

The ENZIAN Classification: A comprehensive framework for Understanding Deep Endometriosis

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Abstract

The ENZIAN classification system offers a comprehensive framework for assessing endometriosis, taking into account various factors beyond traditional staging systems. Developed as an alternative to the ASRM classification, ENZIAN categorizes endometriosis into five stages (P1 to P5) based on a multifactorial assessment that includes symptoms, anatomical location, and depth of infiltration. This classification emphasizes a symptom-based approach, incorporating patient-reported symptoms to guide treatment decisions effectively. ENZIAN provides a detailed anatomical assessment, considering the involvement of different pelvic structures and organs, facilitating surgical planning and personalized treatment strategies. By enhancing clinical management with a nuanced understanding of the disease's severity and complexity, ENZIAN classification aims to improve treatment outcomes and patient satisfaction in the management of endometriosis.

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Introduction

Endometriosis is a chronic gynaecological disorder characterized by the presence of endometrial-like tissue outside the uterus, often causing pelvic pain and infertility [1]. Accurate classification of endometriosis is crucial for effective management and treatment. The ENZIAN classification system, developed by the World Endometriosis Society in 2020, offers a comprehensive approach to categorizing endometriosis based on its extent, nature, and zygosity. This chapter aims to provide an in-depth understanding of the ENZIAN classification and its clinical implications [2]. The 2021 revision of the classification, under the Scientific Endometriosis Foundation (SEF), was the result of a rigorous multi-round expert consensus involving gynecologists, sonographers, and radiologists with extensive experience in the diagnosis and treatment of endometriosis [3].

Historical Context of Endometriosis Classification

Historically, endometriosis classification systems have evolved from descriptive to more structured approaches. The American Society for Reproductive Medicine (ASRM) classification, introduced in 1973, was based primarily on anatomical staging. However, limitations in predicting symptom severity and treatment outcomes prompted the development of more nuanced classification systems like the ENZIAN.

Introduction to the ENZIAN Classification

The ENZIAN classification system encompasses three main components:

- A. E (Extent of Endometriosis): Defines the anatomical distribution and severity of endometriotic lesions.
- B. N (Nature of Endometriosis): Describes the morphological characteristics and histological features of endometriotic lesions.
- C. Z (Zygosity of Endometriosis): Indicates the presence or absence of bilateral involvement of the ovaries and/or fallopian tubes.

Clinical Application of the ENZIAN Classification

The ENZIAN classification system serves as a valuable tool for guiding clinical decision-making in the management of endometriosis. By accurately stratifying patients based on disease severity and biological characteristics, clinicians can tailor treatment strategies to individual needs. Furthermore, the ENZIAN classification facilitates communication among healthcare providers and enhances prognostic accuracy [4]. It is endorsed by major societies including European Society for Gynecological Endoscopy, European Society of Human Reproduction and Embryology, and World Endometriosis Society [3].

The Enzian classification

The Enzian classification is for Deep Endometriosis using three compartments:

- A: Vagina, Recto Vaginal Space (RVS)
- B: Utero Sacral Ligaments (USL) / cardinal ligaments/pelvic sidewall and
- C: Rectum
- F: Far locations such as the urinary bladder (FB), the Ureters (FU), and other extra-genital lesions (FO), Intestinal locations

(sigmoid colon, small bowel; FI)

P: Peritoneum (P)

O: Ovary (O)

T: Adhesions, involving the tubo-ovarian unit (T), and, tubal patency can also be assessed and noted

- A. Individual compartments or organ involvement are identified with capital letters (P, O, T, A, B, C, F). The extent of endometriosis is represented by the numbers 1, 2 and 3 in compartments P, O, T, A, B, and C.
- B. Each compartment is graded 1 (<1cm), 2 (1-3cm), or 3 (>3cm).
- C. Paired organs (Ovary, Tube, USL, Parametrium, Ureter): the severity is arranged separately after the letter (left / right).
- D. Missing / invisible ovary or tube are described with suffix (m, missing; x, unknown).
- E. The individual anatomical locations and their annotation are annotated in a bracket, i.e. (r) or (l)
- F. The classification is applicable via all diagnostic modalities: Transvaginal Sonography (TVS), MRI, or surgery-annotated with prefixes (u), (m), and (s) (Figure 1).

