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**DIAGNOSTIC PARTICULARITIES OF  
DEEP ENDOMETRIOSIS AND ITS IMPACT  
ON WOMEN'S QUALITY OF LIFE**

**321.15 - OBSTETRICS AND GYNECOLOGY**

**Abstract of the doctoral thesis in medical sciences**

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## LIST OF ABBREVIATIONS

|                            |                                                                    |
|----------------------------|--------------------------------------------------------------------|
| <b>#Enzian</b>             | Classification System for Endometriosis (2019)                     |
| <b>A</b>                   | Rectovaginal and vaginal compartment (#Enzian)                     |
| <b>ART</b>                 | Assisted Reproductive Technologies                                 |
| <b>AUC</b>                 | Area under the curve                                               |
| <b>B</b>                   | Sacruterine ligaments and pelvic sidewall compartment (#Enzian)    |
| <b>B&amp;B</b>             | Biberoglu and Behrman                                              |
| <b>C</b>                   | Rectal and sigmoid colon compartment (#Enzian)                     |
| <b>CI</b>                  | Confidence interval                                                |
| <b>CPP</b>                 | Chronic pelvic pain                                                |
| <b>DIE</b>                 | Deep infiltrating endometriosis                                    |
| <b>df</b>                  | Degrees of Freedom                                                 |
| <b>Dm</b>                  | Dysmenorrhoea                                                      |
| <b>Dp</b>                  | Dyspareunia                                                        |
| <b>Du</b>                  | Dysuria                                                            |
| <b>Dh</b>                  | Dyschezia                                                          |
| <b>E</b>                   | Endometriosis                                                      |
| <b>EIQ</b>                 | Endometriosis Impact Questionnaire                                 |
| <b>EFI</b>                 | Endometriosis Fertility Index                                      |
| <b>FA</b>                  | Adenomyosis compartment (#Enzian)                                  |
| <b>FB</b>                  | Bladder compartment (#Enzian)                                      |
| <b>FI</b>                  | Intestinal compartment above the rectosigmoid junction (#Enzian)   |
| <b>FU</b>                  | Ureteral compartment (#Enzian)                                     |
| <b>F...</b>                | Other extragenital locations (e.g. diaphragm, lungs, nerves, skin) |
| <b>G1</b>                  | Research group I                                                   |
| <b>G2</b>                  | Research group II                                                  |
| <b>MRI</b>                 | Magnetic resonance imaging                                         |
| <b>O</b>                   | Ovarian endometriosis                                              |
| <b>P</b>                   | Superficial peritoneal endometriosis                               |
| <b>p</b>                   | p-value                                                            |
| <b>rASRM</b>               | Revised American Society for Reproductive Medicine classification  |
| <b>ROC</b>                 | Receiver operating characteristic                                  |
| <b>Se</b>                  | Sensitivity                                                        |
| <b>SF-36</b>               | Short Form – 36                                                    |
| <b>Sp</b>                  | Specificity                                                        |
| <b>SPSS</b>                | Statistical Package for the Social Sciences                        |
| <b>T</b>                   | Tubal endometriosis                                                |
| <b>U</b>                   | Mann–Whitney U test                                                |
| <b>VAS</b>                 | Visual Analogue Scale                                              |
| <b>WHO-5</b>               | The World Health Organization-5 Well-Being Index                   |
| <b><math>\chi^2</math></b> | Chi-square test                                                    |

## INTRODUCTION

### THE THEORETICAL FRAMEWORK OF THE RESEARCH

**Relevance of the Topic.** Deep infiltrating endometriosis (DIE) represents the most aggressive and clinically heterogeneous form of endometriosis [1], capable of affecting various organs and anatomical structures [2,3]. The condition is often resistant to hormonal treatment [4–7] and may continue to progress even during pregnancy [8–10]. It predominantly affects adolescents and young women, with a significant impact on quality of life [11,12]. The prevalence of endometriosis among adolescents (12–20 years) with dysmenorrhoea ranges from 21–44%, while in young women (20–35 years) with chronic pelvic pain it reaches up to 73%, which may indicate an infiltrative process [13,14].

According to global data, endometriosis affects approximately 10% of women of reproductive age, and around 20% present with the infiltrative form, which is responsible for severe pain, infertility, diagnostic errors and repeated surgical interventions [2,15,16]. Despite medical advances, the aetiology and pathogenetic mechanisms of DIE remain insufficiently elucidated. The postulate that “pregnancy cures endometriosis” is now considered outdated, as hormonal changes may lead to disease progression and serious surgical complications, including hydronephrosis, intestinal obstruction, appendicitis and spontaneous pneumothorax [3].

DIE is associated with the most severe pain manifestations [17]. In addition to dysmenorrhoea and dyspareunia, patients report pain during urination and defecation, which may be daily and difficult to control [18]. Diagnosis is frequently delayed because symptoms often lead patients to consult non-gynaecological specialists, while extragenital forms may be confused with other surgical pathologies [3]. Intraoperative detection of extragenital lesions that extend beyond the expertise of the gynaecological team may result in persistent symptoms and the need for further procedures. Consequently, patients with DIE represent a highly vulnerable group with a markedly reduced quality of life.

Although endometriosis is currently regarded as a chronic, life-long disease, research continues to investigate the mechanisms underlying its development and to improve existing therapeutic strategies. Hormonal therapy, which is effective in other phenotypes, is frequently ineffective in DIE, while complete surgical excision requires a multidisciplinary team approach [2,19]. At the same time, the literature demonstrates variability in the diagnostic performance of imaging methods and a lack of universal standardisation of topographical lesion assessment. Moreover, the relationships between lesion localisation, clinical manifestations and the degree of quality-of-life impairment remain insufficiently elucidated, supporting the need for an integrated multidisciplinary diagnostic approach.

Given the disabling nature of the disease, assessment of its impact on quality of life is essential. Chronic pain, infertility and psycho-emotional disturbances impair social and professional functioning, contribute to depression and reduce overall well-being [3,12,20]. Evaluation of quality of life using general and disease-specific standardised questionnaires [3,21] enables objective assessment of the disease burden on physical, psychological, sexual and social health and supports treatment individualisation. Increasing awareness among medical professionals, early interdisciplinary diagnosis and a multidisciplinary surgical approach constitute key prerequisites for improving prognosis and quality of life in women affected by DIE [3].

**Aim of the study.** To optimise the diagnosis of DIE through the development of a multidisciplinary medical diagnostic algorithm and a comparative assessment of the impact of this condition on quality of life.

**Objectives of the study:**

1. To comparatively evaluate the anamnestic, clinical, and paraclinical characteristics of the study groups.
2. To comparatively analyse clinical manifestations in relation to the localisation of deep endometriosis lesions, as well as to the ultrasonographic findings assessed according to the #Enzian classification, with the aim of developing a multidisciplinary diagnostic algorithm.
3. To comparatively assess the determinants of quality of life in the study groups and to evaluate reproductive prognosis according to the Endometriosis Fertility Index (EFI), as a relevant component of quality of life.
4. To assess the impact of endometriosis in the study groups on the level of physical and emotional functioning, mental health, and daily functional potential.

**General research methodology.** The study was conducted between 2021 and 2023 at the Department of Obstetrics and Gynaecology of Nicolae Testemițanu State University of Medicine and Pharmacy and included 190 patients diagnosed with endometriosis, with final confirmation of the disease established intraoperatively (85 patients with DIE and 105 patients without DIE). The minimum required sample size, calculated using Cochran's formula and adjusted by 10% for the non-response rate, was 161 patients. The main indications for surgical intervention were ovarian endometriotic cysts, infertility, and symptomatic uterine fibroids. The research project was approved by the Research Ethics Committee (Approval No. 38 of 21 May 2021). The study results were analysed from a theoretical and scientific perspective in accordance with the established aim and objectives.

The study was carried out according to a structured methodology organised into successive stages, including: problem definition and development of the research plan, collection of factual data through statistical observation, evaluation of clinical and paraclinical parameters of the patients included in the study, statistical analysis, and synthesis of conclusions. Data processing was performed using IBM SPSS Statistics version 21 and MedCalc software packages, applying descriptive, comparative, and diagnostic performance assessment methods, with the threshold for statistical significance set at  $p < 0.05$ .

**Scientific novelty of the research results.** For the first time in the Republic of Moldova and Eastern Europe, the impact of different forms of endometriosis on the determinants of quality of life was assessed using standardized multidimensional questionnaires (EIQ, SF-36, and WHO-5), with statistical evidence demonstrating the disabling impact of DIE. The findings contribute to the advancement of the diagnostic approach to DIE by systematically integrating quality-of-life assessment into clinical decision-making and supporting its recognition as a chronic biopsychosocial condition.

Integration of the #Enzian classification enabled characterization of the extent and distribution of endometriotic lesions, as well as identification of associations between clinical manifestations and lesion location, thereby contributing to presumptive clinical diagnosis and the development of a multidisciplinary diagnostic algorithm. Assessment of reproductive prognosis

using the EFI, in relation to infertility and quality-of-life determinants, revealed particular aspects of its applicability in patients with DIE and highlighted the need for further research in this field.

**Important scientific problem addressed by the research.** The study addresses the scientific problem of optimizing the non-invasive diagnosis of DIE by substantiating a comprehensive approach based on the integration of clinical and anamnestic, imaging, and topographic data using the #Enzian classification. This approach enabled better guidance of the presumptive clinical diagnosis, identification of the affected compartments, assessment of disease extent, and development of a multidisciplinary medical diagnostic algorithm, supporting a non-invasive approach at the diagnostic stage. At the same time, the applicability of the EFI in assessing reproductive prognosis in patients with DIE was evaluated.

Thus, the research complements the understanding of DIE as a multifocal condition requiring a multidisciplinary approach, in which the assessment of quality-of-life determinants, together with clinical, imaging, and reproductive data, contributes to individualized medical management and the integration of patients' needs into the decision-making process.

**Theoretical significance of the research.** The research makes an important theoretical contribution by strengthening the concept of DIE as a chronic, infiltrative, and disabling condition characterized by clinical and topographic heterogeneity and a significant multisystem impact. Integration of the #Enzian classification into clinical assessment allows DIE to be conceptualized not merely as an anatomical entity but as a condition whose clinical manifestations may be correlated with lesion location.

The study provides a theoretical basis for an integrated diagnostic approach to DIE, while simultaneously elucidating the degree of impairment of quality-of-life determinants assessed using standardized and validated instruments, and supports the need for a comprehensive, multidisciplinary, and individualized approach to patients with DIE.

