






COMMENTARY

The #Enzian classification: A comprehensive non-invasive and surgical description system for endometriosis

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Abstract

Advances in preoperative diagnostics as well as in surgical techniques for the treatment of endometriosis, especially for deep endometriosis, call for a classification system, that includes all aspects of the disease such as peritoneal endometriosis, ovarian endometriosis, deep endometriosis, and secondary adhesions. The widely accepted revised American Society for Reproductive Medicine classification (rASRM)

Abbreviations: DE, deep endometriosis; MRI, magnetic resonance imaging; r-ASRM, revised American Society for Reproductive Medicine; RVS, rectovaginal space; TVS, transvaginal sonography; USL, uterosacral ligaments.

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has certain limitations because of its incomplete description of deep endometriosis. In contrast, the Enzian classification, which has been implemented in the last decade, has proved to be the most suitable tool for staging deep endometriosis, but does not include peritoneal or ovarian disease or adhesions. To overcome these limitations, a comprehensive classification system for complete mapping of endometriosis, including anatomical location, size of the lesions, adhesions and degree of involvement of the adjacent organs, that can be used with both diagnostic and surgical methods, has been created through a consensus process and will be described in detail—the #Enzian classification.

KEYWORDS

#Enzian classification, classification system, endometriosis, r-ASRM classification

1 | INTRODUCTION

The accurate and comprehensive classification of endometriosis is crucial to assess the state of disease with respect to its extent, location, and clinicopathological consequences. This not only allows a better communication between surgeons, diagnostic specialties, and doctors specializing in assisted reproductive medicine and techniques, but may also be useful when comparing therapeutic interventions and measuring treatment outcomes to allow proper research in this field. Endometriosis used to be primarily diagnosed through operative procedures. In 1979, the American Fertility Society published a classification scheme, which was revised in 1985,¹ and again in 1997.² Designed to evaluate the extent of endometriosis and function of reproductive organs during an invasive, ie surgical procedure, it is the most commonly used classification system in clinical practice and international literature. Adhesions that partially obscure the pelvis and other lesions of endometriosis are assessed as a major criterion for the severity of the disease when using the revised American Society for Reproductive Medicine (r-ASRM) classification. The stage of disease recorded in the r-ASRM classification does not, however, allow a detailed description of the extent of deep endometriosis (DE). This raises several questions when analyzing the predictive value, when used in terms of symptoms, response to surgical treatment, postoperative pregnancy rate, symptom recurrence, and disease relapse.³ High accuracy in diagnosis of DE through non-invasive methods, such as magnetic resonance imaging (MRI) and transvaginal sonography (TVS), has been demonstrated.^{4,5}

In 2003⁶ and 2005, the SEF (Stiftung Endometriose-Forschung; Scientific Endometriosis Foundation) first published the Enzian classification. Revised in 2011, it has been evaluated in several clinical studies and is recognized as a valid and useful tool for the classification of DE in TVS, MRI and surgical methods.^{7,8,9} As a consequence, recommendations and several guidelines^{10,11} advocate the use of the Enzian classification. However, the Enzian classification has so far neither included ovarian and peritoneal endometriosis nor pelvic adhesions. Hence, the aim of the present consensus work

Key message

Improvements in both non-invasive diagnostic methods and surgical therapy for endometriosis demand an universally usable classification system for all aspects of the disease, that can be used by both surgical and diagnostic specialties—the #Enzian classification.

was to generate a universally applicable classification system for endometriosis.

2 | METHODS

The present manuscript is the result of a consensus process reached by all authors and is based on the opinion of a panel of known gynecologists and sonographers with extensive expertise in the diagnosis and therapy of endometriosis. Criteria used to invite the experts to participate in this consensus process included having significant peer-reviewed publications in the field of diagnosis and management of endometriosis. A first draft was written in December 2019 by a joint effort of the first and last authors (JK and GH), based on the result of the annual working group meeting of the SEF (Scientific Endometriosis Foundation) and sent to all co-authors. All co-authors were invited to comment within a time-frame, participation was considered a precondition for co-authorship. Taking all comments into account, a revised draft was then sent to all co-authors. In case of conflicting opinions, a consensus was proposed after discussion between the first author (JK), the co-author making the comment and the last author (GH). This pathway was repeated until a consensus between all authors was reached. After nine revisions, the manuscript was deemed ready for submission. This consensus opinion includes recommendations regarding how to perform a TVS including measurements of DE when examining patients with suspected or