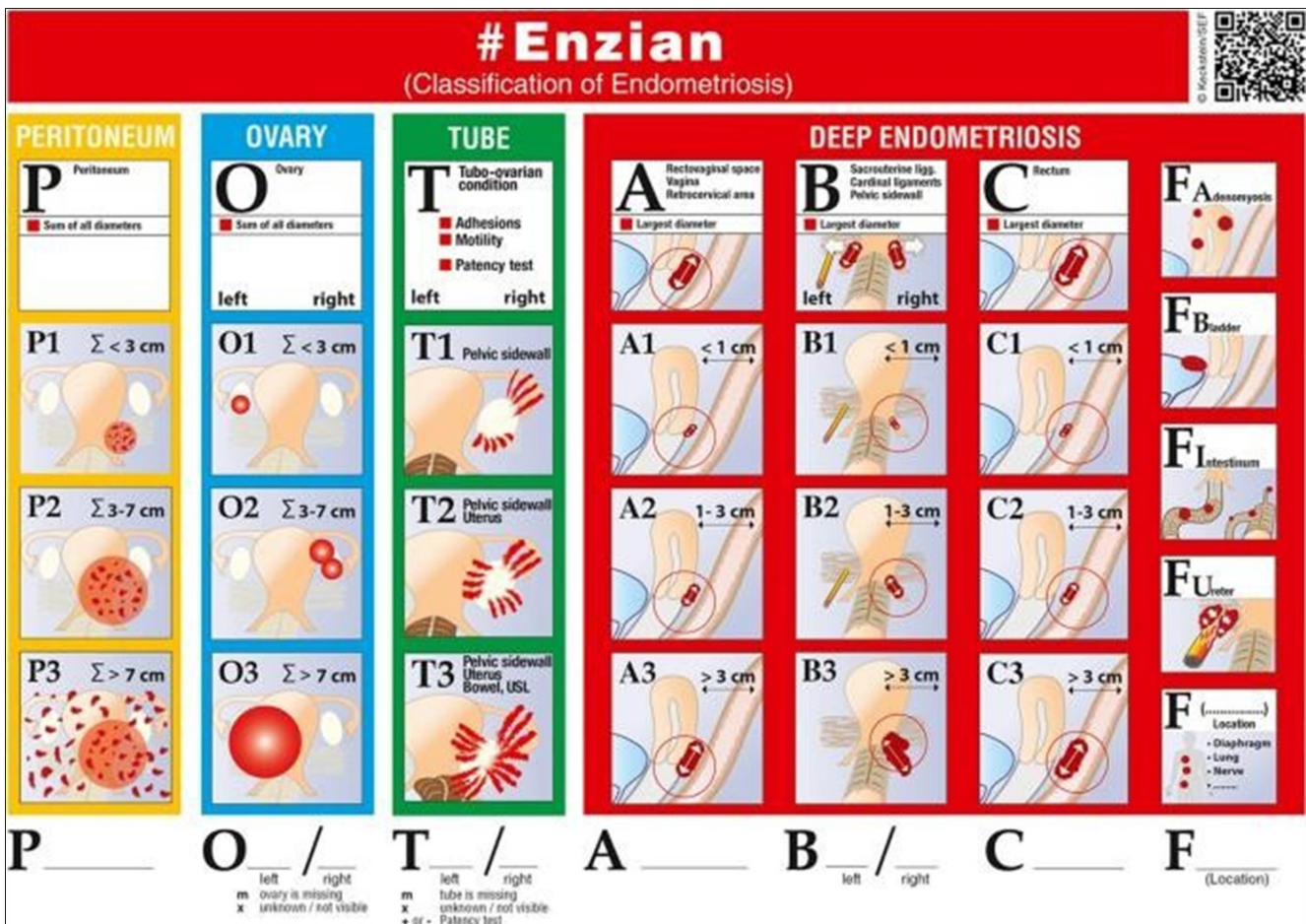


Figure 1: Enzian (Classification of Endometriosis).

Deep Endometriosis (DE)

All lesions exhibiting sub peritoneal infiltration of >5mm is classified as per the DE definition.

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 levels, represented by the compartments:

- A. Compartment A (craniocaudal axis)
- B. Compartment B (mediolateral axis) and
- C. Compartment C (ventro-dorsal axis)

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 (>16cm from the anal verge), Upper sigmoid, Transverse colon, Cecum, Appendix, Small bowel; and other locations (FO) such as the abdominal wall, diaphragm, and nerve.

Compartment A (vagina, rectovaginal space):

Runs in the craniocaudal direction and assesses the posterior vaginal fornix and involvement of the RVS.

- a. The maximal diameter (cm) of the lesion is measured in the sagittal (midline) section.
- b. 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.
- c. The description is as follows: A1 = <1cm, A2 = 1–3cm, A3 = >3cm. (On TVS)

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

This compartment represents the mediolateral axis, which also slightly extends dorso-laterally. 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. Endometriotic lesions causing intrinsic or extrinsic involvement of the ureters with hydro ureteric changes or hydronephrosis will be classified as lesions in compartment FU (ureteral endometriosis).

The description is as follows:

B1 = <1cm maximal diameter,

B2 = 1–3cm,

B3 = >3cm.