**Practical value of the research.** The practical value of the research lies in the development and integration of a set of modern tools applicable to clinical practice, beginning with a diagnostic algorithm aimed at the early and non-invasive identification of DIE, complemented by imaging assessment according to the #Enzian classification, which facilitates multidisciplinary surgical planning; the use of the VAS and B&B scales for the objective assessment of pain and monitoring of clinical evolution; and the application of the EFI, with consideration of its specific features in DIE, for the assessment of reproductive prognosis.

Implementation of the assessment of quality-of-life determinants using the standardized EQ, SF-36, and WHO-5 questionnaires may contribute to integrated management (medical, surgical, reproductive, psychological, and social) within Endometriosis Centres of Excellence, supporting the need for their development.

**Implementation of scientific results.** The research findings were integrated into the teaching process at Nicolae Testemițanu State University of Medicine and Pharmacy and implemented through eight implementation acts at Gheorghe Paladi Municipal Clinical Hospital. Scientific materials developed within the thesis were also used in the development of clinical protocols on endometriosis, including the National Clinical Protocol "Endometriosis" (2025).

**Approval of scientific results.** The main principles of the research were presented and discussed at national and international scientific forums, including the Anniversary International Congress of Nicolae Testemițanu State University of Medicine and Pharmacy (Chișinău, 20–22 October 2025), meetings of the Society of Obstetricians and Gynaecologists of the Republic of

Moldova (29 May 2025), the 11th Annual Congress of the Society of Endometriosis and Uterine Disorders (SEUD) (Prague, Czech Republic, 24–26 April 2025), the 13th National Congress of Obstetrics and Gynaecology in Romania (Bucharest, Romania, 21–23 November 2024), the 7th European Endometriosis Congress (Bucharest, Romania, 6–8 June 2024), the 21st World Congress of Gynaecological Endocrinology (ISGE) (Florence, Italy, 8–11 May 2024), the “Gheorghe Paladi Days” Conference (Chişinău, Republic of Moldova, 17–18 May 2024), the Annual University Conference of Nicolae Testemiţanu State University of Medicine and Pharmacy (Chişinău, Republic of Moldova, 18 October 2023), the Balkan Medical Union Week “Perspectives of Balkan Medicine in the Post-COVID-19 Era” (Chişinău, Republic of Moldova, 7–9 June 2023), as well as a series of Abbott conferences and courses held in Chişinău between 2021 and 2023, and the 7th Congress of the Society of Endometriosis and Uterine Disorders (SEUD) (Stockholm, Sweden, 9–11 December 2021).

**Publications.** On the topic of the thesis, six scientific articles were published, including five papers in peer-reviewed journals. In addition, 20 conference abstracts and six posters were published, and eight innovator certificates were obtained.

**Volume and structure of the thesis.** The thesis is written in Romanian and comprises 114 pages of main text; it includes 50 figures, one formula, 9 tables and 9 appendices. The work consists of an introduction, four chapters, general conclusions, practical recommendations, abstracts in Romanian and English, and a bibliography containing 155 references.

**Keywords.** Endometriosis, deep endometriosis, pain syndrome, clinical diagnosis, #Enzian classification, quality of life, EFI, EIQ, SF-36, WHO-5.

## THESIS CONTENT

### 1. THE PROBLEM OF DEEP ENDOMETRIOSIS AT THE INTERNATIONAL LEVEL

This chapter includes a synthesis of data from the specialised literature regarding the diagnostic features, pathogenesis and management of deep infiltrating endometriosis. Based on numerous international and national bibliographic sources, contemporary concepts of disease aetiopathogenesis, current classifications (#Enzian, rASRM, EFI), imaging diagnostic methods, and conservative and surgical treatment strategies are presented.

A separate section is devoted to differential diagnosis, as deep infiltrating endometriosis may mimic other surgical conditions, such as appendicitis, irritable bowel syndrome, intestinal obstruction and urinary tract pathology, which leads to diagnostic delays and inappropriate treatment.

In addition, data on the impact of deep infiltrating endometriosis on quality of life and reproductive function were critically analysed, together with controversies and limitations regarding the diagnostic performance of imaging methods, the use of classification systems, and therapeutic strategies, highlighting the need for a multidisciplinary approach to the diagnosis and management of this complex condition.

## 2. MATERIALS AND METHODS

An observational, descriptive, cross-sectional, comparative and prospective clinical study was conducted between 2021 and 2023 at the Department of Obstetrics and Gynaecology of Nicolae Testemițanu State University of Medicine and Pharmacy. The minimum required sample size, calculated using Cochran's formula and adjusted by 10% for the non-response rate, was 161 patients; 190 patients with endometriosis were included in the study, with the diagnosis confirmed intraoperatively. The main surgical indications were ovarian endometriotic cysts, infertility and symptomatic uterine fibroids. Based on the obtained data, the diagnostic performance of transvaginal ultrasound and the correlation between clinical manifestations and lesion localisation according to the #Enzian classification were evaluated.

The study was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy (Approval No. 38 of 21 May 2021). All participants provided written informed consent to participate in the study.

Patients were staged according to the #Enzian classification, which allowed the formation of two main study groups: Group 1 (G1) – 85 patients with deep infiltrating endometriosis, and Group 2 (G2) – 105 patients without DIE. This stratification enabled direct comparison of clinical, imaging and intraoperative parameters, reproductive function and quality-of-life indices depending on the presence or absence of DIE.

The inclusion criteria were: women of reproductive age; patients with endometriosis confirmed intraoperatively; patient consent to participate in the clinical study; and the ability to correctly complete clinical and quality-of-life assessment diaries and questionnaires. Exclusion criteria included minors, postmenopausal women, cases of endometriosis with suspected malignant transformation or other genital neoplasms, severe extragenital pathologies, and women who refused participation. In accordance with the principles of the #Enzian classification, cases of adenomyosis were included in compartment FA without further subdivision [22–24].

Data collection was performed through structured interviews, general and gynaecological clinical examinations, analysis of medical records, imaging investigations (transvaginal ultrasound and MRI in selected cases), and evaluation of intraoperative findings. Clinical symptoms, including the classical 4D pain symptom tetrad in endometriosis and catamenial symptoms, were analysed in relation to lesion localisation according to the #Enzian system. Pain intensity was quantified using the Visual Analogue Scale (VAS) and the Biberoglu–Behrman (B&B) scale. Reproductive function was assessed using the Endometriosis Fertility Index (EFI), calculated intraoperatively based on adnexal function, historical factors (age, duration of infertility, previous pregnancies) and surgical factors, with patient stratification according to the probability of spontaneous pregnancy and the need for assisted reproductive technologies [25,26]. The impact of endometriosis on quality of life was assessed using three standardised questionnaires—EIQ, SF-36 and WHO-5—completed by all participants. These instruments enabled a multidimensional evaluation of physical, psychological, social and reproductive health.

All data were systematised in an Excel database and statistically analysed using IBM SPSS Statistics version 21 and MedCalc software. Descriptive statistical methods (frequencies, means, medians, interquartile range, 95% confidence interval) and comparative methods (Pearson's  $\chi^2$  test for qualitative variables, Mann–Whitney U test for non-normally distributed quantitative

variables, and Fisher's exact test for proportion comparison in small samples) were applied. The threshold for statistical significance was set at  $p < 0.05$ . To evaluate the diagnostic performance of transvaginal ultrasound for the diagnosis of DIE, sensitivity and specificity were calculated, and ROC curve analysis was performed using MedCalc.

### **3. ANAMNESTIC, CLINICAL AND PARACLINICAL, REPRODUCTIVE CHARACTERISTICS AND QUALITY-OF-LIFE LEVEL IN WOMEN WITH DEEP INFILTRATING ENDOMETRIOSIS**

**3.1. Localisation of endometriosis according to the #Enzian classification.** To assess the extent of endometriosis, the #Enzian classification was used, which provides a standardised framework for describing the anatomical distribution and severity of lesions, with clinical applicability and predictive value both in assessing treatment difficulty and in estimating the impact on quality of life.

In the analysed sample, the frequency of DIE was 44.7% (95% CI [37.8%–51.8%]), ovarian endometriomas were identified in 50.0% of cases (95% CI [43.0%–57.0%]), and superficial peritoneal endometriosis in 5.3% (95% CI [2.9%–9.4%]).

Stratification of cases based on the #Enzian classification revealed variable involvement of compartments O, T, P, A, B, C and F. Group 1 (G1) included patients with forms of DIE (A, B, C and F), whereas Group 2 (G2) comprised patients with ovarian, tubal or superficial peritoneal forms, without deep infiltration.

Within G1, the most frequent localisation was compartment A, identified in 58.8% of cases (50 patients, 95% CI [48.1%–68.9%]). This was followed by compartments FA and FB, each with a prevalence of 17.6% (95% CI [11.0%–27.1%]). Compartment B was affected in 12.9% of cases (95% CI [7.4%–21.7%]). Involvement of compartment FI was observed in 9.4% of cases (95% CI [3.7%–16.2%]), ureteral infiltration (FU) was reported in 4.7% of patients (95% CI [1.8%–11.5%]), and compartment C was involved in 2.4% of cases (95% CI [0.7%–8.2%]). Extrapelvic localisations (pulmonary, diaphragmatic and cutaneous foci) were identified in 12.9% of cases (95% CI [7.4%–21.7%]). Summary data regarding the distribution of deep endometriotic lesions by compartments according to the #Enzian classification are presented in Table 1.

Associated forms in G1 included ovarian endometriosis (70.6%, 95% CI [60.8%–80.5%]), tubal endometriosis (51.8%, 95% CI [41.0%–62.7%]) and superficial peritoneal endometriosis (34.1%, 95% CI [24.3%–45.0%]). The unfavourable reproductive prognostic sign, “kissing ovaries”, was identified in 15.3% of G1 patients (95% CI [9.2%–24.4%]).

In G2, ovarian endometriosis predominated—90.5% (95% CI [84.7%–95.9%]), distributed as follows: O1 – 34.3% (95% CI [25.2%–44.1%]), O2 – 48.6% (95% CI [39.2%–58.0%]), and O3 – 22.9% (95% CI [15.9%–31.8%]). Localisations T and P were identified in 50.5% (95% CI [40.8%–59.6%]) and 15.2% (95% CI [8.4%–22.4%]) of cases, respectively.

Comparative analysis between the study groups revealed significant differences regarding peritoneal involvement according to the #Enzian staging criteria, with higher prevalences of P2-type lesions ( $\chi^2=5.847$ ,  $df=1$ ,  $p=0.016$ ) and P3-type lesions ( $\chi^2=20.118$ ,  $df=1$ ,  $p<0.001$ ) in G1. In contrast, tubal involvement was similar between the groups ( $\chi^2=0.031$ ,  $df=1$ ,  $p=0.860$ ), with no statistically significant differences.