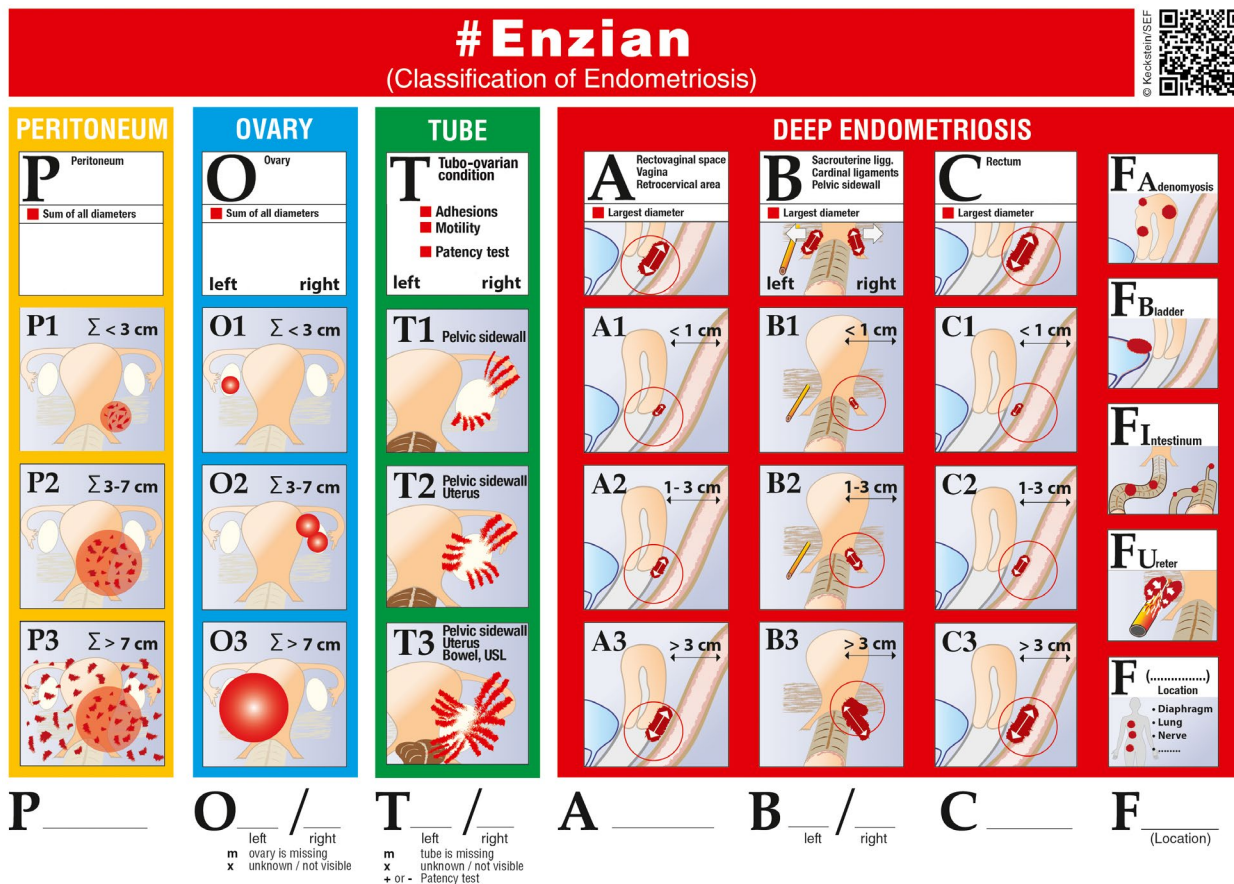


FIGURE 1 #Enzian classification: overview with potentially affected organs and compartments (<https://www.endometriose-sef.de/aktivitaeten/klassifikation-enzian/>)

actual endometriosis and explains the description of endometriosis when performing surgical interventions.

2.1 | The #Enzian classification—description

The #Enzian classification (Figure 1) is based on the known Enzian classification for DE using three compartments (A—vagina, rectovaginal space (RVS); B—uterosacral ligaments (USL) / cardinal ligaments/ pelvic sidewall and C—rectum) as well as so-called F (ie far locations) such as the urinary bladder (FB), the ureters (FU), and other extragenital lesions (FO). It additionally covers the involvement of the peritoneum (P) (Figure 2), ovary (O) (Figure 3), other intestinal locations (sigmoid colon, small bowel; FI), as well as adhesions, involving the tubo-ovarian unit (T) (Figure 4), and, optionally, tubal patency.

- Individual compartments or organ involvement are identified with capital letters (P, O, T, A, B, C, F) and arranged in this order.
- The extent of endometriosis is represented by the numbers 1, 2 and 3 in compartments P, O, T, A, B, and C.
- Paired organs (ovary, tube, USL, parametrium, ureter): the severity is arranged separately after the letter (left / right).
- Missing / invisible ovary or tube are described with suffix (m, missing; x, unknown).

The individual anatomical locations and their annotation are described below and based on the findings during imaging techniques and/or surgery. In case of ureteral involvement, the side is annotated in a bracket, ie (r) or (l).

2.2 | Peritoneum (P)

The classification of peritoneal endometriosis takes into account all superficial (subperitoneal invasion < 5 mm) peritoneal foci located in the pelvis and abdomen above the pelvic rim, that are not considered DE. The diameter of a virtual circle is calculated, in which all endometrial foci can be included. P1 = < 3 cm (sum of all lesions); P2 = 3–7 cm (sum of all lesions), P3 = > 7 cm (sum of all lesions). P can only be documented during the surgical procedure, as peritoneal lesions cannot be directly diagnosed with imaging techniques.