Annotation of the left (l) and right (r) side is separated by a slash (/).

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 maybe necessary because the USL or cardinal ligament are not parallel to the sagittal axis of the uterus.

Compartment C (rectum) runs in the ventrodorsal direction and issued to assess the length of the lesion in the anterior wall of the rectum. Lesions located up to 16cm from the anal verge will be assigned to compartment C. If the lesion is located higher than 16 cm, 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 = <1cm maximal diameter, C2 = 1–3cm, C3 = >3cm. In case of both rectal and sigmoidal DE, both anatomical sites (C and FI) have to be coded.

Peritoneum (P)

The classification of peritoneal endometriosis takes into account all superficial (sub peritoneal invasion <5mm) peritoneal foci located in the pelvis and abdomen above the pelvic rim, that are not considered Deep endometriosis. (Noted during surgery)

The diameter of a virtual circle is calculated, in which all endometrial foci can be included.

P1 = <3cm (sum of all lesions);

P2 = 3–7cm (sum of all lesions),

P3 = >7cm (sum of all lesions).

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 separately calculated for each side. (Can be noted during surgery and during Ultrasound TVS)

O1 = <3cm (sum of all endometriomas);

O2 = 3–7cm (sum of all endometriomas);

O3 = >7cm (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.

Tubo-ovarian condition

The evaluation of the tubo-ovarian condition, specifically the presence of possible adhesions affecting the mobility of the ovaries and tubes, as well as tubal patency, is 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 a slash (/);

m = missing tube,

x = tube not visualized or unknown (only for surgical evaluation).

Tubal patency can optionally be assessed using TVS (hysterosalpingo contrast sonography)

Imaging and Surgical Considerations

TVS is a key diagnostic tool. For compartment A, lesions are measured in the mid-sagittal plane. For B, probe rotation of 20–90° helps visualize USLs. For C, measurements are taken along the rectal axis, with lesions >16cm classified under FI. Tubo-ovarian adhesions are evaluated using the sliding sign and tubal patency can be assessed with hysterosalpingo contrast sonography (HyCoSy)

Coding of the Enzian classification

Individual compartments are written with capital letters in an order: #Enzian P_ O_/_ T_/_ A_ B_/_ C_ F

- 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 (e.g.: 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.

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

Validation and Reliability of ENZIAN Classification

Several studies have validated the ENZIAN classification system, demonstrating its reliability and predictive value in clinical practice. These studies have highlighted the system's ability to correlate with symptom severity, surgical outcomes, and disease recurrence. Additionally, the ENZIAN classification has shown good interobserver agreement among expert endometriosis specialists, supporting its widespread adoption in clinical settings.

Challenges and Limitations

Despite its merits, the ENZIAN classification system has some limitations. Variability in lesion morphology and histopathological interpretation may pose challenges to accurate classification. Additionally, the complexity of the ENZIAN system may require specialized training for healthcare providers to ensure consistent application. Further research is needed to address these challenges and refine the ENZIAN classification for improved clinical utility.

Endometriosis Fertility Index (EFI)

The EFI system was developed to predict pregnancy rates in patients with surgically confirmed endometriosis. Proposed by Adamson & Pasta [5], the EFI system considers historical factors such as age, duration of infertility, and previous pregnancies. Successful pregnancy requires proper functioning of the fallopian tube, fimbria, and ovary. The functional score assesses the ability of the embryo to implant in the uterus, the uterus's capacity to support early embryo development, and the fallopian tubes' efficiency in picking up the ovum.

Score is calculated by evaluating the function of the ovary, fallopian tube, and fimbria on each side, then summing the lowest scores from the left and right. Surgeons determine functional scores, which range from 0 to 4: 0 for absent or nonfunctional, 1 for severe dysfunction, 2 for moderate dysfunction, 3 for mild dysfunction, and 4 for normal function. In addition to the least functional score, other surgical factors like the rASRM total score and the endometriosis lesion score of rASRM are included (Figure 2).

ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score	Description		Left	Right
4	= Normal		<input type="text"/>	<input type="text"/>
3	= Mild Dysfunction	Fallopian Tube	<input type="text"/>	<input type="text"/>
2	= Moderate Dysfunction	Fimbria	<input type="text"/>	<input type="text"/>
1	= Severe Dysfunction	Ovary	<input type="text"/>	<input type="text"/>
0	= Absent or Nonfunctional			

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

Lowest Score	<input type="text"/>	+	<input type="text"/>	=	<input style="border: 1px dashed black;" type="text"/>		
	Left		Right		LF Score		

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age	If age is ≤ 35 years	2	LF Score	If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile	If years infertile is ≤ 3	2	AFS Endometriosis Score	If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy	If there is a history of a prior pregnancy	1	AFS Total Score	If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: Historical + Surgical = EFI Score

ESTIMATED PERCENT PREGNANT BY EFI SCORE

Figure 2: Endometriosis Fertility Index (EFI) Surgery form.

