for Prevention and Management of Refeeding Syndrome in Adults. In; 2018**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Guideline **Relevant recommendations/ statements**	Management of the Refeeding Syndrome - Assess risk - Prescribe thiamine - Feed and hydrate gradually - Monitor electrolytes o Monitor serum potassium, magnesium, phosphate daily for Days 1 – 10 It is not necessary to correct electrolyte levels before starting feeding. However, blood levels of potassium, magnesium and phosphate should be measured daily and aggressively corrected as feeding proceeds. For most patients daily blood levels will need to be done for the first ten days.		

187.	**Friedli N, Stanga Z, Culkin A et al. Management and prevention of refeeding syndrome in medical inpatients: An evidence-based and consensus-supported algorithm. Nutrition 2018; 47: 13-20. doi:10.1016/j.nut.2017.09.007 [556]**		
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Expert opinion			

4 **Relevant recommendations/ statements**	Based on the available evidence, we developed a practical algorithm for risk assessment, treatment and monitoring of RFS in medical inpatients. In daily routine clinical care, this may help to optimize and standardize the management of this vulnerable patient population. We encourage future quality studies to further refine these recommendations. **How should high risk patients be treated to prevent RFS?** Patients at high risk for RFS should receive substitution of lower-than normal electrolytes (Mg <0.70-0.75mmol/l, PO4 <0.80mmol/l, K <3.5mmol/l). Additionally, patients should be treated with vitamin B1 (thiamine) and multivitamins. In those patients nutritional therapy should be started with reduced caloric targets and a slow increase to the full caloric amount over 5-10 days according to the individual risk category for RFS. Fluid overload should be prevented by restricted use of fluid and sodium restricted diet within the first 7 days. We recommend prophylactic supplementation of electrolytes, thiamine and minerals before initiation of nutritional support in patients at risk for RFS. No iron substitution within the first 7 days even when patients have iron deficiency. (Moderate) **How should we monitor patients at risk for RFS?** Electrolyte concentrations should be monitored daily during the first 72h of nutritional therapy with additional clinical examination to detect signs and symptoms of fluid overload in patients at risk for RFS. (Strong) **How should we treat imminent or manifest RFS?** In case of an imminent or manifest RFS, electrolyte supplementation should be started or adapted. If patients suffer from manifest RFS with edema, lung or heart failure, the caloric target should be reduced as in high risk patients and adequate treatment for those conditions is needed.

Empfehlung 157

Moderat bis schwer kranke Patienten mit zunehmenden Beschwerden wie Ödemen, Tachykardie und Tachypnoe oder mit schwerer Dyselektrolythämie (definiert als Serum Phosphat <0,991 mg/dldL (<0,32 mmol/l/L), Kalium <9,77 mg/dldL (<2,5 mmol/l/L) oder Magnesium <1,217 mg/dldL (<0,5 mmol/l/L) sollten nach Möglichkeit stationär behandelt werden und der Elektrolytausgleich intravenös erfolgen.

Empfehlungsgrad B

188. da Silva JSV, Seres DS, Sabino K et al. ASPEN Consensus Recommendations for Refeeding Syndrome. Nutr Clin Pract 2020; 35: 178-195. doi:10.1002/ncp.10474 [545]	
Consensus Recommendations	Although many prior definitions [of the refeeding syndrome] have, for historic reasons, focused solely on hypophosphatemia, it is proposed here that the decrement in any of the 3 electrolytes [phosphorus, potassium, magnesium] may signal total-body deficit and warrant monitoring or intervention.

Relevant recommendations/ statements	- A decrease in any 1, 2, or 3 of serum phosphorus, potassium, and/or magnesium levels by 10%–20% (mild RS), 20%–30% (moderate RS), or >30% and/or organ dysfunction resulting from a decrease in any of these and/or due to thiamin deficiency (severe RS). - Check serum potassium, magnesium, and phosphorus before initiation of nutrition. - Monitor every 12 hours for the first 3 days in high-risk patients. May be more frequent based on clinical picture. - Replete low electrolytes based on established standards of care.

