

## Ziel der Evidenztable:

Einschätzung der gegenwärtigen Evidenzlage zum Thema als Informationsgrundlage zur Formulierung und Graduierung von Empfehlungen

## Evidenztable zu Ergebnissen der Literatursuche (2015 – 2021) zu Risikofaktoren (mit statistischer Betrachtung):

Referenz Studientyp	Teilnehmer*innen (Anzahl und Charakteristika)	Drop-out Rate	Inter- vention	Kontrolle	Ziel- größe(n)	Hauptergebnis	Bemerkung/ Evidenzgrad (SIGN)
	insgesamt						Limitationen
Huang et al. 2017 Eine Meta- Analyse von Kohortenstudien (Fall- Kontrollstudien- siehe Artikel)	Artikel identifiziert durch Datenbanksuche, letztlich 8 Artikel eingeschlossen. Hierin waren 307 RAV- Fälle in der hHcy Gruppe und 542 Kontrollen.	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	<b>Primären Zielgröße:</b> <b>Hyperhomocysteinämie in RAV-Patienten vs. Kontrollen</b>  <b>Sekundäre Zielgröße:</b> <b>Plasma- Konzentration Homocystein</b>	<b>Ergebnisse der <u>primären</u> Zielgrößen:</b> Six studies evaluated hyperhomocysteinemia (hHcy) in retinal artery occlusion Patients and controls; the incidence of hHcy in Patients with RAO was higher than the control and the pooled odds ratio (OR) was 6.64 (95% confidence interval (CI): 3.42, 12.89). Subgroup analyses showed that the ORs were 4.77 (95% CI: 2.69, 8.46) in Western countries, 22.19 (95% CI: 2.46, 200.37) in Asian countries, 9.70 (95% CI: 4.43, 21.20) in the age matched group, 11.41 (95% CI: 3.32, 39.18) in the sex matched group, 9.70 (95% CI: 4.37, 21.53) in the healthy control group, and 6.82 (95% CI: 4.19, 11.10) in the sample size >30.	<b>Meta-Analyse von Fall- Kontroll- Studien</b>  <b>2++</b>  RoB der eingeschlossenen Studien NOS > 5  Keine subst. Heterogenität und keine Indirektheit
Romiti et al. 2020 Eine systematische Übersichtsarbeit mit Meta-Analyse	Artikel identifiziert durch systematische Datenbanksuche.	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	<b>Primären Zielgröße:</b> <b>Thrombophilie Veränderunge n in RAV- Patienten</b>	Ninety-five studies were included; FVL and F-II mutations were found in 7% (95% CI: 2-13) and 3% (95% CI: 1-6) of individuals with RAO, respectively, whereas AT-III (3%), PC and PS activity deficiencies were found in 2% of RAO. The MTHFR C677T homozygous polymorphism were observed in 23% in RAO, respectively; 13% presented APL antibodies in RAO. Conclusions: Compared with healthy subjects, Patients with retinal vascular occlusion showed similar prevalence of inherited and acquired thrombophilias. These findings do not support routine thrombophilia screening in individuals with RAO or RVO.	<b>Systematische Übersichtsarbeit mit Meta- Analyse von Fall-Kontroll- Studien</b>  <b>2++</b>  Keine subst. Heterogenität und keine Indirektheit