2.3 | Ovary (O)

All endometriomas and infiltrating ovarian surface foci (≥ 5 mm) are considered as ovarian endometriosis. In the case of multilocular endometriomas, the sum of the maximal diameter of all lesions is

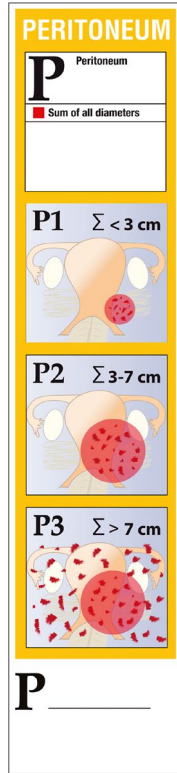
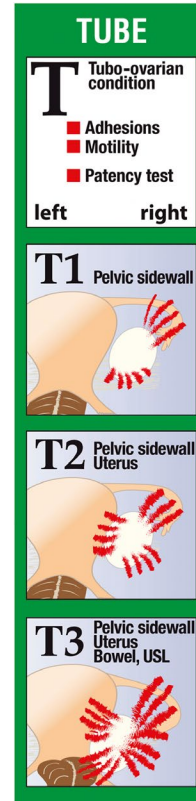
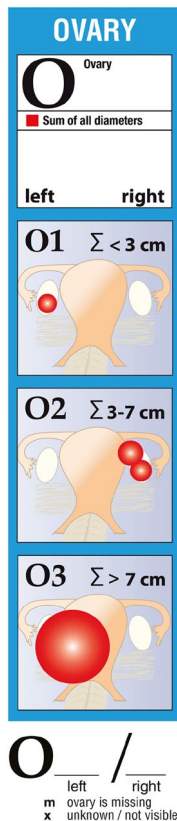


FIGURE 2 #Enzian classification for peritoneal disease, P



T ____ / ____
 left / right
 m tube is missing
 x unknown / not visible
 + or - Patency test

FIGURE 4 #Enzian classification for the tubo-ovarian condition, T



O ____ / ____
 left / right
 m ovary is missing
 x unknown / not visible

FIGURE 3 #Enzian classification for ovarian endometriosis, O

separately calculated for each side. O1 = <3 cm (sum of all endometriomas); O2 = 3–7 cm (sum of all endometriomas); O3 = >7 cm (sum of all endometriomas). Annotation of the left (l) and right (r) side is separated by a slash (/); m = missing organ (ovary), x = not visualized or unknown. These criteria are used in both operative and non-invasive diagnostics. For TVS, optionally, criteria described by the International Ovarian Tumor Analysis (IOTA) group can be used for describing the sonomorphological appearance of ovarian endometriotic cysts in detail.¹²

2.4 | Tubo-ovarian condition

Assessment of the tubo-ovarian condition, namely possible adhesions with regard to mobility of the ovaries and tubes and tubal patency, are described as follows: T1 = adhesions between the ovary and pelvic sidewall +/- tubo-ovarian adhesions; T2 = T1 plus adhesions to the uterus or isolated adhesions between the adnexa and uterus; T3 = T2 plus adhesions to the USL and/or bowel or isolated adhesions between the adnexa and the USL and/or bowel. Optionally, tubal patency can be annotated with “+” (patent) or “-” not patent. Annotation of the left (l) and right (r) side is separated by