**Table 1. Distribution of DIE foci according to the #Enzian classification**

| Compartment<br>#Enzian | Absolute frequency | Relative frequency, % | 95% CI (%) |
|------------------------|--------------------|-----------------------|------------|
| A                      | 50                 | 58.8                  | 48.1–68.9  |
| B                      | 11                 | 12.9                  | 7.4–21.7   |
| C                      | 2                  | 2.4                   | 0.7–8.2    |
| FA                     | 15                 | 17.6                  | 11.0–27.1  |
| FB                     | 15                 | 17.6                  | 11.0–27.1  |
| FI                     | 8                  | 9.4                   | 3.7–16.2   |
| FU                     | 4                  | 4.7                   | 1.8–11.5   |
| F...                   | 11                 | 12.9                  | 7.4–21.7   |

*Note: A – rectovaginal and vaginal DIE; B – DIE of the uterosacral ligaments and pelvic walls; C – DIE of the rectum and sigmoid colon; FA – adenomyosis; FB – bladder DIE; FU – ureteral DIE; FI – intestinal DIE above the rectosigmoid junction; F... – other DIE localisations (lungs, diaphragm, nerves, skin).*

These results highlight the substantial prevalence of deep infiltrating endometriosis and the complex distribution of lesions according to the #Enzian classification.

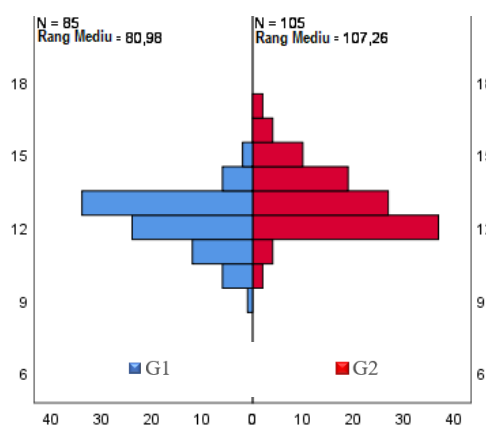
### 3.2. Anamnestic data.

**Age of the patients.** Analysis of the age-group distribution did not reveal significant differences between the study groups, indicating adequate demographic homogeneity of the sample ( $\chi^2=1.115$ ,  $df=5$ ,  $p=0.953$ ). The mean age of the patients did not differ significantly between the two groups, being 32.4 years in G1 (95% CI [30.8–34.0]) and 30.3 years in G2 (95% CI [28.9–31.6]) ( $U=4520.00$ ,  $p=0.879$ ).

#### Gynaecological History.

**The age at menarche** differed significantly between the groups, with a mean of 12.3 years in G1 (95% CI [11.9–12.7]) compared with 13.2 years in G2 (95% CI [12.8–13.6]), a difference that was statistically confirmed ( $U=5697.00$ ,  $p=0.001$ ) (Figure 1).

**Regularity of the menstrual cycle.** A regular menstrual cycle was reported in 60.0% of patients in G1 (95% CI [48.9%–70.7%]) compared with 81.9% in G2 (95% CI [73.5%–88.1%]), while an irregular cycle was present in 40.0% and 18.1% of patients, respectively. The difference was statistically significant ( $\chi^2=11.206$ ,  $df=1$ ,  $p=0.001$ ), indicating a higher prevalence of menstrual disorders among patients with deep infiltrating endometriosis.



**Figure 1. Age at menarche (years), G1 vs G2**

**Duration of the menstrual cycle and menstruation.** The mean duration of the menstrual cycle was 27.5 days in G1 (95% CI [26.5–28.4]) compared with 28.9 days in G2 (95% CI [28.2–29.5]); the difference reached the threshold of statistical significance ( $U=5152.50$ ,  $p=0.046$ ). The mean duration of menstruation was similar between the groups—5.5 days in G1 (95% CI [4.9–6.2]) and 5.1 days in G2 (95% CI [4.6–5.6])—with no statistically significant difference ( $U=3840.50$ ,  $p=0.086$ ).

**Volume of menstrual bleeding.** Heavy menstrual bleeding and premenstrual spotting were significantly more frequent in G1 ( $p<0.001$ ), demonstrating their association with deep infiltrating endometriosis.

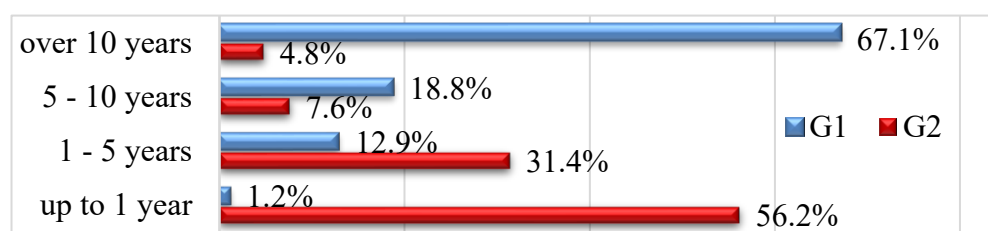
#### **General medical history and time to diagnosis.**

**Disease History.** Compared with G2, patients in G1 demonstrated notable differences in disease history. An uncomplicated course was reported in 16.5% of patients in G1 (95% CI [8.6%–25.3%]) versus 25.9% in G2 (95% CI [19.4%–32.4%]). Infertility was significantly more frequent in G1, occurring in 83.5% of cases (95% CI [74.2%–89.9%]), compared with 58.1% in G2 (95% CI [48.6%–67.5%]). Chronic pelvic pain was reported by 67.1% of patients in G1 (95% CI [56.5%–76.1%]) versus 41.9% in G2 (95% CI [32.9%–51.5%]). Dysmenorrhoea with onset during adolescence was present in 36.5% of cases in G1 (95% CI [27.0%–47.1%]), compared with only 8.6% in G2 (95% CI [4.6%–15.5%]). Extragenital symptoms (dysuria, dyschezia, haematuria, catamenial cough, etc.) were reported in 80.0% of patients with deep infiltrating endometriosis (95% CI [70.3%–87.1%]) and were not identified in G2. Previous surgical interventions were significantly more frequent in G1—35.3% (95% CI [26.0%–46.0%]) versus 18.1% in G2 (95% CI [11.9%–26.5%]). A positive family history of endometriosis was reported in 12.9% of patients in G1 (95% CI [7.4%–21.7%]) compared with 8.6% in G2 (95% CI [4.6%–15.5%]).

Overall comparison of anamnestic variables revealed a statistically significant difference between the groups ( $\chi^2=81.844$ ,  $df=6$ ,  $p<0.001$ ), with higher frequencies of chronic pelvic pain, infertility and extragenital manifestations in G1.

**Time to diagnosis.** The time to diagnosis, defined as the interval between the onset of first symptoms and diagnostic confirmation, showed marked differences between the groups. In patients with DIE, this interval exceeded 10 years in 67.1% of cases (95% CI [56.5%–76.1%]), was 5–10 years in 18.8% (95% CI [11.9%–28.4%]), 1–5 years in 12.9%, and up to 1 year in 1.2% of cases. In contrast, in G2 diagnosis was established earlier: 56.2% of women (95% CI [46.3%–65.6%]) received the diagnosis within the first year after symptom onset, 31.4% (95% CI [23.3%–40.8%]) within 1–5 years, and only 12.4% (95% CI [7.4%–20.0%]) after more than 5 years of disease evolution (Figure 2).

The differences between the groups were statistically significant ( $\chi^2=112.487$ ,  $df=3$ ,  $p<0.001$ ), demonstrating a considerable diagnostic delay in patients with deep infiltrating endometriosis.



**Figure 2. Time to diagnosis of endometriosis (%), G1 vs. G2**

**Reproductive history.** The frequency of *reproductive losses* was comparable between the groups, being recorded in 15.3% of patients in G1 and 10.5% in G2. The confidence intervals overlapped (G1: 95% CI [9.2%–24.4%]; G2: 95% CI [6.0%–18.0%]), and statistical analysis did not reveal a significant difference between the two groups ( $U=4463.000$ ,  $p=0.839$ ).

With regard to *infertility*, it was reported in 83.5% of patients in G1 (95% CI [74.2%–89.9%]) and in 58.1% in G2 (95% CI [48.6%–67.5%]). Comparative analysis ( $\chi^2=14.34$ ,  $df=1$ ,  $p<0.001$ ) demonstrated a significantly higher frequency of infertility in patients with deep infiltrating endometriosis (Figure 3).

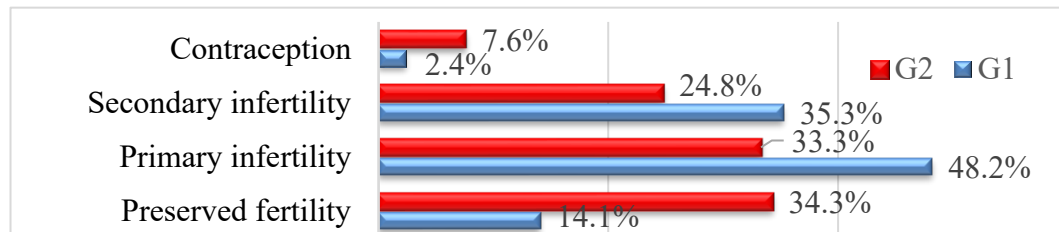


Figure 3. Fertility status (%), G1 vs. G2

### 3.3. Clinical symptoms in the patient sample.

**General description of patient complaints.** Analysis of symptomatology in patients with endometriosis reveals a markedly different clinical picture between the groups, with a higher prevalence of pain and catamenial symptoms among patients with deep infiltrating endometriosis. Severe chronic pelvic pain ( $VAS \geq 7$ ) was reported by 88.2% of patients in G1 (75 cases, 95% CI [79.7%–93.5%]), compared with 18.1% in G2 (19 cases, 95% CI [11.9%–26.5%]). Severe dyspareunia was present in 82.4% of women with deep infiltrating endometriosis (70 cases, 95% CI [72.9%–89.0%]) and in only 8.6% of patients in G2 (95% CI [4.6%–15.5%]). Severe dysmenorrhoea had a high prevalence in both groups but was more pronounced in G1—96.5% (95% CI [90.1%–98.8%]) versus 69.5% in G2 (95% CI [60.2%–77.5%]).