<p><b>Christiansen et al. 2018</b> Retrospektive Sekundärdatenanalyse</p>	<p>Retrospektive Analyse von Daten des Danish National Patient Register</p> <p>N=706 Fälle und N=3530 Kontrollen, 70,7 Jahre alt, 49,7% weiblich.</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p><b>Primären Zielgröße: Neu-Auftreten von Vorhofflimmern bei RAV-Patienten</b></p>	<p>The rate of incident AF amongst all cases with retinal vascular occlusion was 1.74 per 100 person-years (95% confidence interval (CI), 1.47-2.06) compared to 1.22 (95% CI, 1.12-1.33) in the matched control group. The rate of AF in RAO was 2.01 (95% CI, 1.6-2.52) per 100 person-years.. HRs of incident AF adjusted for cardiovascular comorbidities were 1.45 (95% CI; 1.10-1.89, p = 0.015) for RAO.</p>	<p><b>Sekundärdatenanalyse einer Registerstudie</b></p> <p><b>2+</b></p> <p>Risiko der Indirektheit durch Verwendung von KK-Kodierung. Risiko für Selektions-Bias gering.</p>
<p><b>Lavin et al. 2018</b> Retrospektive Kohortenstudie</p>	<p>Retrospektive Kohortenstudie an einer Universitätsklinik</p> <p>N=103, 65,1 ± 12,8 Jahre, 45,6% weiblich</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p><b>Primären Zielgröße: Risikofaktoren bei RAV-Patienten</b> <b>Sekundäre Zielgrößen: Mortalität und Schlaganfall nach RAV-Ereignis</b></p>	<p>In this academic-hospital based cohort (2009 to 2017) of 103 Patients with CRAO and systematic risk factor screening, 36.7% of Patients had critical carotid disease, 37.3% had coincident acute stroke, 33.0% presented with hypertensive emergency, 20.0% had a myocardial infarction or critical structural cardiac disease, 25% underwent an urgent surgical intervention, and 93% had a change in medication as a result of the inpatient evaluation. Patients with CRAO had similar risk of subsequent stroke, myocardial infarction, and death as Patients with high-risk transient ischemic attack</p>	<p><b>Krankenhausbasierte Kohortenstudie</b></p> <p><b>2-</b></p> <p>Risiko für Selektions-Bias aufgrund von hohen Non-Responder-Raten für die einzelnen diagnostischen Verfahren und retrospektivem Studiendesign. Keine Indirektheit.</p>
<p><b>Fallico et al. 2020</b> systematische Übersichtsarbeit mit Meta-Analyse</p>	<p>Artikel identifiziert durch systematische Datenbanksuche, N=254 für ZAV und N=120 für VAV</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p><b>Primären Zielgröße: Schlaganfallrisiko in RAV-Patienten</b></p>	<p>For the primary outcome, the pooled proportion of acute cerebral ischaemia was 0.30 (CI 0.24-0.36) in the CRAO cohort, and 0.25 (CI 0.16-0.37) in the BRAO cohort, without statistical heterogeneity. The rate of acute cerebral ischaemia was 11.8% in the TMVL cohort. For the secondary outcome, the pooled proportion of asymptomatic acute cerebral ischaemia was 0.22 (CI 0.16-0.28) in the CRAO cohort, 0.29 (CI 0.20-0.41) in the BRAO cohort and 0.08 (CI 0.05-0.15) in the TMVL cohort, with no statistical heterogeneity.</p>	<p><b>Meta-Analyse von Studien, die MRT nach RAV-Ereignis durchführten.</b></p> <p><b>1-</b></p> <p>RoB der eingeschlossenen Studien NOS &gt; 6 Keine Indirektheit.</p>
<p><b>Zhou et al. 2020</b> systematische Übersichtsarbeit mit Meta-Analyse</p>	<p>Artikel identifiziert durch systematische Datenbanksuche,</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p>Nicht zutreffend</p>	<p><b>Primären Zielgröße: Risiko einer zerebrovaskulären</b></p>	<p>When compared with individuals without retinal vascular occlusions, individuals with retinal artery occlusion (RAO) (odds ratio [OR] = 2.01, 95% confidence interval [CI]: 1.21-3.34; P = 0.005) had higher risks of developing CVD. Additionally, both individuals with central retinal artery occlusion (CRAO) (OR = 2.00, 95% CI:</p>	<p><b>Systematische Übersichtsarbeit mit Meta-Analyse von Fall-Kontroll-Studien und</b></p>