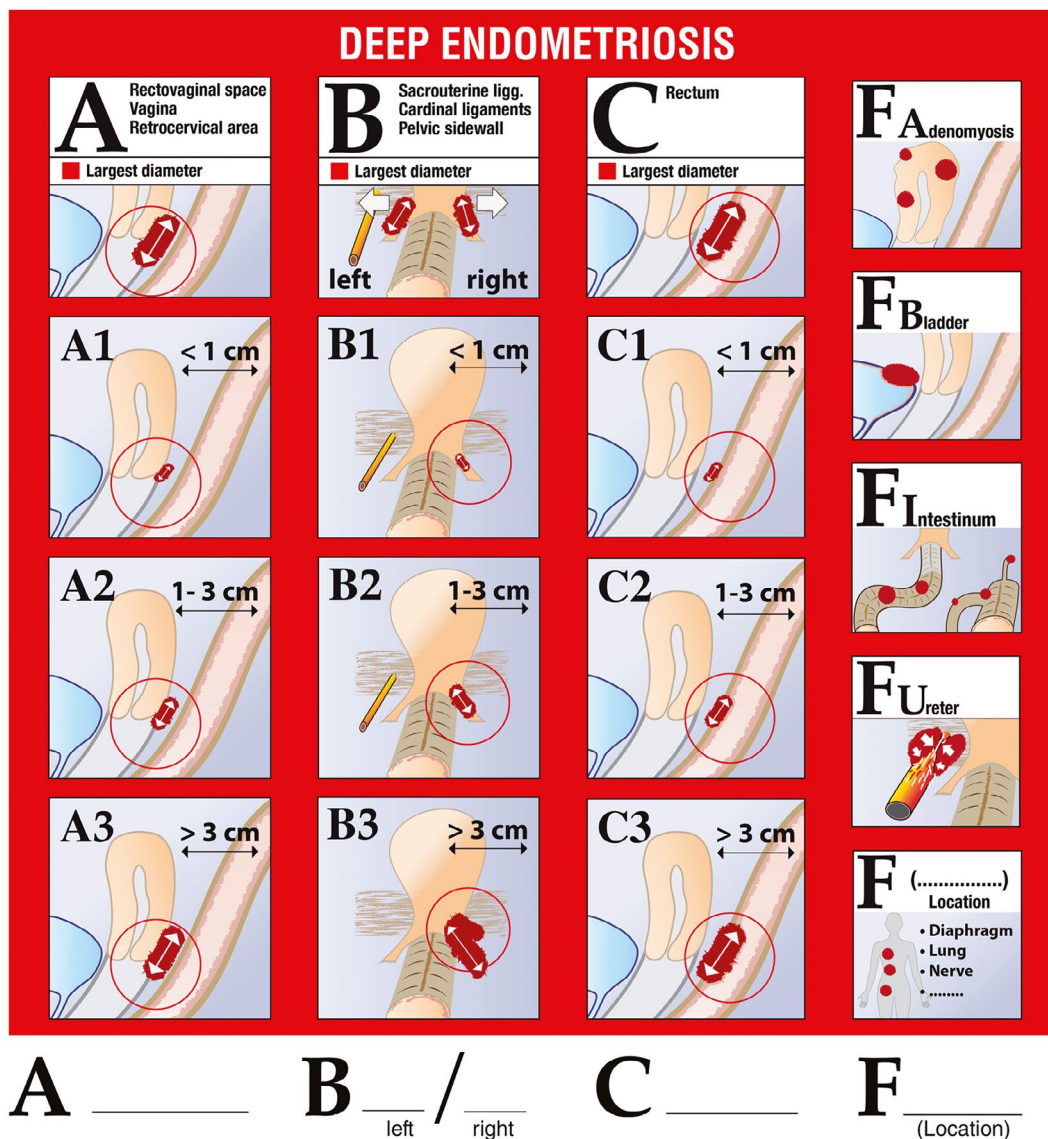


FIGURE 5 #Enzian classification for compartments A, B and C

a slash (/); m = missing tube, x = tube not visualized or unknown (only for surgical evaluation).

In case of description by TVS, assessment is also carried out separately for the left and the right side by dynamic ultrasound using the sliding sign of the named structures.⁵ Reflected by TVS, reduced mobility or loss of mobility between these structures is demonstrated. Tubal patency can optionally be assessed using TVS (hysterosalpingo contrast sonography).

2.5 | Deep endometriosis

All lesions exhibiting subperitoneal infiltration of >5 mm are classified as per the DE definition.¹³ The description takes into account the different extent of the disease in terms of size, site, and different organ involvement. The #Enzian classification comprises three axes or levels, represented by the compartments A (craniocaudal axis), B (mediolateral axis), and C (ventrodorsal axis, Figure 5).

Uterine and other extragenital locations (F) are also described: adenomyosis (FA); bladder involvement (FB); extrinsic and/or intrinsic ureteric involvement with signs of obstruction (FU); bowel disease (FI) cranial to the rectosigmoid junction (>16 cm from the anal verge), upper sigmoid, transverse colon, cecum, appendix, small bowel; and other locations (FO) such as the abdominal wall, diaphragm, and nerve.

2.6 | Compartment A (vagina, rectovaginal space)

Compartment A (Figure 6) runs in the craniocaudal direction and assesses the posterior vaginal fornix and involvement of the RVS. The maximal diameter (cm) of the lesion is measured in the sagittal (midline) section. In cases of combined involvement of the vagina and RVS, the maximal diameter of the whole (vagina and RVS) lesion will be measured in the sagittal (midline) plane. The description is as follows: A1 = <1 cm, A2 = 1-3 cm, A3 = >3 cm.

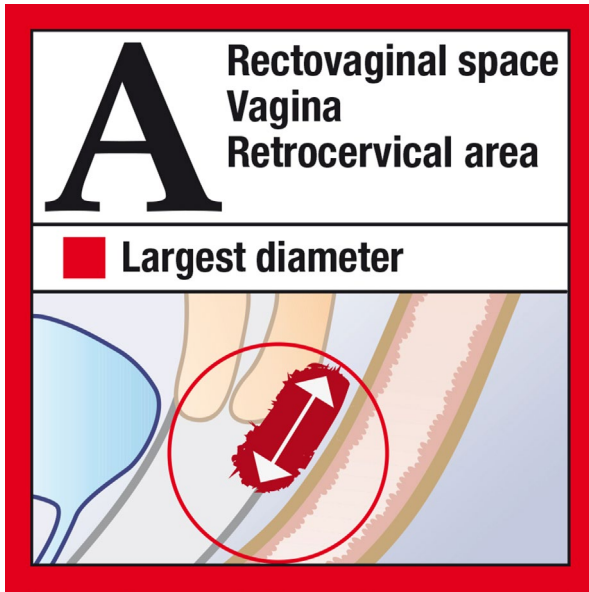


FIGURE 6 #Enzian classification for compartment A

In cases of diagnosis by TVS, the criteria are used as described above. Anatomical structures are measured sonographically according to the proposal by the International Deep Endometriosis Analysis (IDEA) group.⁵ The maximum diameter of the lesion in the vagina should be evaluated in the mid-sagittal section cranio-caudally, which varies somewhat slightly from the IDEA proposal stating "...the dimensions of the vaginal wall DE nodule should be measured in three orthogonal planes."⁵ In cases of multiple involvement of these structures, the maximal diameter of the whole (vagina, RVS and retrocervical area) lesion will be measured in the sagittal (midline) section.