Catamenial extragenital symptoms were mainly characteristic of deep infiltrating endometriosis. From the urinary tract, bladder tenesmus was observed in 17.7% of patients in G1 (15 women), compared with 0.0% in G2. Cases of hydronephrosis requiring ureteral stenting accounted for 4.7% (4 patients, 95% CI [1.8%–11.5%]), occurring exclusively in deep infiltrating endometriosis; severe dysuria was reported in 18.8% of patients in G1 (16 patients, 95% CI [11.9%–28.4%]) versus 0.0% in G2. Haematuria, a manifestation specific to deep forms, was identified exclusively in G1 (10.6%, 95% CI [5.7%–18.9%]) and was absent in G2.

Severe dyschezia was reported by 40.0% of patients in G1 (34 patients, 95% CI [30.2%–50.6%]) versus 0.0% in G2. Rectal tenesmus was observed in 48.2% of patients in G1 (41 cases, 95% CI [37.9%–58.7%]) compared with approximately 1% in G2. Defecation disorders of the constipation/diarrhoea type were present in 44.7% of patients in G1 (38 cases, 95% CI [34.6%–55.3%]) and were absent in G2. Meteorism was reported by 9.4% of patients (8 cases, 95% CI [4.9%–17.5%]), and signs of subintestinal obstruction by 5.9% (5 cases, 95% CI [2.5%–13.0%]), all occurring in G1.

Heavy menstrual bleeding was reported by 42.4% of patients in G1 (36 cases, 95% CI [32.4%–53.0%]) compared with 17.1% in G2 (18 cases, 95% CI [11.1%–25.5%]).

Extrapelvic manifestations were rare but specific to deep infiltrating endometriosis: catamenial cutaneous lesions—5.9% (5 patients, 95% CI [2.5%–13.0%]); hiccups and phrenic

nerve symptoms—3.5% (3 patients, 95% CI [1.2%–9.9%]). Catamenial cough and haemoptysis were reported in 2.4% of cases (2 patients), and cyclic chest pain also in 2.4%.

Systemic symptoms showed marked differences: the Benjamin symptom was identified in 83.5% of patients with deep infiltrating endometriosis in G1 (71 cases, 95% CI [74.2%–89.9%]) compared with 22.9% in G2 (24 cases, 95% CI [15.9%–31.8%]); weakness was reported by 72.9% of patients in G1 (62 cases, 95% CI [62.7%–81.2%]) and by 13.3% in G2 (14 cases, 95% CI [8.1%–21.1%]).

These results highlight the multiorgan and polymorphic nature of deep infiltrating endometriosis and the high frequency of catamenial and extragenital symptoms.

**Pain intensity according to the VAS score in the study groups.** Assessment of pain using the VAS scale showed that patients with deep infiltrating endometriosis presented, for most of the analysed pain types, mean pain values  $\geq 7$ , indicating a pronounced pain syndrome. In contrast, in G2 pain intensity was significantly lower, predominantly falling within the range of moderate or mild pain, with differences evident across all evaluated pain categories (Table 2). Dysuria and dyschezia were reported exclusively in the group with deep infiltrating endometriosis, suggesting symptom characteristics associated with infiltrative forms.

**Table 2. Pain intensity according to VAS (points)**

| Type of pain  | G1, mean (95% CI) | G2, mean (95% CI) | U test  | P      |
|---------------|-------------------|-------------------|---------|--------|
| CPP           | 7.9 (7.5 – 8.3)   | 2.4 (1.5 – 3.3)   | 706.00  | < 0.01 |
| Dysmenorrhoea | 9.0 (8.7 – 9.4)   | 5.3 (4.2 – 6.4)   | 1254.00 | < 0.01 |
| Dyspareunia   | 7.9 (7.2 – 8.5)   | 2.2 (1.2 – 3.1)   | 699.50  | < 0.01 |
| Dysuria       | 7.4 (6.8 – 7.9)   | 0.0               | —       | < 0.01 |
| Dyschezia     | 6.0 (5.6 – 6.5)   | 0.0               | —       | < 0.01 |

**Pain intensity according to the B&B score.** Pain assessment using the Biberoglu–Behrman (B&B) scale revealed marked differences between the study groups across all three analysed components. Self-assessed pain, representing the subjective component of the scale and integrating the patient’s perception of chronic pelvic pain, dysmenorrhoea and dyspareunia, showed mean values of 7.6 points in G1 (95% CI [7.2–8.0]) compared with 2.9 points in G2 (95% CI [2.2–3.7]), with a statistically significant difference (U=512.50,  $p<0.001$ ).

Pain on physical examination, the objective component of the scale derived from pain sensitivity and limitation of organ mobility during bimanual palpation, was also significantly more intense in G1—4.0 points (95% CI [3.3–4.2]) versus 2.0 points in G2 (95% CI [1.5–2.5]), with a highly statistically significant difference (U=2146.00,  $p<0.001$ ).

The total B&B score, integrating both perceived pain intensity and objectively elicited pain on examination, reached 11.5 points in G1 (95% CI [10.7–12.1]), exceeding the threshold corresponding to very severe pain. In G2, the total score was significantly lower—4.9 points (95% CI [3.7–6.1]), corresponding to moderate pain (U=735.00,  $p<0.01$ ).

VAS and B&B scores demonstrated a significantly more severe pain syndrome in patients with deep infiltrating endometriosis compared with G2.

**Catamenial clinical symptoms associated with #Enzian compartments.** Analysis of symptoms according to #Enzian compartments demonstrated a clear association between the localisation of deep infiltrating endometriosis lesions and the severity of clinical manifestations.

In **compartment A**, the most characteristic symptoms were severe chronic pelvic pain—85.1% (95% CI [73.8%–93.0%]) ( $\chi^2=36.497$ ,  $df=2$ ,  $p<0.001$ ), severe dysmenorrhoea—97.9%

(95% CI [89.5%–99.6%]) ( $\chi^2=18.914$ ,  $df=2$ ,  $p<0.001$ ), severe dyspareunia—93.6% (95% CI [83.8%–97.9%]) ( $\chi^2=70.103$ ,  $df=2$ ,  $p<0.001$ ), severe dyschezia—53.2% (95% CI [40.4%–67.0%]) ( $\chi^2=81.874$ ,  $df=3$ ,  $p<0.001$ ), catamenial rectal tenesmus—57.4% (95% CI [43.2%–72.7%]) ( $\chi^2=45.298$ ,  $df=1$ ,  $p<0.001$ ), defecation disorders of the constipation/diarrhoea type—57.4% (95% CI [44.2%–70.7%]) ( $\chi^2=54.730$ ,  $df=1$ ,  $p<0.001$ ), the Benjamin symptom—85.1% (95% CI [75.0%–94.7%]) ( $\chi^2=30.786$ ,  $df=1$ ,  $p<0.001$ ), and weakness—74.5% (95% CI [61.2%–86.7%]) ( $\chi^2=30.913$ ,  $df=1$ ,  $p<0.001$ ).

In **compartment B**, the most frequent symptoms were severe chronic pelvic pain—100.0% (95% CI [74.1%–100.0%]) ( $\chi^2=7.422$ ,  $df=2$ ,  $p=0.024$ ), severe dyspareunia—100.0% (95% CI [74.1%–100.0%]) ( $\chi^2=10.212$ ,  $df=2$ ,  $p=0.006$ ), severe dyschezia—42.9% (95% CI [19.5%–70.0%]) ( $\chi^2=8.756$ ,  $df=3$ ,  $p=0.033$ ), and rectal tenesmus—71.4% (95% CI [28.6%–100.0%]) ( $\chi^2=10.268$ ,  $df=1$ ,  $p=0.001$ ).

For **compartment C**, no statistically significant association with symptoms was identified (Fisher's exact test,  $p>0.05$ ).

In **compartment FA**, predominant symptoms were chronic pelvic pain and severe dysmenorrhoea—100.0% (95% CI [79.6%–100.0%]) ( $\chi^2=16.632$ ,  $df=2$ ,  $p<0.001$ ), severe dyspareunia—86.7% (95% CI [62.2%–96.3%]) ( $\chi^2=13.774$ ,  $df=2$ ,  $p=0.001$ ), dyschezia—46.7% (95% CI [24.8%–69.9%]) ( $\chi^2=20.410$ ,  $df=3$ ,  $p<0.001$ ), heavy menstrual bleeding with premenstrual spotting—100.0% (95% CI [79.6%–100.0%]) ( $\chi^2=41.016$ ,  $df=1$ ,  $p<0.001$ ), rectal tenesmus—73.3% (95% CI [50.0%–92.9%]) ( $\chi^2=24.821$ ,  $df=1$ ,  $p<0.001$ ), constipation/diarrhoea—60.0% (95% CI [33.3%–85.7%]) ( $\chi^2=16.286$ ,  $df=1$ ,  $p<0.001$ ), the Benjamin symptom—80.0% (95% CI [54.8%–93.0%]) ( $\chi^2=5.863$ ,  $df=1$ ,  $p=0.015$ ), and weakness—80.0% (95% CI [54.8%–93.0%]) ( $\chi^2=10.857$ ,  $df=1$ ,  $p=0.001$ ).

In **compartment FB**, the following were identified: severe chronic pelvic pain—86.7% (95% CI [62.2%–96.3%]) ( $\chi^2=10.011$ ,  $df=2$ ,  $p=0.007$ ), severe dysuria—86.7% (95% CI [62.2%–96.3%]) ( $\chi^2=147.310$ ,  $df=3$ ,  $p<0.001$ ), haematuria—60.0% (95% CI [35.75%–80.18%]) ( $\chi^2=110.221$ ,  $df=1$ ,  $p<0.001$ ), bladder tenesmus—100.0% (95% CI [79.6%–100.0%]) ( $\chi^2=41.016$ ,  $df=1$ ,  $p<0.001$ ), the Benjamin symptom—93.3% (95% CI [78.6%–100.0%]) ( $\chi^2=12.232$ ,  $df=1$ ,  $p<0.001$ ), and weakness—73.3% (95% CI [50.0%–94.4%]) ( $\chi^2=7.540$ ,  $df=1$ ,  $p=0.006$ ).

In **compartment FI**, the most frequent symptoms were severe dyschezia—87.5% (95% CI [52.9%–97.8%]) ( $\chi^2=28.645$ ,  $df=3$ ,  $p<0.001$ ), catamenial defecation disorders of the constipation/diarrhoea type—100.0% (95% CI [67.6%–100.0%]) ( $\chi^2=33.407$ ,  $df=1$ ,  $p<0.001$ ), intestinal subocclusion—62.5% (95% CI [22.3%–100.0%]) ( $\chi^2=116.824$ ,  $df=1$ ,  $p<0.001$ ), catamenial meteorism—87.5% (95% CI [60.0%–100.0%]) ( $\chi^2=143.648$ ,  $df=1$ ,  $p<0.001$ ), the Benjamin symptom—100.0% (95% CI [67.6%–100.0%]) ( $\chi^2=8.352$ ,  $df=1$ ,  $p=0.004$ ), and weakness—87.5% (95% CI [60.0%–100.0%]) ( $\chi^2=7.851$ ,  $df=1$ ,  $p=0.005$ ).