	<b>N= 324,518 Studienteilnehmer</b>				<b>Erkrankung in RAV-Patienten</b>	1.12-3.56; P = 0.02) and branch retinal artery occlusion (BRAO) (OR = 1.60, 95% CI: 1.03-1.48; P = 0.04) were significantly associated with increased risk of CVD	<b>Kohortenstudien 2+</b>  Keine Indirektheit, Heterogenität bei nur 3 eingeschlossenen Studien zu RAV.
<b>Mir et al. 2019 Retrospektive Sekundärdatenanalyse</b>	<b>Retrospektive Sekundärdatenanalyse von Abrechnungsdaten  N=17 117 ZAV-Fälle, Alter: 68.4 ± 0.1 Jahre</b>	<b>Nicht zutreffend</b>	<b>Nicht zutreffend</b>	<b>Nicht zutreffend</b>	<b>Primären Zielgröße: Schlaganfallrisiko in RAV-Patienten</b>	There were an estimated 17 117 CRAO in Patient admissions in the US between 2003-2014. The incidence of in-hospital stroke and acute MI were 12.9% and 3.7%. The incidence of stroke showed an increasing trend over the years, almost doubling in 2014 in comparison to 2003 (15.3% vs 7.7%). The combined risk of in-hospital stroke, transient ischemic attack, acute MI, or mortality was 19%. Female sex, hypertension, carotid artery stenosis, aortic valve disease, smoking, and alcohol dependence or abuse were positive predictors of in-hospital stroke.	<b>Sekundärdatenanalyse 2-</b>  Risiko der Indirektheit durch Verwendung von KK-Kodierung. Risiko für Selektion-Bias gering.
<b>Scoles et al. 2021 Retrospektive Sekundärdatenanalyse</b>	<b>Retrospektive Sekundärdatenanalyse von Abrechnungsdaten  N= 16,193 ZAV-Patienten, Alter: 74.6 ±8.4 Jahre</b>	<b>Nicht zutreffend</b>	<b>Nicht zutreffend</b>	<b>Nicht zutreffend</b>	<b>Primären Zielgröße: Schlaganfallrisiko in RAV-Patienten</b>	The SCCS included 16,193 Patients with RAO using a US medical claims database. The incidence rate ratio (IRR) of new stroke in the month after RAO was increased compared to all periods >2 months before and all months after the index date (IRRs: 1.68-6.40, p < 0.012). Risk was increased in the week immediately following the index date compared to most weeks starting 2 weeks prior to and all weeks immediately after the index date (IRRs: 1.93-29.00, p < 0.026). The cohort study analysed 18,213 propensity-matched Patients with RAO vs. hip fracture. The HR for having a stroke after RAO compared to a hip fracture was elevated in all analyses (All RAO HR: 2.97, 95% CI: 2.71-3.26, p < 0.001; CRAO HR: 3.24, 95% CI: 2.83-3.70, p < 0.001; BRAO HR: 2.76, 95% CI: 2.43-3.13, p < 0.001).	<b>Sekundärdatenanalyse 2-</b>  Risiko der Indirektheit durch Verwendung von KK-Kodierung. Risiko für Selektion-Bias gering.