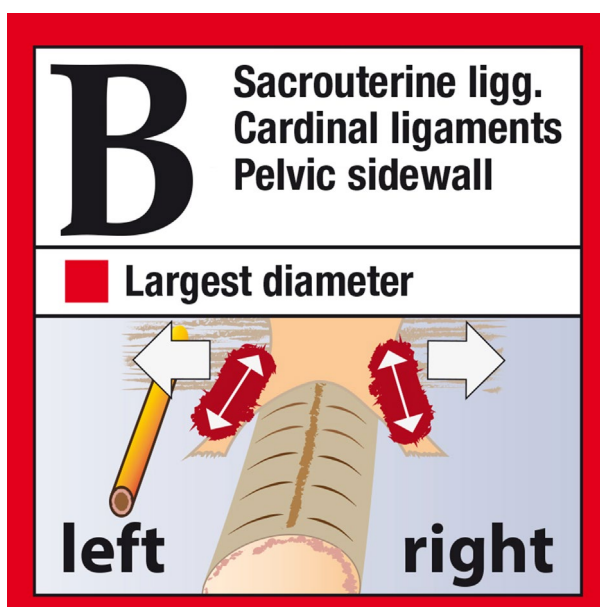


FIGURE 7 #Enzian classification for compartment B

2.7 | Compartment B (USL, cardinal ligaments, and pelvic sidewall)

This compartment (Figure 7) represents the mediolateral axis, which also slightly extends dorsolaterally. Hereby, the participation of the parametrial area and USL are taken into account. Measurement then follows according to the shape of the anatomical structures. The right and left sides will be recorded separately. This is in contrast to the previous version of the Enzian classification, where only the larger lesion was recorded in case of bilateral involvement. Endometriotic lesions causing intrinsic or extrinsic involvement of the ureters with hydroureteric changes or hydronephrosis will be classified as lesions in compartment FU (ureteral endometriosis). The description is as follows: B1 = <1 cm maximal diameter, B2 = 1–3 cm, B3 = >3 cm. Annotation of the left (l) and right (r) side is separated by a slash (/). In contrast to the previous Enzian classification, B3 no longer stands for ureter involvement and/or hydronephrosis. In case of multiple lesions on one side, diameters are counted together.

In diagnosis by TVS, the probe is inserted in the posterior vaginal fornix and the cervix is visualized defining the mid-sagittal plane by visualization of the cervical canal. Visualization of the USL is achieved via horizontal movement of the TVS probe by 20 degrees (cervical insertion of the USL) laterally. Rotation of the probe may be necessary because the USL or cardinal ligament are not parallel to the sagittal axis of the uterus. Any DE lesion within this visualization process should be measured in its most lateral extension (see Figures 8 and 9). This is in slight contrast to the IDEA proposal,⁵ but is necessary to distinguish the midline, left and right USL involvement.

2.8 | Compartment C (rectum)

Compartment C (Figure 10) runs in the ventrodorsal direction and is used to assess the length of the lesion in the anterior wall of the rectum. Lesions located up to 16 cm from the anal verge will be assigned to compartment C. If the lesion is located higher than 16 cm (definition of the anatomical rectum by the International Union Against Cancer 2003), it will be classified as a lesion in #Enzian compartment FI. Severity grade is determined by the maximal diameter of the lesion measured in the sagittal section along the axis of the rectum as follows: C1 = <1 cm maximal diameter, C2 = 1–3 cm, C3 = >3 cm. In case of both rectal and sigmoidal DE, both anatomical sites (C and FI) have to be coded.

In diagnosis by TVS, anatomical structures are measured according to the proposal made by the IDEA group.⁵ In cases of multifocal lesions of DE in the bowel, the total length of the sum of DE lesions of the bowel segment involved (from caudal to cephalic aspect) should be measured.

2.9 | Adenomyosis and other extragenital deep endometriosis

Presence of adenomyosis (Figure 11) is based on surgical findings, which are obvious for adenomyosis (appearance, consistency, size

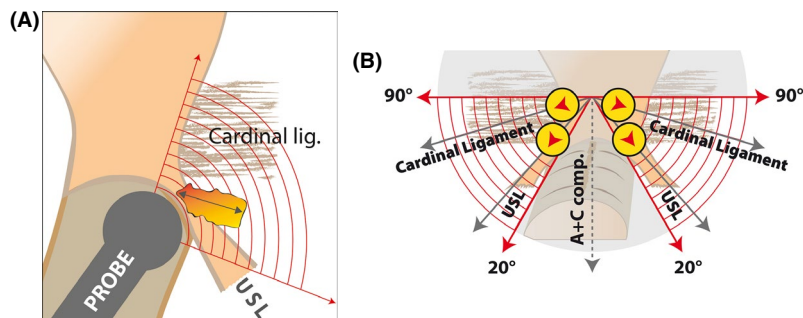


FIGURE 8 (A,B) Schematic drawing of transvaginal sonography (TVS) measurement of deep endometriosis affecting compartment B using the oblique plane. (A) The ultrasound probe, which is located in the posterior vaginal fornix, is turned slightly (20–30 degrees) laterally to show the area of the uterosacral ligaments (USL). (B) Schematic representation of the positions of the TVS probe and the corresponding planes for representing the USL (>20 degrees), and the various parts of the cardinal ligament (20–90 degrees)