In **compartment FU**, lumbar pain associated with hydronephrosis and ureteral stenting was present in 100.0% of patients (95% CI [51.0%–100.0%]) (Fisher's exact test,  $p<0.001$ ).

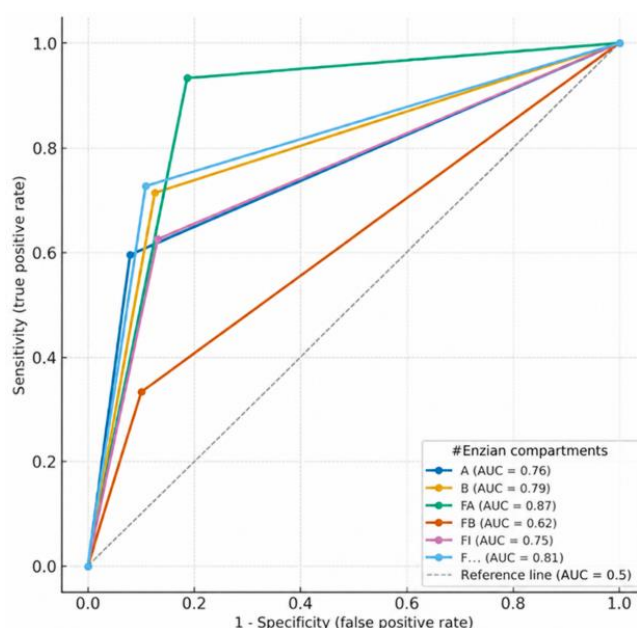
In **compartment F...**, characteristic symptoms included severe chronic pelvic pain—90.91% (95% CI [62.2%–98.3%]) ( $\chi^2=8.352$ ,  $df=2$ ,  $p=0.015$ ), catamenial cough and haemoptysis—18.2% (95% CI [0.0%–44.4%]) ( $\chi^2=32.892$ ,  $df=1$ ,  $p<0.001$ ), catamenial chest pain—18.2% (95% CI [0.0%–44.4%]) ( $\chi^2=32.892$ ,  $df=1$ ,  $p<0.001$ ), bleeding scar—45.5% (95% CI [14.3%–77.8%]) ( $\chi^2=83.563$ ,  $df=1$ ,  $p<0.001$ ), hiccups—27.3% (95% CI [0.0%–60.0%]) ( $\chi^2=49.601$ ,  $df=1$ ,  $p<0.001$ ), and the phrenic symptom—27.3% (95% CI [0.0%–60.0%]) ( $\chi^2=49.601$ ,  $df=1$ ,  $p<0.001$ ).

Statistical analysis demonstrated significant associations between the clinical manifestations of deep infiltrating endometriosis and lesion localisation within the #Enzian compartments.

**3.4. Objective findings in the study groups.** Clinical evaluation revealed significant differences between the groups. Uterine retroversion was more frequent in G1—88.2% (95% CI [79.7%–93.5%]) compared with 65.7% (95% CI [56.2%–74.1%]),  $p=0.0003$ , while the fixed uterine position was observed in 29.4% versus 13.3%,  $p=0.0065$ . Large adnexal masses were identified in 45.9% of patients in G1 and 69.5% in G2,  $p=0.001$ ; cervical deviation was noted in 40.0% versus 48.6%,  $p=0.2$ . Specific signs of deep infiltrating endometriosis included subcutaneous formations—7.1%,  $p=0.0049$ ; retrocervical nodular lesions—35.3%,  $p<0.0001$ ; enlarged globular uterus—17.6%,  $p<0.0001$ ; rectovaginal nodules—48.2%,  $p<0.0001$ ; and induration of the uterosacral ligaments—5.9%,  $p=0.0139$ . The objective findings described above were significantly more frequent in patients with deep infiltrating forms of endometriosis.

**3.5. Imaging investigation results of the present study.** The results of imaging investigations confirmed the value of transvaginal ultrasound in the diagnosis of deep infiltrating endometriosis. Uterine retroflexion was observed in 81.2% of patients in G1 versus 31.4% in G2 ( $p<0.0001$ ), organ dystopia in 48.2% versus 20.9% ( $p=0.0001$ ), and pelvic organ immobility in 48.2% versus 11.4% ( $p<0.0001$ ). Other ultrasound signs specific to deep infiltrating endometriosis included a globular uterus (11.8%,  $p<0.001$ ), thickened or disrupted junctional zone (14.1%,  $p<0.001$ ), negative “sliding sign” (31.8%,  $p<0.001$ ), hypoechoic layers within anatomical structures (24.7%,  $p<0.001$ ), and “kissing ovaries” (15.3%,  $p<0.001$ ).

Analysis of the diagnostic performance of ultrasound based on the #Enzian classification demonstrated variable sensitivity and specificity across compartments. Compartments FA and O showed the best performance: FA with sensitivity (Se) 93.3% (95% CI [68.1%–99.8%]) and specificity (Sp) 81.4% (95% CI [70.3%–89.7%]), and O with Se 91.6% (95% CI [86.1%–95.5%]) and Sp 94.3% (95% CI [80.8%–99.3%]). In addition, compartments A, B and FI showed higher specificity than sensitivity (A: Se 59.6%, Sp 92.1%; B: Se 71.4%, Sp 87.5%; FI: Se 62.5%, Sp 87.0%).



**Figure 4. ROC curves for the diagnosis of DIE according to #Enzian compartments**

In the overall analysis of ultrasound performance for the diagnosis of DIE according to the #Enzian compartments, the mean sensitivity was 65.5%, while the mean specificity was 87.8%.

Ultrasound performance was lower for the FB and T compartments, with sensitivities of 33.3% and 28.9%, respectively.

ROC curve analysis showed AUC values ranging from 0.62 to 0.87, demonstrating variable diagnostic performance of ultrasound depending on the #Enzian compartment (Figure 4).

Based on the study findings, a diagnostic algorithm for deep infiltrating endometriosis according to the #Enzian classification was developed, integrating clinical and imaging assessment and contributing to the non-invasive identification of lesion localisation.

**3.6. Volume of surgical intervention performed.** As the primary aim of the research was to evaluate the diagnostic features of deep infiltrating endometriosis and its impact on quality of life, analysis of surgical extent did not constitute a central objective. Nevertheless, in order to describe the therapeutic approaches applied within the study sample, the extent of surgical interventions performed in both groups was assessed. Histopathological examination revealed no evidence of malignant transformation in the examined specimens.

Analysis of operative extent demonstrated clear differences in the types and frequencies of interventions performed between the study groups. In G1, the most frequent procedure was laparoscopic cystectomy with or without diathermocoagulation, performed in 34.1% of cases (95% CI [24.7%–44.7%]). Laparoscopic diathermocoagulation of lesions was performed in 15.3% (95% CI [9.2%–24.4%]). Chromosalpingoscopy with or without adhesiolysis accounted for 11.8% (95% CI [6.5%–20.3%]). Laparoscopic drainage of lesions with biopsy, with or without diathermocoagulation, represented 5.9% (95% CI [2.5%–13.0%]). Laparoscopic ethanol sclerotherapy was applied in 2.4% (95% CI [0.7%–8.2%]). Laparotomic cystectomies accounted for 2.4% (95% CI [0.7%–8.2%]), while laparotomic adnexectomy/tubectomy with or without cystectomy represented 3.5% (95% CI [1.2%–9.9%]). Laparotomic hysterectomy ± adnexectomy/tubectomy was performed in 2.4% of patients in G1 (95% CI [0.7%–8.2%]). Thoracic surgery was carried out in 2.4% (95% CI [0.7%–8.2%]), and excision of cutaneous lesions in 7.1% (95% CI [3.3%–14.6%]). Endometrial biopsy combined with conservative treatment accounted for 5.9% (95% CI [2.5%–13.0%]), while conservative treatment alone was applied in 2.4% of cases (2/85; 95% CI [0.7%–8.2%]).

In G2, laparoscopic cystectomy ± diathermocoagulation was performed in 42.9% of cases (95% CI [33.0%–52.4%]). Laparoscopic diathermocoagulation of lesions accounted for 30.5% (95% CI [22.5%–39.8%]). Laparoscopic adnexectomy/tubectomy with or without cystectomy was performed in 13.3% (95% CI [8.1%–21.1%]). Chromosalpingoscopy with or without adhesiolysis accounted for 6.7% (95% CI [3.3%–13.1%]). Laparoscopic drainage with biopsy was performed in 4.8% (95% CI [2.1%–10.7%]). Laparotomic hysterectomy ± adnexectomy/tubectomy was carried out in 1.0% (95% CI [0.2%–5.2%]), and conservative treatment in 1.0% (95% CI [0.2%–5.2%]).

Comparison of operative volumes between the two groups revealed statistically significant differences ( $\chi^2=36.911$ ,  $df=13$ ,  $p<0.001$ ), with distinct distributions of the applied surgical procedures. In both groups, endometriotic lesions were evaluated intraoperatively according to the #Enzian classification. In cases of extragenital localisations identified in G1 (intestinal, ureteral,

bladder and diaphragmatic), patients were referred for interdisciplinary consultations to determine optimal therapeutic management.

### 3.7. Reproductive Prognosis

**Uterine tubal patency.** Assessment of uterine tubal patency, as an essential indicator of fertility potential, demonstrated similar results between the study groups. In G1 compared with G2, bilateral tubal patency was observed in 85.9% (95% CI [76.9%–91.7%]) versus 81.9% (95% CI [73.5%–88.1%]), unilateral patency in 4.7% (95% CI [1.8%–11.5%]) versus 10.5% (95% CI [6.0%–17.8%]), tubal occlusion in 2.4% (95% CI [0.7%–8.2%]) versus 1.0% (95% CI [0.2%–5.2%]), and tubectomy was performed in 7.1% (95% CI [3.3%–14.6%]) versus 6.7% (95% CI [3.3%–13.1%]). No statistically significant differences were identified between the distributions of the four categories ( $\chi^2=2.664$ ,  $df=3$ ,  $p=0.446$ ).

**Endometriosis fertility index.** Given the impact of endometriosis on fertility, reproductive prognosis was assessed using the Endometriosis Fertility Index (EFI), which estimates the likelihood of spontaneous conception and guides therapeutic decision-making.