## Evidenztabelle zu Ergebnissen der Literatursuche (2015 – 2021) zu Therapien:

Referenz Studientyp	Teilnehmer*innen (Anzahl und Charakteristika)		Drop- out Rate	Intervention	Kontrolle	Ziel- größe(n)	Hauptergebnis	Bemerkung/ Evidenzgrad
	insgesamt							
Dumitrascu et al. 2020 Systematische Übersichtsarbeit	Systematische Datenbanksuche und deskriptiver Bericht der Studienergebnisse		Nicht angegeb en	IV or IA thrombolysis: early treatment (4,5h, 6h)	IV or IA thrombolys is: late treatment (4,5h, 6h)	Primären Zielgröße: Sehschärfe	Ergebnisse der primären Zielgröße: Use of IV thrombolysis with alteplase was reported in 7 articles encompassing 111 patients, with 54% of them receiving IV tPA within 4.5 hours of symptom onset, and none developing symptomatic intracranial or ocular hemorrhage. Six studies described IA alteplase administration, with only 18 of a total of 134 patients (13.4%) treated within the first 6 hours after visual loss. The reported adverse events were minimal. Visual outcomes post-IV and IA thrombolysis were heterogeneously reported; however, most studies demonstrated benefit of the respective reperfusion therapies when administered very early.	Retrospektive, prospektive und RCT-Daten wurden gepoolt. 3  Risiko der Verzerrtheit durch verschiedene Studiendesigns und post-hoc Analyse mit verschiedenen Zeitgrenzen.
	Pro Arm							
	-	-						
Hoyer et al. 2021 Fallserie	Fallserie, n=101, Alter: 72.13 +/-12.64 Jahre, 57.6% männlich		Nicht angegeb en	Nicht zutreffend	Nicht zutreffend	Primären Zielgröße: Analyse der Versorgungs situation	Almost 60% of all Patients presented outside of the 4.5-h time window for thrombolysis; by far the most common reason not to deliver intravenous thrombolysis in our cohort was a prehospital delay to presentation (58.8%), with 44.4% of Patients having consulted a private-practice ophthalmologist first. A total of 25 (32.5%) of 77 Patients who underwent magnetic resonance imaging (MRI) had accompanying acute ischaemic stroke lesions on diffusion-weighted MRI of the brain. A possible aetiology of CRAO was identified in 41.4% of Patients.	Krankenhaus- basierte Fallserie 3  Keine Kontrollgruppe, keine funktionellen Ergebnisse.
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Huang et al. 2018 Systematische Übersichtsarbeit mit Meta-Analyse	Systematische Datenbanksuche und Meta-Analyse	Nicht angegeb en	IVT with alteplase	No IVT treatment	Primären Zielgröße: Sehschärfe	Ergebnisse der <u>primären</u> Zielgröße: We included 8 studies enrolling 316 CRAO Patients, among them, 157 Patients received IVT with alteplase while 159 Patients did not. The rate of best BCVA improvement was 47% (95% CI 33–62%) in the CRAO Patients treated with IVT, which was higher than that of 12% (95% CI 1–23%) in those without IVT (OR 5.97, 95% CI [2.77–12.86]). In the setting of similar baseline BCVA (MD [logMAR] 0.16, 95% CI [- 0.15 to 0.46]), compared with those who did not receive IVT, the CRAO Patients who received IVT had better best BCVA (MD [logMAR] - 0.23, 95% CI [- 0.44 to - 0.02]), but had no significant better final BCVA (MD [logMAR] - 0.10, 95% CI [- 0.32 to 0.12]). Two CRAO Patients had complicated symptomatic intracranial hemorrhage after IVT.	Retrospektive, prospektive und RCT-Daten wurden gepoolt. 2+  Keine Indirektheit, geringe Heterogenität, keine Bewertung der Studienqualität präsentiert.
	Pro Arm						
Page et al. 2018 Systematische Übersichtsarbeit mit Meta-Analyse	Systematische Datenbanksuche und Meta-Analyse	Nicht angegeb en	IAT treatment	Standard treatment	Primären Zielgröße: Sehschärfen verbesserun g	Ergebnisse der <u>primären</u> Zielgröße: Five retrospective controlled studies and one randomized clinical trial were identified satisfying all inclusion criteria resulting in the analysis of 236 Patients treated with IAT and 255 Patients treated with ST. A pooled fixed effects analysis resulted in an estimated odds ratio of 2.52, 95% CI (1.69, 3.77) (P < 0.0001) favoring IAT.	Retrospektive und RCT-Daten wurden gepoolt. 2+  Keine Indirektheit, geringe Heterogenität, individuelle Studien mit relevantem RoB.
	Pro Arm						
Pielen et al. 2015 RCT	Sekundäranalyse eines RCTs  71% männlich, Alter: 65 (24–75) Jahre	Nicht angegeb en	Local intra- arterial fibrinolysis	Conservati ve standard treatment	Sekundäre Zielgröße: Therapeutisc hes Ansprechen in Bezug auf Alter etc.	Ergebnisse der <u>primären</u> Zielgröße: Patients with coronary heart disease (CHD) presented worse BCVA at baseline (0.39 logMAR, p = 0.0097). Patients with time from occlusion to treatment <12 h showed a trend to better vision gain at month 1 (- 0.23 logMAR, p = 0.086), similarly smoking (-0.24 logMAR, p = 0.077). Predictive effect: Age (<60 years favours LIF -0.54 logMAR; >70 years favours CST 0.28 logMAR; interaction p = 0.070) and CHD	Analyse einer sekundären Zielgröße der EAGLES Studie 1-  Studie abgebrochen, daher
	Pro Arm						

	36	36					(favours CST 0.44 logMAR; interaction p = 0.073) might be predictors of therapeutic outcome. There were no strong effects in multivariate analysis.	geringe Power. RoB aufgrund des Studiendesigns gering. Keine Indirektheit.
Schultheiss et al. 2018 Fallserie	50% weiblich, Alter: 72.8±10.9 Jahre		Nicht zutreffend	Intravenous thrombolysis	-	Primären Zielgröße: Sehschärfe	Ergebnisse der <u>primären</u> Zielgröße: Until August 2016, 20 Patients received IVT within 4.5 hours after NA-CRAO with a median onset-to-treatment time of 210 minutes (IQR 120-240). Visual acuity improved from baseline mean logarithm of the minimum angle of resolution 2.46±0.33 (SD) (light perception) to 1.52±1.09 (Snellen equivalent: 6/200) at d5 (p = 0.002) and 1.60±1.08 (Snellen equivalent: 6/240) at d30. Compared to the EAGLE CST-arm, functional recovery to reading ability occurred more frequently after IVT: 6/20 (30%) versus 1/39 (3%) at d5 (p = 0.005) and at d30 5/20 (25%) versus 2/37 (5%) (p = 0.045). Two Patients experienced serious adverse events (one angioedema and one bleeding from an abdominal aortic aneurysm) but recovered without sequelae.	Fallserie 3  RoB, da keine Kontrollgruppe. Keine Indirektheit.
	Pro Arm							
	20	-						
Wu et al. 2018 Meta-Analyse	Datenbanksuche mit Meta-Analyse		Nicht angegeben	Sauerstoff-Therapie	Keine Sauerstofftherapie	Primären Zielgröße: Sehschärfeverbesserung	Seven randomized controlled trials (RCTs) met the inclusion criteria. Patients who received oxygen therapy exhibited probability of visual improvement about 5.61 times compared with the control group who did not receive oxygen therapy (OR = 5.61; 95% CI, 3.60-8.73; p < 0.01). No statistically significant difference was observed between oxygen inhalation methods (Chi2 = 0.18, df = 1, p = 0.67), combined therapy (Chi2 = 0.21, df = 1, p = 0.64), or RAO type (Chi2 = 0.06, df = 1, p = 0.81). Conversely, 100% oxygen (Chi2 = 4.55, df = 1, p < 0.05) and hyperbaric oxygen (Chi2 = 4.55, df = 1, p < 0.05) significantly improved VA in RAO Patients. Better effect was showed in period within 3 months (Chi2 = 5.76, df = 1, p < 0.05). The most effective treatment length was over 9 hours (Chi2 = 6.58, df = 1, p < 0.05).	Meta-Analyse 2++  Keine Indirektheit, keine subst. Heterogenität. RoB assessment der Einzelstudien positiv oder unklar.
	Pro Arm							
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**Evidenztable zu Ergebnissen der Literatursuche (2015 – 2021): Übersichtsarbeiten ohne statistische Betrachtung):**