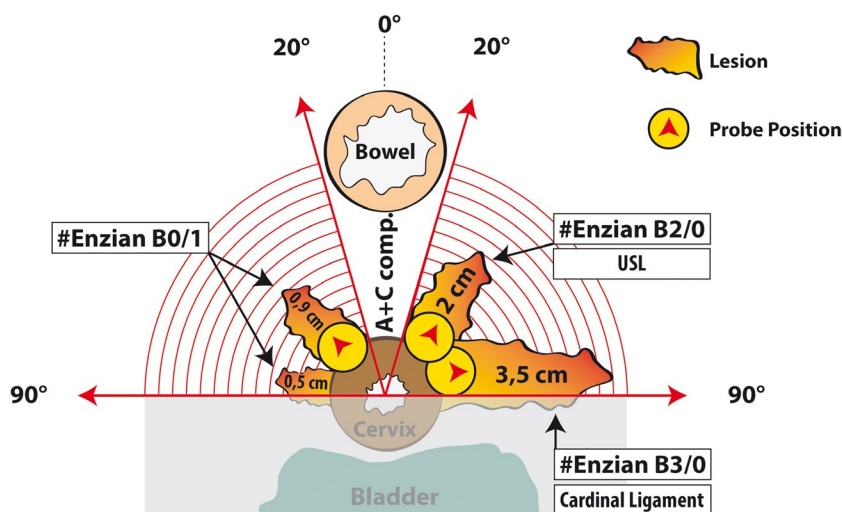


FIGURE 9 Schematic demonstration of transvaginal sonography (TVS) of the medial limit of #Enzian compartment B (view from above) starting from 20 degrees rotating laterally (probe positions for right and left uterosacral ligaments [USL] and parametrial deep endometriosis), depicting possible lesion sizes. The pathological changes caused by deep endometriosis which are located in the area between 0 and 20 degrees are assigned to the compartments A and C. In this figure each lesion is classified separately in order to demonstrate the code (eg, #Enzian B2/0 for a 2-cm lesion in the left cardinal ligament)

etc.), histological diagnosis (if available), and/or TVS findings. Within this, adenomyosis should be assessed sonographically using the Morphological Uterus Sonographic Assessment (MUSA) criteria.¹⁴ Deep lesions of the urinary bladder (FB) with involvement of the muscular layer or ureteric disease (extrinsic and/or intrinsic; FU) are based on surgical findings, that are obvious for DE (appearance, consistency, size) and histological diagnosis (if available). In cases of ureteral DE, FU correlates to obstruction-related dilatation in a funnel-shape either caused by a lesion corresponding to DE (usually parametrial origin) or by DE of the urinary bladder with or without hydronephrosis.

In cases of diagnosis by TVS, a ureteral diameter ≥ 6 mm is interpreted as a congestion sign correlating to ureteric obstruction.¹⁵ TVS diagnosis of ureteric endometriosis causing hydroureteric involvement can either be made by visualization of hydroureteric dilatation¹⁶ or hydronephrosis in the presence of DE. However, it should be noted that early stages of ureteral dilatation may not be accompanied by hydronephrosis. Ureteric obstruction may also occur due

to DE lesions of non-parametrial origin infiltrating the upper pelvic sidewall. This may not be visible using TVS, but can be identified with transabdominal ultrasound. Annotation of the left (l) and right (r) sides are given in brackets.

FI describes DE involving other intestinal structures besides the rectum: lesions cranial to the rectosigmoid junction (above 16 cm from the anus—upper sigmoid, transverse colon, cecum, appendix, and small bowel). Lesions on other locations such as the abdominal wall, diaphragm, lung, and nerve, are annotated as F (...). Instead of previous O for “other”, the #Enzian classification cites the localization directly in brackets, eg F(umbilicus) or F(diaphragm right) or F(plexus sacralis, right).

2.10 | Coding of the #Enzian classification

Individual compartments are written with capital letters in an order:

#Enzian P_, O_/, T_/, A_, B_/, C_, F_().....