The EFI score, ranging from 0 to 10, is derived by summing historical and surgical scores, with 10 indicating the best prognosis and 0 the worst. The EFI system is advantageous for predicting pregnancy outcomes, outperforming the rASRM classification. According to Zeng et al [6], the pregnancy rates for rASRM stages I, II, III, and IV were 53.6%, 36.0%, 51.7%, and 41.7%, respectively, with no statistically significant difference ($p= 0.246$). However, the EFI score showed statistically significant pregnancy rates: 8.3% for scores 0 to 3, 41.2% for scores 4 to 7, and 60.9% for scores 8 to 10 ($p< 0.001$) [6]. Similarly, Wang et al. [7] found that IVF outcomes were better for patients with an EFI score of 6 or higher compared to those with a score of 5 or lower.

However, the EFI system has some drawbacks. It does not correlate with pain, and the least functional score can vary subjectively between surgeons, leading to inconsistent total scores. No studies have yet assessed the interobserver reliability and interobserver reproducibility of the EFI system. Additionally, the EFI score is more complex to use than the rASRM classification and ENZIAN score due to the need to calculate and sum scores from various categories.

Future Directions

The ENZIAN classification represents a significant advancement in the field of endometriosis classification, but ongoing research is

essential to enhance its efficacy and relevance. Future directions include integrating molecular markers and imaging modalities into the classification system to provide a more comprehensive understanding of endometriosis pathophysiology. Additionally, large-scale prospective studies are needed to validate the ENZIAN classification across diverse patient populations and healthcare settings.

Conclusion

The ENZIAN classification of endometriosis offers a comprehensive framework for characterizing the extent, nature, and zygosity of the disease. By providing detailed insights into disease severity and biological behaviour, the ENZIAN classification facilitates personalized treatment approaches and improves clinical outcomes for patients with endometriosis. Continued research and collaboration are essential to refine and validate the ENZIAN classification for optimal patient care.

Key Points

- A. Multifactorial assessment:** ENZIAN considers various factors beyond the traditional ASRM staging, such as symptoms, anatomical location, and depth of infiltration.
- B. Five stages:** It categorizes endometriosis into five stages (P1 to P5), with each stage reflecting the severity and complexity of the disease.
- C. Symptom-based classification:** ENZIAN emphasizes symptomatology, incorporating patient-reported symptoms into the classification to guide treatment decisions.
- D. Detailed anatomical assessment:** It provides a more detailed anatomical assessment, considering the involvement of different pelvic structures and organs.
- E. Surgical planning:** The classification aids in surgical planning by providing a comprehensive evaluation of the extent and

severity of endometriosis, helping surgeons determine the most appropriate approach.

- F. Tailored treatment:** Allows for a more personalized and tailored approach to treatment, considering both the severity of the disease and the patient's symptoms and preferences.
- G. Improved clinical management:** ENZIAN classification enhances clinical management by providing a more nuanced understanding of endometriosis, leading to improved treatment outcomes and patient satisfaction.

References

1. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, et al. (2014) ESHRE guideline: management of women with endometriosis. *Hum Reprod* 29: 400-412.
2. Tuttles F, Keckstein J, Ulrich U, Possover M, Schweppe KW, et al. (2005) ENZIAN- score, a classification of deep infiltrating endometriosis. *Zentralbl Gynakol* 127(5): 275-281.
3. Keckstein J, Saridogan E, Ulrich UA, Sillem M, Oppelt P, et al. (2021) The #Enzian classification: A comprehensive non- invasive and surgical description system for endometriosis. *Acta Obstet Gynecol Scand* 100(7): 1165-1175.
4. Di Paola V, Manfredi R, Castelli F, Negrelli R, Mehrabi S, et al. (2015) Detection and localization of deep endometriosis by means of MRI and correlation with the ENZIAN score. *Eur J Radiol* 84(4): 568-574.
5. Adamson GD, Pasta DJ (2010) Endometriosis fertility index: The new, validated endometriosis staging system. *Fertil Steril* 94(5): 1609-1615.
6. Zeng C, Xu JN, Zhou Y, Zhou YF, Zhu SN, et al. (2014) Reproductive performance after surgery for endometriosis: Predictive value of the revised American Fertility Society classification and the endometriosis fertility index. *Gynecol Obstet Invest* 77(3):180-185.
7. Wang W, Li R, Fang T, Huang L, Ouyang N, et al. (2013) Endometriosis fertility index score maybe more accurate for predicting the outcomes of in vitro fertilisation than r-AFS classification in women with endometriosis. *Reprod Biol Endocrinol* 11: 112.