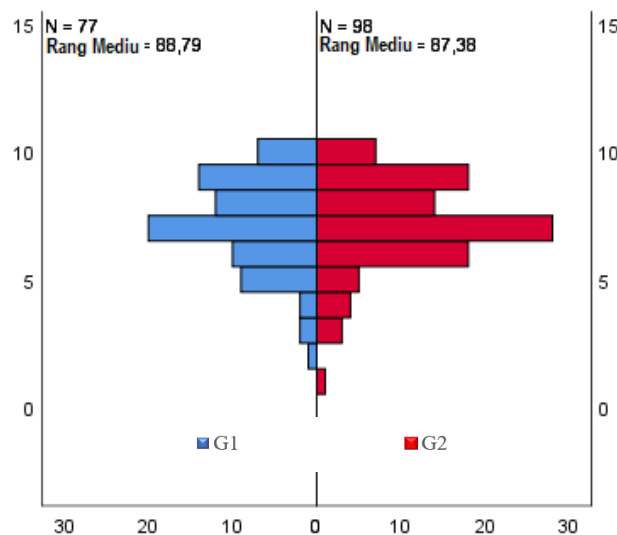


Figure 5. Endometriosis Fertility Index (EFI) score, G1 vs. G2

In G1 versus G2, the median EFI was identical—7.0 points, with mean values of 7.2 [6.7–7.7] and 7.1 [6.6–7.7], respectively, without statistically significant differences ( $U=3712.000$ ,  $p=0.852$ ) (Figure 5). Despite similar EFI scores, the frequency of infertility was significantly higher in G1. Severe deep dyspareunia ( $VAS \geq 7$  points) was identified in 82.4% of patients with deep infiltrating endometriosis ( $U=699.500$ ,  $p<0.01$ ).

### 3.8. Quality of life of the patients included in the study

**Quality of life in the study groups according to the EIQ.** Analysis of the EIQ questionnaire demonstrated a significantly more severe impact of deep infiltrating endometriosis on all determinants of quality of life compared with other forms of endometriosis (Figure 6). Analysis of the impact of endometriosis on quality of life revealed marked differences between the groups across all evaluated domains. **Physical impact** reached mean values of 64.5% in G1 (95% CI [57.6%–71.3%]) compared with 14.1% in G2 (95% CI [9.3%–19.0%];  $U=479.000$ ,  $p<0.01$ ), encompassing limitations in daily activities, reduced mobility and impaired overall functioning.

The **psychological component** was also profoundly affected in deep infiltrating endometriosis, with values of 70.3% (95% CI [64.1%–76.5%]) versus 14.1% (95% CI [8.6%–19.6%]; U=311.000, p<0.01), encompassing anxiety, emotional distress and negative perception of health status.

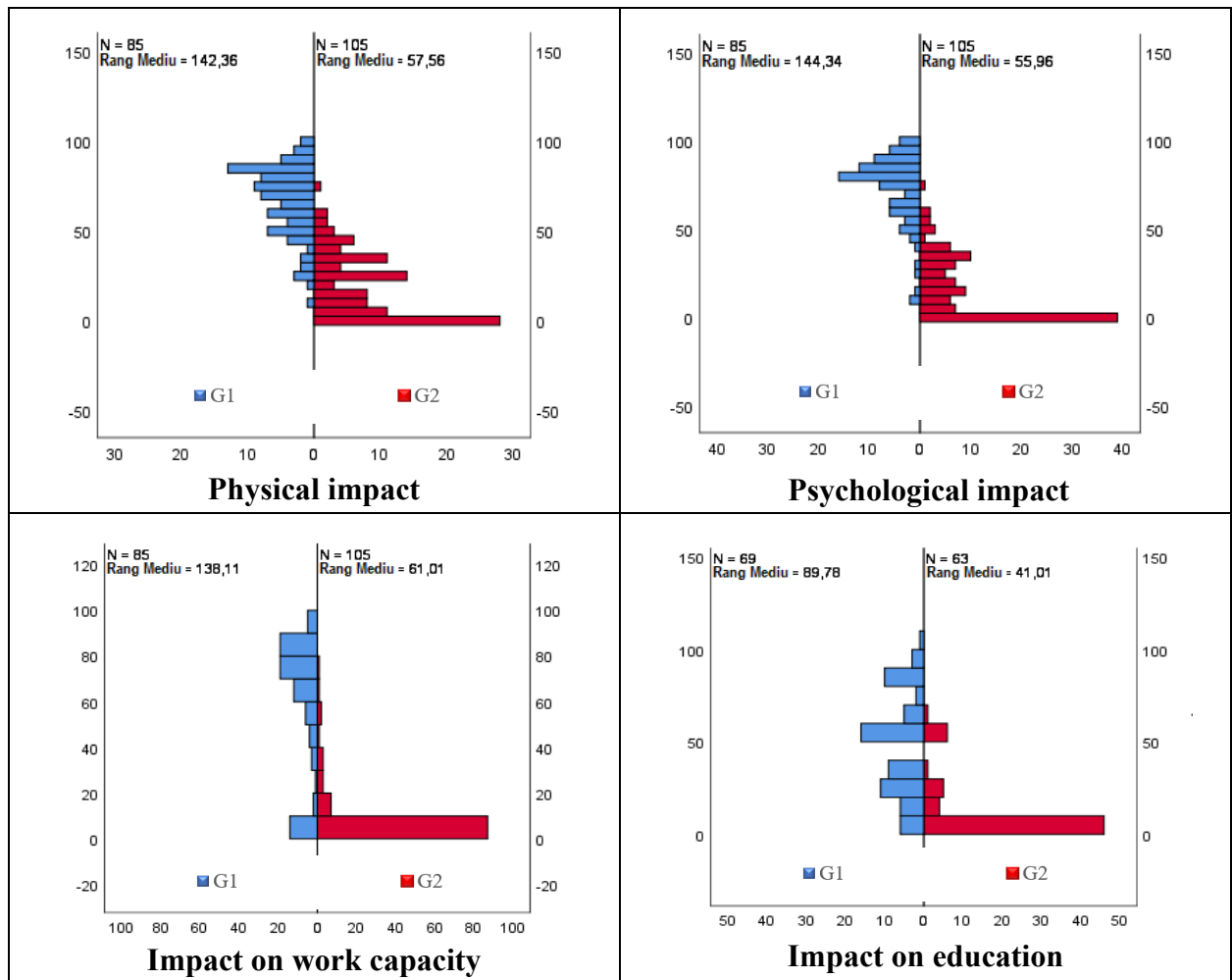


Figure 6. Impact of endometriosis on quality of life according to the EIQ (%), G1 vs. G2

**Social impact** amounted to 52.7% in G1 (95% CI [43.8%–61.6%]) compared with 4.7% in G2 (95% CI [1.0%–8.4%]; U=701.500, p<0.01), covering family and social relationships, participation in activities and social interactions. The **sexual domain** was affected in 64.9% of cases in G1 (95% CI [55.7%–74.1%]) versus 12.7% in G2 (95% CI [6.8%–18.7%]; U=690.500, p<0.01), including dyspareunia-related limitations, reduced frequency of sexual intercourse and decreased sexual satisfaction. The **reproductive component** showed the highest impact: 90.9% in G1 (95% CI [83.8%–98.1%]) and 79.9% in G2 (95% CI [68.9%–90.9%]; U=1107.500, p=0.001), encompassing concerns regarding infertility, unsuccessful conception attempts and the associated emotional burden. **Work capacity** was affected in 58.8% of cases in G1 (95% CI [49.5%–68.0%]) compared with 4.8% in G2 (95% CI [1.7%–7.9%]; U=841.000, p<0.01), covering reduced productivity, absenteeism and professional limitations. In the **educational domain**, the impact of deep infiltrating endometriosis was 44.3% (95% CI [36.0%–52.6%]) versus 3.6% (95% CI [1.0%–6.3%]; U=567.500, p<0.01), including difficulties with concentration, absenteeism and reduced academic performance. **Lifestyle** was affected in 53.0% of cases in G1 (95% CI [41.8%–64.2%]) compared with 2.3% in G2 (95% CI [0.0%–4.8%]; U=850.000, p<0.01), encompassing limitations

in daily activities, hobbies, physical activity and personal autonomy. The EIQ results demonstrated a significantly greater impact of deep infiltrating endometriosis across all assessed domains compared with G2.

**Quality of life in the study groups according to SF-36.** For a comprehensive and objective assessment of quality of life, the generic SF-36 questionnaire was applied, the scores of which reflect the level of achievement of quality-of-life determinants (higher values indicating better functional status and a lower impact of the disease).

