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Interdisciplinary S2k Guidelines for the Diagnosis and Treatment of Endometriosis

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Interdisziplinäre S2k-Leitlinie für die Diagnostik und Therapie der Endometriose

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1 Information on these guidelines

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1.2 Funding

Compilation of the present guidelines was in part financially supported by the German Society for Obstetrics and Gynecology and its Working Group Gynecologic Endoscopy (Arbeitsgemeinschaft Gynäkologische Endoskopie, AGE).

1.3 Lead professional organizations

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1.5 Additional information

The present short version is based on the full version of the S2k Guidelines for the Diagnosis and Treatment of Endometriosis, accessible via internet as follows:

<http://www.awmf.org/leitlinien/aktuelle-leitlinien.html>

<http://www.dggg.de>

<http://www.oeggg.at>

<http://www.sggg.de>

<http://leitlinien.net>

<http://AG-Endoskopie.de>

Additional information on the topic is available through:

Endometriosis Research Foundation (Stiftung Endometrioseforschung,

<http://www.endometriose-sef.de>)

The Royal College of Obstetricians and Gynaecologists Clinical Green-Top
Guidelines for the Investigation and Management of Endometriosis

(<http://www.rcog.org.uk/>)

ESHRE Guideline for the Diagnosis and Treatment of Endometriosis

(<http://www.eshre.eu>).

The American College of Obstetrics and Gynecology Committee on Practice Bulletins

(<http://www.acog.org/>)

Guidelines report of the present guidelines (see full version).

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1.7 Abbreviations used in this paper

Abbreviation	Comment
AFS	American Fertility Society
AGE	Arbeitsgemeinschaft Gynäkologische Endoskopie der DGGG (Working Group Gynecologic Endoscopy of the DGGG)

AGO	Arbeitsgemeinschaft Gynäkologische Onkologie der DGGG und der Deutschen Krebsgesellschaft (Working Group Gynecologic Oncology of the DGGG and the German Cancer Society)
CT	Computed tomography
DGGG	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (German Society for Obstetrics and Gynecology)
DIE	Deep infiltrating endometriosis
EEL	Europäische Endometriose Liga (European Endometriosis League)
ENZIAN	Name of a hotel in Weissensee, Carinthia (Austria) where the classification of DIE was first established by an SEF expert group in 2002
GnRHa	Gonadotropin-releasing hormone analog
HRT	Hormone replacement therapy
ICSI	intracytoplasmatic sperm injection
IUD	Intrauterine device
IUI	intrauterine Insemination
IVF	in-vitro fertilization
MRI	Magnetic resonance imaging
OC	Oral contraceptive (orales, hormonelles Antikonzeptivum)
OEGGG	Österreichische Gesellschaft für Gynäkologie und Geburtshilfe (Austrian Society for Obstetrics and Gynecology)
rASRM	(revised) American Society for Reproductive Medicine (-classification)
SEF	Stiftung Endometrioseforschung (Endometriosis Research Foundation)

2 Special notes

While a company's brand name, or a registered trade mark, respectively, are not necessarily given in the present paper, it must not be presumed that such name or mark was free.

As medical science is a rapidly developing field, informations and recommendations given in these guidelines do represent the state-of-the-art knowledge as it stands at the time of submission of the paper. Utmost care has been taken by the expert panel to extract that knowledge from the scientific literature as well as their personal experience. Having said that, the user remains fully liable for all applications based upon recommendations given in the present paper.

The reader's attention is drawn to the fact that oral contraceptives (OCs) and intrauterine levonorgestrel-releasing systems are not specifically approved in

Germany for the treatment of endometriosis. Thus, their therapeutic application for the treatment of endometriosis is made off label.

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3 Introduction and general comments

3.1 Definition and epidemiology

Statements:

a) Endometriosis – one of the most common gynecologic diseases – is defined as the occurrence of endometrium-like cell formations outside the uterine cavity.

b) The cardinal symptom is chronic pelvic pain. Infertility is common.

There are about 20.000 hospital admissions per year for endometriosis in Germany (Haas et al. 2012). Pathologically and histologically, endometriosis is a benign disease. However, infiltrative growth into adjacent organs is possible requiring extensive surgical procedures.

3.2 Etiology, pathology, and staging

Statement:

Etiology and pathogenesis of endometriosis are not fully understood. Therefore, a causal therapy is not known to date.

Recommendation:

All staging systems known to date have their limitations. In order to ensure the international comparability of data, the use of the rASRM staging system – and in cases of deep infiltrating endometriosis the additional use of the ENZIAN classification – is recommended.

Endometriosis and malignancy

Statements:

- a) In rare cases, malignancy – usually ovarian cancer – may arise from endometriosis.
- b) Aside from this, the association of other, non-gynecologic malignancies with endometriosis has been described in the literature. The clinical significance of this observation is not understood.

4 Diagnosis and treatment of endometriosis

Statements:

a) Indications for endoscopic diagnosis and treatment of endometriosis are as follows:

- Chronic pelvic pain,
- Destruction of organs, *and/or*
- Infertility.

b) For control of symptoms, the surgical removal of endometriotic lesions is considered as "gold standard" (Abbott et al. 2004, Deguara et al. 2012, Garry 2004).

Recommendations:

In general, the diagnosis of endometriosis is to be established histologically. Hence, diagnostic laparoscopy is essential for the diagnostic work-up (Walter et al. 2001).

4.1 General comments

Some affected women have no symptoms. Also, there is no correlation between stage of the disease and grade of symptoms. Asymptomatic endometriosis in a woman without infertility is no indication of surgical or other medical interventions (exception: endometriosis-related hydronephrosis). Almost every woman with symptomatic endometriosis suffers from dysmenorrhea. If this cardinal symptom is lacking, other differential diagnoses are to be considered (see Guidelines for Chronic Pelvic Pain in Women, AWMF Registry No. 016-001, Sillem u. Teichmann 2003, Siedentopf et al. 2009).