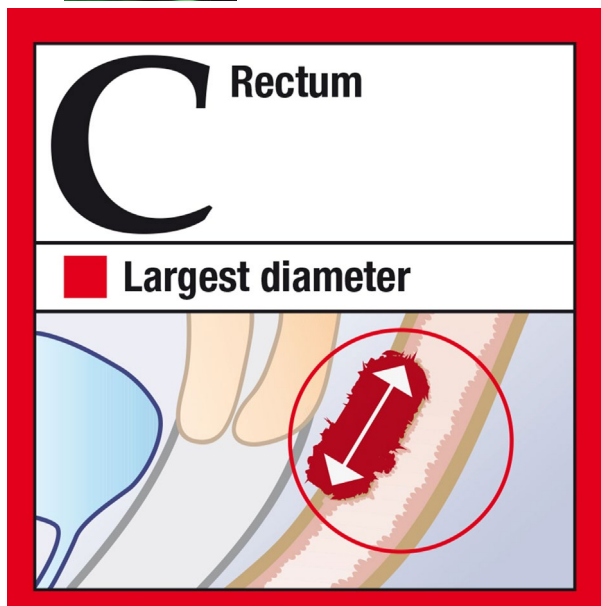


FIGURE 10 #Enzian classification for compartment C

The individual stages (numbers) according to the specification are written directly after the letter: number 0 is used in case of no involvement. There is a comma between each individual compartment. Paired organs (eg ovary, tube) are annotated according to the side. A slash separates left and right (/). In the case of paired organs, both sides are annotated, even if only one side is affected.

#Enzian classification summarized in the code (as an example):

- Superficial endometriosis on the peritoneum <3 cm (P) = P1
- Ovarian endometriosis, right 4 cm (O) = O0/2
- No adhesions on the tubo-ovarian unit (T) = T0/0
- No lesion in the A compartment=A0
- DE left USL <1 cm, right USL 1-3 cm (B) = B1/2
- DE in the rectum 2 cm (C) = C2
- Hydroureter right (FU) = FU(r)
- Endometriosis in the appendix (FI) = FI(App.)

For better readability only affected compartments and organs should be listed (Figure 12):

#Enzian P1, O0/2, B1/2, C2, FU(r), FI (Appendix)

This code should be used independently of the imaging modality (TVS, MRI) and type of surgery. A prefix can be used optionally in brackets following the word #Enzian (ie #Enzian(s) P1, ...) in order to depict the modality of evaluation of the disease when using the #Enzian:

#Enzian (u) assessment by ultrasound

#Enzian (m) assessment by MRI

#Enzian (s) assessment by surgery

If the surgical #Enzian (s) classification of a particular compartment (ie in case of severe obliteration of the pouch of Douglas or hidden

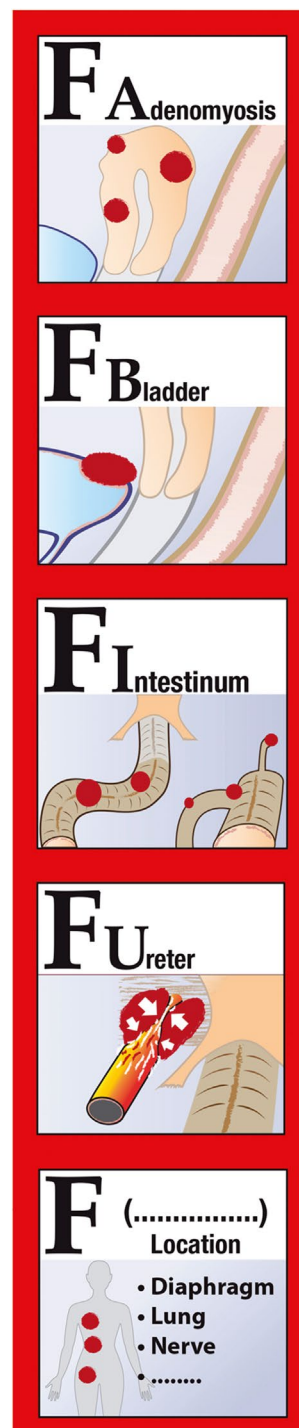


FIGURE 11 #Enzian classification of adenomyosis and other extragenital localizations F

extraperitoneal lesions) cannot be completed at surgery, the "x" suffix should be used after the compartment code.

An example of this is,

#Enzian (s)P2, O1/0, T3-/0+, B2/0, Cx, F(diaphragm);

Cx indicates that the rectum cannot be assessed surgically (Figure 12). In the presence of the relevant imaging finding for these missing compartments, #Enzian(s) classification can be completed