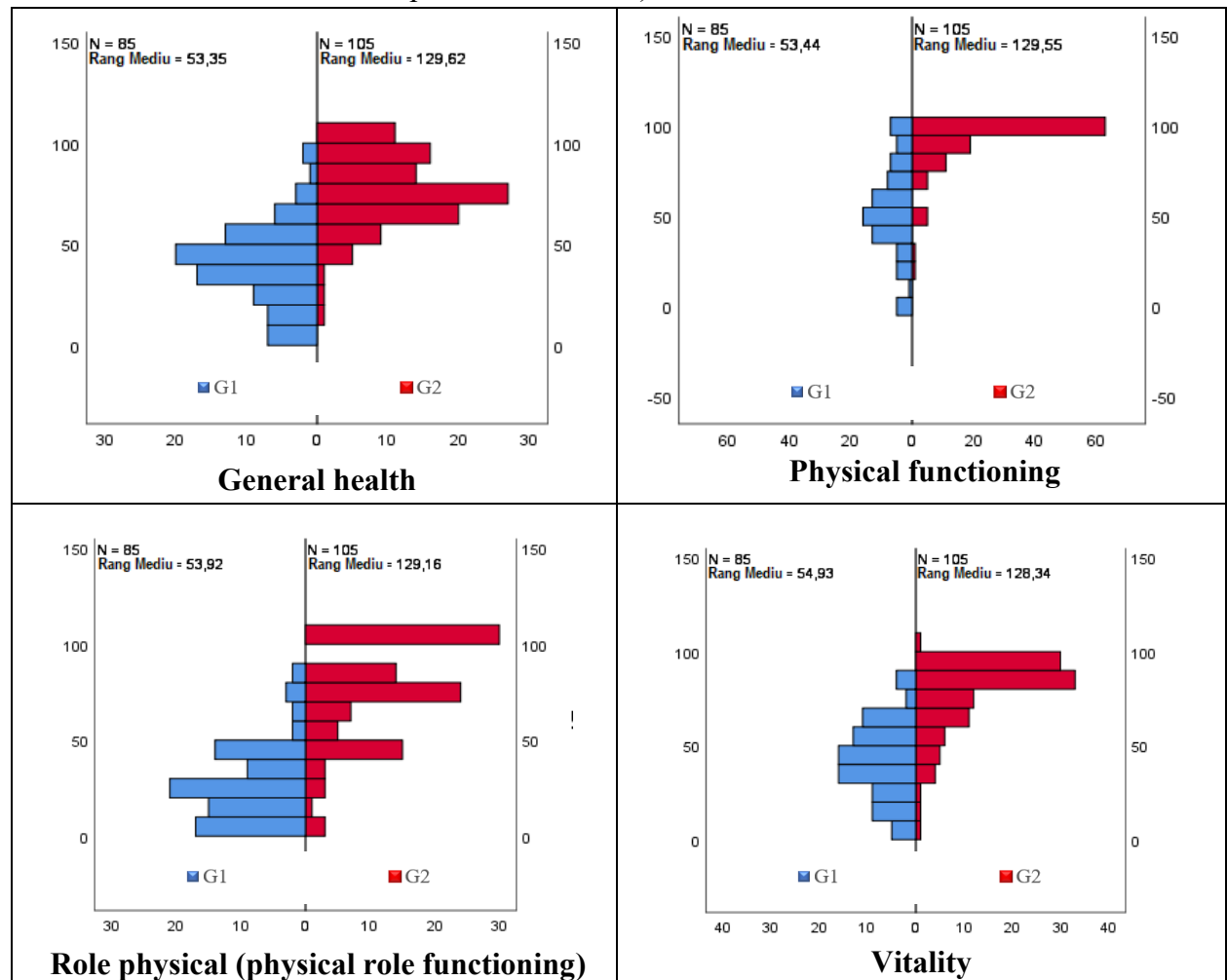


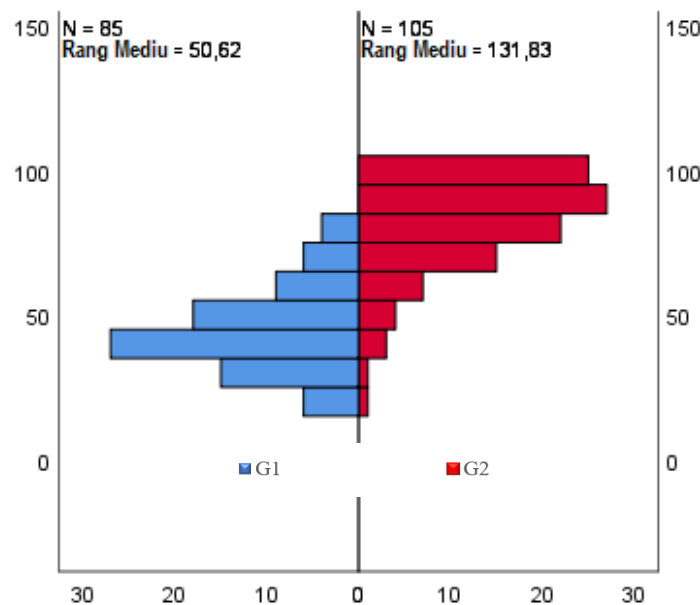
Figure 7. Quality of life according to the SF-36 (%), G1 vs. G2

The analysis showed that, in patients with deep infiltrating endometriosis, all SF-36 dimensions—except social functioning—recorded significantly lower mean scores compared with G2, indicating a multidimensional impairment of quality of life (Figure 7).

Thus, **General Health** (GH) was significantly reduced in G1—42.2% (95% CI [35.2%–49.1%]) compared with 76.2% (95% CI [70.1%–82.3%]) in G2 ( $U=8045.500$ ,  $p<0.01$ ), while **Physical Functioning** (PF) recorded scores of 58.5% (95% CI [50.2%–66.9%]) in G1 versus 92.2% (95% CI [88.2%–96.1%]) in G2 ( $U=8037.500$ ,  $p<0.01$ ), indicating marked functional limitations in patients with deep infiltrating endometriosis. **Role Physical** (RP) also reflected substantial impairment, with values of 39.6% (95% CI [29.2%–50.1%]) in G1 compared with 89.1% (95% CI [82.2%–96.0%]) in G2 ( $U=7852.500$ ,  $p<0.01$ ). **Bodily Pain** (BP) showed one of the most pronounced discrepancies, with scores of 28.3% (95% CI [21.5%–35.1%]) in G1 versus 77.5% (95% CI [68.7%–86.3%]) in G2 ( $U=7997.000$ ,  $p<0.01$ ), confirming the severe pain impact

in deep infiltrating endometriosis. **Social Functioning** (SF) was the only dimension without statistically significant differences—47.1% (95% CI [45.1%–49.2%]) in G1 and 51.4% (95% CI [49.4%–53.5%]) in G2 (U=4689.000, p=0.473). At the same time, **Role Emotional** (RE) and **Mental Health** (MH) were significantly compromised in patients with deep infiltrating endometriosis: RE—37.8% (95% CI [28.6%–47.0%]) versus 85.6% (95% CI [77.5%–93.7%]) (U=7715.000, p<0.01), and MH—47.3% (95% CI [42.5%–52.1%]) versus 77.2% (95% CI [71.2%–83.2%]) (U=7991.500, p<0.01). **Vitality** (VT) was also significantly reduced—42.4% (95% CI [36.8%–48.1%]) in G1 compared with 76.3% (95% CI [69.6%–83.0%]) in G2 (U=7911.000, p<0.01), reflecting pronounced fatigue. Overall, SF-36 scores were significantly lower in patients with deep infiltrating endometriosis across all assessed dimensions except Social Functioning, demonstrating a more pronounced multidimensional impairment of quality of life.

**Quality of life in the study groups according to the WHO-5 Well-Being Index.** The mean score in G1 was 44.3% (95% CI [40.2%–48.4%]) compared with 81.4% (95% CI [75.9%–86.9%]) in G2, with a statistically significant difference (U=8277.000, p<0.01) (Figure 8).



**Figure 8. Psychological well-being according to the WHO-5 (%), G1 vs. G2**

The EIQ, SF-36 and WHO-5 results demonstrate a significantly more pronounced impairment of quality of life and psychological well-being in patients with deep infiltrating endometriosis compared with other forms of endometriosis.

## GENERAL CONCLUSIONS

1. DIE is a condition affecting young women, the diagnosis of which is frequently delayed by more than 10 years ( $p < 0.001$ ), and is associated with a younger age at menarche ( $p = 0.001$ ), severe multiorgan manifestations and a more pronounced pain spectrum (VAS  $\geq 7$  points, B&B  $\geq 11$  points;  $p < 0.01$ ), as well as more frequent previous surgical interventions (35.3% vs 18.1%;  $p < 0.01$ ). Despite the diagnostic challenges, expert ultrasound performed according to the #Enzian compartments demonstrated clinically relevant diagnostic performance, with a mean sensitivity of 65.5% and a mean specificity of 87.8%.

2. The study identified statistically significant associations ( $p < 0.05$ ) between symptoms and the localisation of DIE lesions according to the #Enzian classification, which contributed to the development of a non-invasive diagnostic algorithm. Additionally, the identification of multiorgan involvement and clinical manifestations with inflammatory features supported the chronic and inflammatory nature of endometriosis and its multisystemic character.
3. The use of the standardised EIQ questionnaire demonstrated a complex and pronounced impact of DIE on the determinants of quality of life ( $p < 0.01$ ), with pronounced and very pronounced impairment of both the intimate sphere (68.2% of patients;  $p < 0.01$ ) and a perceived very pronounced impact on fertility (92.6% of patients;  $p = 0.001$ ). These aspects may further contribute to reproductive difficulties, in the context of a higher frequency of infertility among patients with DIE (83.5% vs 58.1%;  $p < 0.001$ ), although the EFI was comparable between the two groups, with no statistically significant differences in the likelihood of achieving spontaneous pregnancy.
4. Assessment of physical and emotional functioning, mental health, and daily functional potential using the SF-36, as well as psychological well-being using the WHO-5, demonstrated significantly greater impairment in patients with deep endometriosis compared with patients with other forms of endometriosis ( $p < 0.01$ ). These findings support the recognition of deep endometriosis as a chronic condition with severe functional impact and potentially disabling consequences, thereby justifying the development of an integrated model of medical and social management.

### **PRACTICAL RECOMMENDATIONS**

- ✓ The presence of severe dysmenorrhoea and catamenial chronic pelvic pain raises clinical suspicion of deep endometriosis and warrants further targeted evaluation.
- ✓ Pain assessment should be performed using validated scales, such as VAS and B&B, which allow objective quantification of symptom severity and monitoring of treatment response over time.
- ✓ The association of chronic pelvic pain with infertility and signs of extragenital involvement constitutes a major clinical indicator of deep endometriosis, particularly in the context of repeated surgical interventions without a clear diagnosis.
- ✓ In patients with an ovarian endometrioma associated with severe pelvic pain (VAS  $\geq 7$  points), expert gynaecological ultrasonography for endometriosis is indicated to identify deeply infiltrating lesions and systematically assess the #Enzian compartments.
- ✓ Application of the non-invasive diagnostic algorithm for deep endometriosis developed in this study may facilitate the early identification of patients at increased risk and optimise the diagnostic pathway through the integration of clinical and imaging data and standardised assessment tools.
- ✓ Suspicion of deep endometriosis requires a multidisciplinary approach from the stage of non-invasive diagnosis onwards, as well as in surgical management, to ensure complete identification and appropriate treatment of the lesions.
- ✓ Implementation of the #Enzian classification as a standardised tool for clinical, imaging and intraoperative assessment enables characterisation of disease extent and facilitates communication between the specialties involved in patient management.

- ✓ Expert gynaecological ultrasonography demonstrated clinically relevant diagnostic performance in the assessment of deep endometriosis lesions, with variations according to the #Enzian compartments. MRI may complement the assessment in selected cases, while standardised reporting according to #Enzian may facilitate lesion mapping.
- ✓ Intraoperative calculation of the EFI score is recommended in patients with endometriosis and infertility to estimate reproductive prognosis. In patients with deep endometriosis, the score should be interpreted with caution, as it does not incorporate the impact of severe pain, dyspareunia and sexual dysfunction.
- ✓ Assessment of quality of life using standardised instruments (EQ, SF-36 and WHO-5) is recommended to evaluate the multidimensional impact of the disease and to individualise long-term medical, psychological and social management.