189. Hofer M, Pozzi A, Joray M et al. Safe refeeding management of anorexia nervosa inpatients: an evidence-based protocol. Nutrition 2014; 30: 524-530. doi:10.1016/j.nut.2013.09.019 [549]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Retrospective, observational case study 3	**Countries:** Switzerland **Centers:** Bern University Hospital **Setting:** Internal Medicine, Psychosomatic Medicine **Funding Sources:** research funds from the Department of General Internal Medicine of the University Hospital of Bern, Switzerland **Dropout rates:** n/a **Study limitations:** The limitations of the study are the retrospective data collection that relies on accuracy of record charts written by the medical staff. Moreover, we performed only clinical anthropometric parameters without bioimpedance	**Total no. Patients:** 65 **Inclusion criteria:** Anorexia nervosa patients aged >16 years, diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision fulfilled, hospitalized for multimodal Anorexia nervosa therapy, signed treatment contract **Exclusion criteria:** younger than 16 years of age, no signed treatment contract	Multimodal treatment After admission, a multidisciplinary and an interprofessional team, consisting of specialists in the field of psychosomatics, psychiatry, internal medicine, clinical nutrition, dietetics, psychology, recreational therapy, and physical therapy assessed all patients. Nutritional replenishment therapy Nutritional replenishment therapy (energy and protein supply), fluids administration, electrolyte, and micronutrient supplementation were started on day 1 for a duration of 10 d (days 1–10), according to the ESPEN guidelines.

	measurements of the body composition.		
Notes	**Author's Conclusion:** This data indicate that evidence-based RF regimens are able to avoid mortality and reduce refeeding syndrome-related complications to a minimum in high-risk patients with Anorexia nervosa		
Outcome measures/results	None defined.		During the RF phase, two cases (2.3%) showed severe hypokalemia (<2.5 mmol/L); none of the cases showed severe hypophosphatemia (<0.32 mmol/L) or severe hypomagnesemia (<0.5 mmol/L) as defined previously. During RF, 41 (47.7%) cases received potassium (32 orally, 5 combined orally/intravenously, 1 intravenously), 28 (32.6%) received phosphate (25 orally, 1 combined orally/ intravenously, 2 intravenously), and 35 (40.7%) received magnesium (32 orally, 1 combined orally/intravenously, 2 intravenously). There was no need for supplementation of potassium in 45 patients (53.3%), phosphate in 57 (66.3%), or magnesium in 46 (53.5%). After the RF phase through day 30 of treatment, one patient received a combined substitution of phosphate and magnesium; three were substituted orally with magnesium, three with phosphate, and nine with potassium.

190. Rio A, Whelan K, Goff L et al. Occurrence of refeeding syndrome in adults started on artificial nutrition support: prospective cohort study. BMJ open 2013; 3: e002173. doi:10.1136/bmjopen-2012-002173 [558]			
Study Type/ Evidence Level	**Study details/limitations**	**Patient characteristics**	**Interventions**
Prospective Cohort Study 2+ NOS 7/9	**Countries:** UK **Centers:** King's College Hospital, London **Setting:** n/a **Funding Sources:** n/a **Dropout rates:** n/a **Study limitations:** Risk of Bias: moderate Inconsistency: n/a Indirectness: high Impreciseness: moderate Publication bias: n/a Inherent bias of narrow selection criteria, exclusion	**Total no. Patients:** 484 **Inclusion criteria:** adults >18 years of age started on artificial nutrition support for the first time during that hospital admission **Exclusion criteria:** previous artificial nutrition support during hospital admission, artificial nutrition support started at the previous institution, participants <18 years of age or failure to obtain consent/assent due to serious illness or lack of next of kin	n/a

	of participants who were able to take oral nutritional intake. A large number of potentially eligible participants could not be recruited due to difficulty in obtaining consent. A further reduction in potential participants was death within 24 h of commencing artificial nutrition support.		
Notes	**Author's Conclusion:** Refeeding syndrome was a rare, survivable phenomenon that occurred during hypocaloric nutrition support in participants identified at risk. Independent predictors for refeeding syndrome were starvation and baseline low-serum magnesium concentration. Intravenous carbohydrate infusion prior to artificial nutrition support may have precipitated the onset of the syndrome.		
Outcome measures/results	Primary outcome measure: occurrence of refeeding syndrome Secondary outcome measure: analysis of the risk factor at predicting refeeding syndrome Tertiary outcome measure: mortality due to refeeding syndrome and all-cause mortality	The research team confirmed the diagnosis of refeeding syndrome in three participants, asymptomatic electrolyte depletion in two participants and the remaining 238 participants did not develop symptoms. There were 133 participants with risk factors for refeeding syndrome of which 68 were men. Mortality was not attributed to refeeding syndrome either during feeding (5.3%, 13/243) or hospital admission (28%, 68/243). Cause of death in these participants was due to underlying disease with mortality by location: ward 45/153, high dependency unit 14/46 and intensive care 9/44.	

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