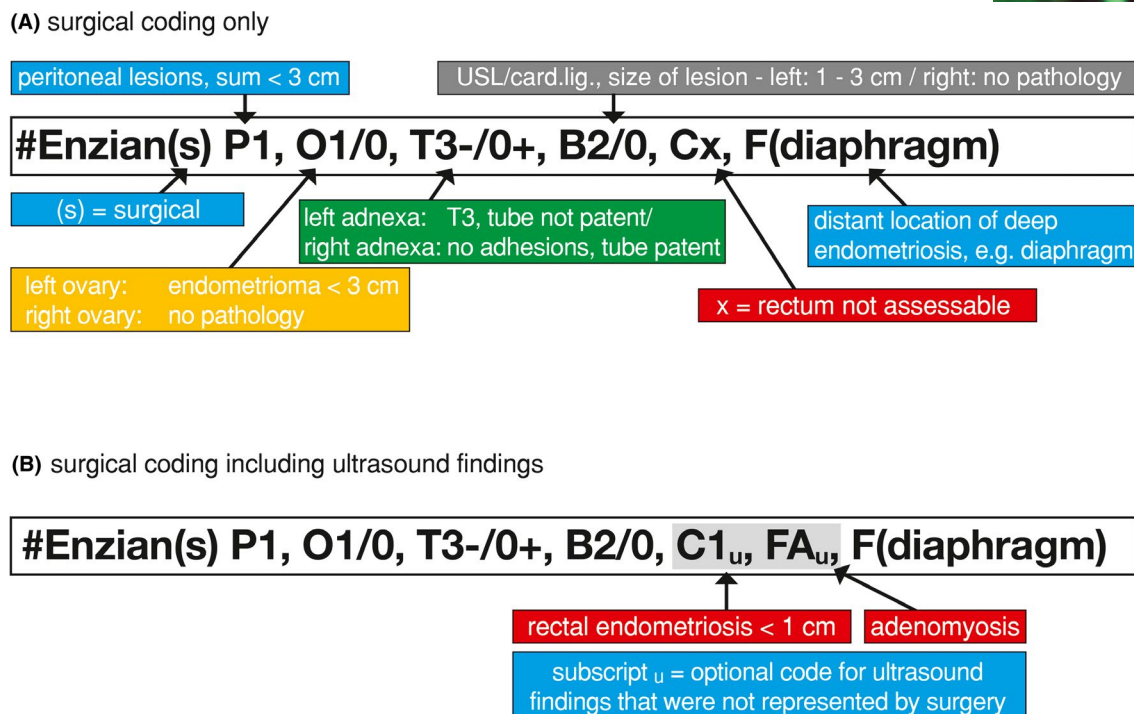


FIGURE 12 Explanation of the different components of the formula when coding (surgically) with the #Enzian classification in an example: (A) surgical coding only; (b) Surgical coding including the transvaginal sonography findings that were not identified during surgery

optionally, using this finding by adding a subscript letter of 'm' or 'u' to specify the method after the compartment code (same example:

#Enzian (s)P2, O1/0, T3-/0+, B2/0, C1_u, FA_u, F(diaphragm);

C1_u, FA_u = sonographically identified DE of the rectum <1 cm and adenomyosis (Figure 12).

3 | DISCUSSION

Our current proposal is the first of its kind to universally describe superficial and deep endometriosis, ovarian endometriosis and adenomyosis by using a classification system that can be applied by gynecologists, surgeons, sonographers, and radiologists following the same principles. The r-ASRM score was primarily designed to record intra-abdominal lesions, including adhesions, but not DE, which affects the extraperitoneal space, such as the bowel, bladder, RVS, or ureters as well as adenomyosis. In a study based on 63 patients with DE including rectosigmoid endometriosis, 21% were found to have only stage 1 or 2 according to the r-ASRM scoring system.¹⁷ Haas et al confirmed these data in 160 patients with DE.¹⁸

The lack of adequate classification of DE using the r-ASRM is underlined by Montanari et al,⁸ showing a significant correlation between the extent of DE and symptoms, when classified by the Enzian score.^{19,20} Further studies observed a direct correlation between the complexity of surgical procedures and the extent of DE described by the Enzian classification.²⁰⁻²² As a consequence of these data the working group of the European Society of Gynaecological Endoscopy (ESGE), the European Society of Human

Reproduction and Embryology (ESHRE), the World Endometriosis Society (WES) and the Consolidated Standards of Reporting Trials (CONSORT) group included the Enzian classification in their recommendations. Also the guidelines of the German, Swiss, Czech, and Austrian Societies for Obstetrics and Gynecology recommend, that the Enzian classification should be used for classification of DE.^{11,23,24}

The newly proposed #Enzian classification now includes endometriosis of the peritoneum, the ovaries, and the extent of adnexal adhesions. Peritoneal lesions are considered by the #Enzian classification using the sum of all visible affected areas. The choice of the diameter >3 cm and >7 cm was adapted in line with the r-ASRM classification. Obviously, the extent of the disease may be only diagnosed by a surgical procedure. When assessing ovarian endometriosis, the size, number, and involvement of the respective organs are taken into account. The division of the different stages according to the diameter was adapted not only to the r-ASRM classification, but also to the recommendations of the European Society of Gynaecological Endoscopy (ESGE), European Society of Human Reproduction and Embryology (ESHRE), and the World Endometriosis Society (WES).²⁵ Endometriomas smaller than 3 cm are usually not treated surgically, whereas lesions larger than 3 cm are more often subjected to surgery, either by stripping or vaporization procedures. A diameter larger than 7 cm was recommended by our group as the critical limit of size for organ-preserving surgery. Adhesions in the area of the adnexa and the cul-de-sac, including the intestine, are classified both sonographically (sliding sign) and surgically. The patency of the fallopian tubes may be

documented with (hysterosalpingo contrast sonography) and/or pertubation during surgery.

Taken together, this consensus provides a classification system that is anatomically logical and should be easy to use. Further studies are ongoing and are needed to provide proof for the applicability, reproducibility, and accuracy of the #Enzian classification for the description of endometriosis. The correlation between preoperative and surgical staging, on the basis of the #Enzian scheme allows for a consistent and clear classification of endometriosis, especially DE but also secondary adhesions. Endometriosis can be mapped with one single classification system applicable by pre-invasive (TVS, MRI) and invasive methods thereby enabling the use of one common language for describing endometriosis. Future studies are needed to validate this classification regarding its clinical validity, accuracy, and reproducibility.

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