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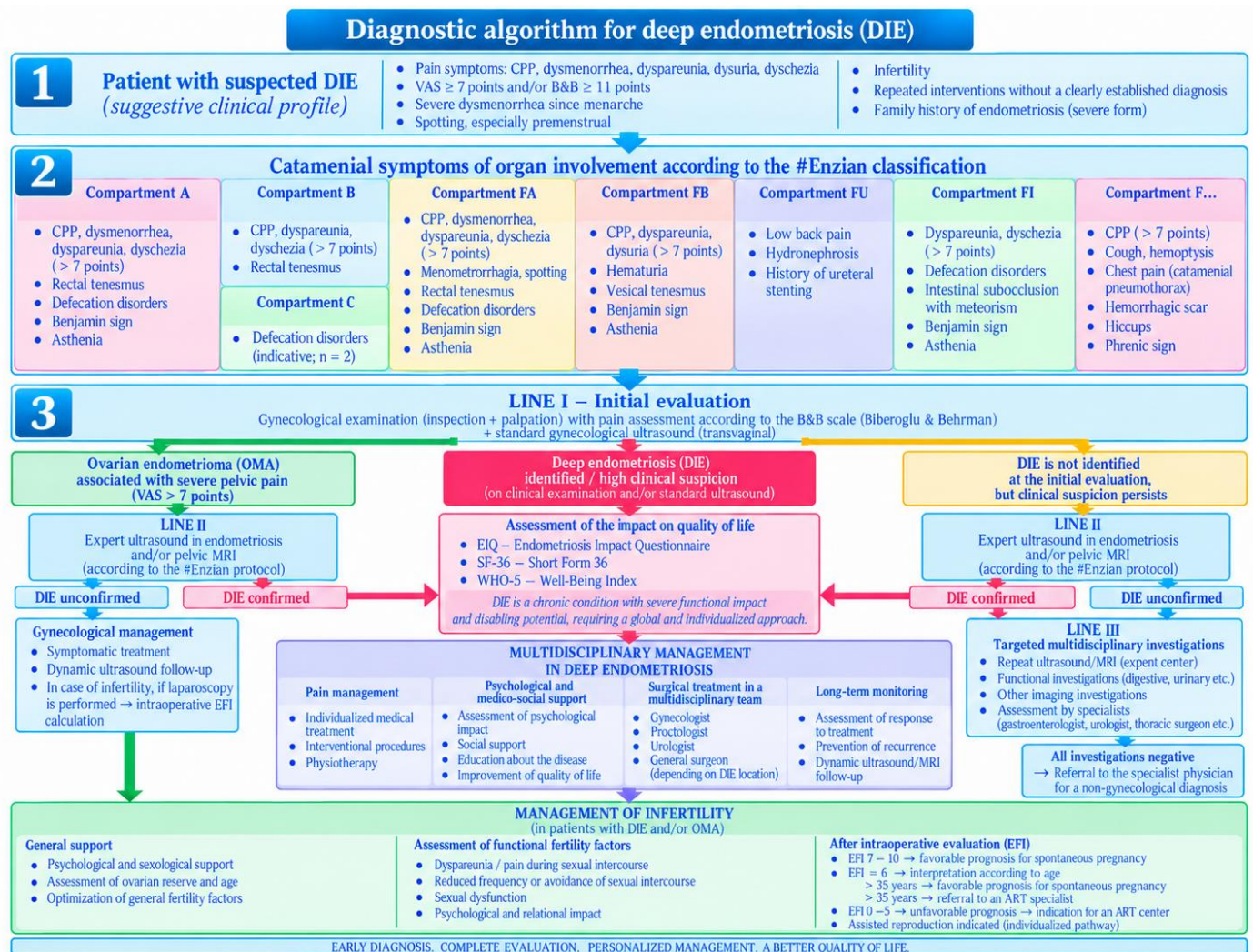
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## Appendix 1. Algorithm for establishing the diagnosis of DIE



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- **Articles in Scopus-indexed journals and other international databases**

1. **Иванова Е.Г.**, Кодряну Н.П. Глубокий эндометриоз – сравнительное исследование болевого синдрома и распространенности клинических симптомов согласно классификации #ENZIAN. In: *Проблемы репродукции*. 2025;31(4):96–101. doi:10.17116/repro20253104196.

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## ADNOTARE

Ivanova Elena

### *Particularitățile de diagnostic ale endometriozei profunde și impactul asupra calității vieții femeilor*

*Teză de doctor în științe medicale. Chișinău, 2026*

**Actualitatea cercetării.** Endometrioza profundă (EP) reprezintă o formă severă a bolii, asociată cu un diagnostic întârziat, durere pelvină complexă, afectare multiorganică și reducerea calității vieții femeilor.

**Scopul lucrării.** Optimizarea diagnosticului EP prin elaborarea unui algoritm medical multidisciplinar și studiul comparativ al impactului acestei patologii asupra calității vieții.

**Obiectivele cercetării.** Evaluarea comparativă a particularităților anamnestice, clinice și paraclinice în loturile investigate; analiza manifestărilor clinice și ecografice ale EP conform clasificării #Enzian; aprecierea prognosticului reproductiv și a impactului endometriozei asupra calității vieții; evaluarea nivelului de funcționare fizică și emoțională și a sănătății mintale în loturi.

**Noutatea și originalitatea științifică.** Studiul evidențiază impactul sever al EP asupra calității vieții și potențialul său dizabilant, asocierile dintre manifestările clinice și localizarea leziunilor conform #Enzian, precum și particularitățile aplicabilității și limitele utilizării indicelui EFI în aprecierea prognosticului reproductiv la paciențele cu EP.

**Rezultatele majore noi obținute.** Diagnosticul EP a fost întârziat peste 10 ani la 67,1% dintre paciente. Au fost identificate asocieri semnificative între manifestările clinice și compartimentele #Enzian, iar ultrasonografia ginecologică de expertiză a demonstrat o sensibilitate medie de 65,5% și o specificitate medie de 87,8%, cu variații între compartimente. EIQ, SF-36 și WHO-5 au evidențiat afectarea semnificativ mai pronunțată a calității vieții în EP. Infertilitatea a fost semnificativ mai frecventă la paciențele cu EP, în timp ce indicele EFI a fost comparabil între grupuri, evidențiind limitele aplicabilității acestuia în prognosticul reproductiv.

**Problema științifică importantă soluționată.** Optimizarea diagnosticului neinvaziv al EP prin integrarea datelor clinico-anamnestice și imagistice conform clasificării #Enzian, cu elaborarea unui algoritm medical multidisciplinar de diagnostic și evaluarea aplicabilității indicelui EFI în prognosticul reproductiv.

**Semnificația teoretică.** Rezultatele consolidează conceptul de EP ca afecțiune cronică, infiltrativă, cu impact multisistemic și potențial dizabilant și fundamentează necesitatea unei abordări diagnostice integrate, multidisciplinare și individualizate.

**Valoarea aplicativă.** A fost elaborat un algoritm medical multidisciplinar orientat spre diagnosticul precoce și neinvaziv al EP, prin integrarea datelor clinice și imagistice conform #Enzian și utilizarea instrumentelor standardizate pentru evaluarea durerii, prognosticului reproductiv și calității vieții.

**Implementarea rezultatelor științifice.** Rezultatele cercetării au fost integrate în procesul didactic al IP USMF „Nicolae Testemițanu” și valorificate în practica medicală prin acte de implementare și protocoale clinice privind endometrioza.

**Structura tezei.** Lucrarea cuprinde 114 pagini de text de bază, introducere, 4 capitole, concluzii generale, recomandări practice, 155 de surse bibliografice, 50 de figuri, o formulă, 9 tabele și 9 anexe. Rezultatele sunt publicate în 26 de lucrări științifice.

**Cuvinte-cheie:** endometrioza, endometrioza profundă, sindrom algic, diagnostic clinic, clasificarea #Enzian, calitatea vieții, EFI, EIQ, SF-36, WHO-5.

## ANNOTATION

Elena Ivanova

### *Diagnostic particularities of deep endometriosis and its impact on women's quality of life*

*Doctoral thesis in medical sciences. Chişinău, 2026*

**Relevance of the research.** Deep infiltrating endometriosis (DIE) is a severe form of the disease associated with delayed diagnosis, complex pelvic pain, multiorgan involvement and reduced quality of life in women.

**Aim of the study.** To optimise the diagnosis of DIE through the development of a multidisciplinary medical diagnostic algorithm and a comparative assessment of the impact of this condition on quality of life.

**Research objectives.** Comparative assessment of anamnestic, clinical and paraclinical characteristics; analysis of clinical and ultrasonographic manifestations of DIE according to #Enzian; assessment of reproductive prognosis and the impact of endometriosis on quality of life; evaluation of the level of physical and emotional functioning and of mental health in the study groups.

**Scientific novelty and originality.** The study highlights the severe impact of DIE on quality of life and its disabling potential, associations between clinical manifestations and lesion location according to #Enzian, and the applicability and limitations of the EFI in assessing reproductive prognosis in patients with DIE.

**Major new results obtained.** DIE diagnosis was delayed by over 10 years in 67.1% of patients. Significant associations were found between clinical manifestations and #Enzian compartments. Expert gynaecological ultrasonography showed mean sensitivity of 65.5% and specificity of 87.8%, varying by compartment. EQ, SF-36 and WHO-5 showed significantly greater impairment of quality of life in DIE. Infertility was significantly more frequent in DIE, while the EFI was comparable between groups, highlighting its limitations in reproductive prognosis.

**Scientific problem solved.** Optimisation of non-invasive DIE diagnosis through integration of clinical, anamnestic and imaging data according to #Enzian, development of a multidisciplinary diagnostic algorithm and assessment of the applicability of the EFI in reproductive prognosis.

**Theoretical significance.** The results support the concept of DIE as a chronic, infiltrative condition with multisystem impact and disabling potential and the need for an integrated, multidisciplinary and individualised diagnostic approach.

**Practical value.** A multidisciplinary medical algorithm was developed for early, non-invasive DIE diagnosis by integrating clinical and imaging data according to #Enzian and standardised tools for assessing pain, reproductive prognosis and quality of life.

**Implementation of scientific results.** The findings were integrated into teaching at Nicolae Testemiţanu State University of Medicine and Pharmacy and implemented in clinical practice through implementation acts and clinical protocols on endometriosis.

**Thesis structure.** The thesis comprises 114 pages of main text, an introduction, 4 chapters, general conclusions, practical recommendations, 155 references, 50 figures, one formula, 9 tables and 9 appendices. The results were published in 26 scientific papers.

**Keywords:** endometriosis, deep infiltrating endometriosis, pain syndrome, clinical diagnosis, #Enzian classification, quality of life, EFI, EQ, SF-36, WHO-5.