4.2 Peritoneal endometriosis

Statements:

a) The diagnosis of peritoneal endometriosis is made laparoscopically.

b) Treatment of choice is the laparoscopic removal of the implants.

Recommendation:

Following hormonal suppression of the ovarian function, endometriotic implants may undergo regression. For the reduction of endometriosis-associated symptoms, progestins, OCs, or GnRH analogs may be used in order to induce therapeutic amenorrhea (Abou-Setta et al. Cochrane Review 2013, Brown et al. Cochrane Review 2012, Allen et al. Cochrane Review 2009).

4.3 Ovarian endometriosis (endometriomas)

Statement:

The diagnosis of ovarian endometriomas is primarily made by transvaginal ultrasound.

Recommendations:

a) For primary treatment of ovarian endometriomas, the cyst wall should be removed surgically. Fenestration alone is considered insufficient.

b) Endocrine drug treatment alone is neither effective in eliminating an ovarian endometrioma (and, consequently, to replace its surgical removal) – nor in compensating for incomplete surgical removal. Therefore, it is not recommended.

Differential diagnosis

In ovarian endometriomas, often a typical echogenic pattern is found (Hudelist et al. 2009b). However, there are also sonographically complex ovarian masses with heterogeneous appearance making it sometimes difficult to differentiate between functional ovarian cysts on the one side and dermoid cysts, kystomas, or ovarian malignant neoplasms on the other side. If a laparoscopic approach is scheduled in unclear ovarian findings, the DGGG S1 Guidelines for Laparoscopic Surgery of

Ovarian Tumors apply (AWMF Registry No. 015-003). Any unclear ovarian mass must be clarified histologically.

As the CA-125 level in endometriosis patients is consistently elevated, its assessment is not recommended routinely. The same applies to the serum level of human epididymal protein (HE4, Lenhard et al. 2011, Zheng and Gao 2012).

4.4 Deep infiltrating endometriosis

Statements:

a) Deep infiltrating endometriosis (DIE) is defined as involvement of the rectovaginal septum, vaginal fornix, retroperitoneum (pelvic side wall, parametrium), bowel, ureters, and urinary bladder.

b) The primary diagnosis of DIE is made clinically with rectovaginal palpation, inspection with divided specula, vaginal ultrasound, and transabdominal ultrasound of the kidneys being mandatory.

Recommendations:

a) For treatment, complete resection of DIE should be performed. Nonetheless, compromises must be made as preservation of fertility often is imperative. Considering that the disease is benign and potentially relevant complications may occur, the extent of resection should be thoroughly discussed and agreed upon with the patient.

b) Treatment of DIE should be carried out in specialized centers with a multidisciplinary approach (Ebert et al. 2013).

c) If patients with DIE are to be managed conservatively – as well as pre- and postoperatively – sonographic examination of the kidneys is mandatory in order to avoid overlooking silent hydronephrosis. DIE-associated hydronephrosis is an absolute indication of appropriate diagnosis and treatment.

Hormone replacement therapy in patients with endometriosis

Premenopausal patients who have undergone hysterectomy because of endometriosis – proper indication provided – should receive a combined estrogen-progestin HRT. In postmenopause, in view of the fact that there is a potential risk of malignancy (see paragraph on endometriosis-associated malignancy), combined estrogen-progestin HRT – or tibolone – is recommended as well (Moen et al. 2010, Soliman and Hillard 2006). Nonetheless, the problem of breast cancer risk has to be balanced against that – and an individual decision made together with the patient (see also S3 Guidelines for HRT in the peri- and postmenopause, AWMF Registry No. 015-062).

4.5 Adenomyosis

Statement:

The diagnosis of adenomyosis is primarily established clinically by vaginal ultrasonography and/or MRI. Most often, it is only the histological result after hysterectomy that is proving.

Recommendations:

- a) Given completion of family planning and presence of respective symptoms, hysterectomy can be recommended.

- b) If the patient opts for preservation of the uterus, a therapeutic amenorrhea may be induced, or a progestin-releasing IUD inserted (Garcia and Isaacson 2011).

5 Endometriosis and infertility

Statements:

- a) While a causal relationship has not been resolved yet, endometriosis and infertility are often associated.

- b) For the treatment of women with both endometriosis and infertility, appropriate skills and experience in infertility surgery, as well as cooperation with centers for reproductive medicine are required.

Recommendations:

a) In women with both infertility and endometriosis, the implants should be surgically removed for the improvement of fertility.

b) In cases of recurrence, assisted reproductive technologies are superior to repeated surgery in terms of pregnancy rate. In repeat operations for ovarian endometriosis, the surgery-related reduction of ovarian reserve is to be considered.

c) Postoperative treatment with GnRH analogs was ineffective in improving spontaneous pregnancy rates and is, therefore, not recommended.

d) Any drug treatment for endometriosis alone does not improve fertility and should not be applied from a reproductive-medicine perspective.

6 Psychosomatic aspects

Recommendation:

Psychosomatic aspects in the treatment of patients with endometriosis should be considered and integrated early on.

7 Complementary and integrative treatment approaches

No statements, no recommendations.

8 Rehabilitation, follow-up, and self-help

Statement:

After extensive surgery – especially for deep infiltrating endometriosis, after repeat endometriosis operations, or in patients with chronic pain, there often is a need for rehabilitation.

Recommendation:

This need mentioned should be assessed, and measures of rehabilitation, or after-care, respectively, be initiated.

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