Referenz Studientyp	Teilnehmer*innen (Anzahl und Charakteristika)	Drop-out Rate	Inter- vention	Kontrolle	Ziel- größe(n)	Hauptergebnis	Bemerkung/ Evidenzgrad (SIGN)
	insgesamt						
Biousse et al. 2018 Selektive Literatur- übersicht	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	keine	Because the risk of stroke is maximum within the first few days after the onset of visual loss, prompt diagnosis and triage are mandatory. Eye care professionals must make a rapid and accurate diagnosis and recognize the need for timely expert intervention by immediately referring patients with acute retinal arterial ischemia to specialized stroke centers without attempting to perform any further testing themselves.	<b>Selektive Literaturübersicht, daher keine Eingruppierung nach SIGN.</b>
Flaxel et al. 2018 Leitlinie, basierend auf systematischen Literaturrecherchen	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	Nicht zutreffend	keine	An ophthalmic artery occlusion (OAO), central retinal artery occlusion (CRAO), or, less commonly, a branch retinal artery occlusion (BRAO) can be associated with life-threatening conditions (e.g., carotid occlusive or cardiac valve disease). In patients over 50 years of age, one must additionally suspect giant cell arteritis (GCA) and should consider urgent systemic corticosteroid therapy when GCA is diagnosed or very likely in an attempt to preserve or recover	<b>Leitlinie, basierend auf systematischer Literaturrecherche, daher keine Eingruppierung nach SIGN.</b>

					<p>vision in the affected eye and preserve in the contralateral eye.</p> <p>An OAO or retinal artery occlusion (RAO) occurring in a patient of any age should prompt a systemic evaluation for carotid occlusive and thromboembolic disease. Generally, this would be a workup for vasculitis or hypercoagulability in younger patients (under 50 years old) and an embolic workup in older patients (over 50 years old).</p> <p>Acute, symptomatic OAO, CRAO, or BRAO from embolic etiologies should prompt an immediate referral to the nearest stroke referral center for prompt assessment for consideration of an acute intervention. The precise timing of evaluation for patients with an asymptomatic but newly diagnosed CRAO or BRAO is unclear, though these patients still warrant a timely referral.</p> <p>In general, there are no proven treatments to reverse the vision loss caused by CRAO, BRAO, or OAO.</p> <p>In vascular occlusive disorders of the eye, there is an increased risk for posterior and/or anterior segment neovascularization. Patients with greater ischemia require closer and more frequent follow-up. Panretinal photocoagulation (PRP) treatment is recommended for patients who develop iris or retinal neovascularization.</p>	
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<p><b>MacGrory et al. 2018</b> <b>Literatur-übersicht</b></p>	<p><b>Nicht zutreffend</b></p>	<p><b>Nicht zutreffend</b></p>	<p><b>Nicht zutreffend</b></p>	<p><b>Nicht zutreffend</b></p>	<p><b>keine</b></p>	<p>Acute CRAO is a medical emergency. Systems of care should evolve to prioritize early recognition and triage of CRAO to emergency medical attention. There is considerable variability in management patterns among practitioners, institutions, and subspecialty groups. The current literature suggests that treatment with intravenous tissue plasminogen activator may be effective. Patients should undergo urgent screening and treatment of vascular risk factors.</p>	<p><b>Selektive Literaturübersicht, daher keine Eingruppierung nach SIGN.</b></p>
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