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Endometriosis/Adenomyosis and Congenital Uterine Malformations: Correlation of ESHRE/ESGE classes to #ENZIAN compartments

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Abstract

Purpose

Identify the association between endometriosis/adenomyosis and Congenital Uterine Malformations (CUMs), determine the malformation most commonly associated and detect the #Enzian compartment most frequently involved.

Methods

This retrospective cohort study included 304 patients with CUMs diagnosed by three-dimensional transvaginal ultrasound (3D-TVS) according to the ESHRE/ESGE classification, referred to our Gynecological Ultrasound Unit between January 2022 and December 2025. Concurrent endometriosis/adenomyosis was assessed by 2D/3D-TVS, and lesion distribution was analyzed according to the #Enzian classification.

Results

Among the 304 patients, 44 (14.5%) had dysmorphic uterus (ESHRE U1), 193 (63.5%) septate uterus (U2), 30 (9.8%) bicorporeal uterus (U3), 35 (11.5%) hemi-uterus (U4), and 2 (0.6%) aplastic uterus (U5). Overall, 116 patients (38.2%) showed at least one ultrasound sign of endometriosis/adenomyosis: 22/44 (50%) U1, 80/193 (41.5%) U2, 5/30 (16.7%) U3, 9/35 (25.7%) U4, and none with U5. U3 showed the lowest association with endometriosis/adenomyosis (OR 0.29). Multivariate logistic regression identified significant associations for U1 (OR 5.0) and U2 (OR 3.5). Analysis of the #Enzian compartments showed that U1 was associated with the FA compartment (OR 8.00), whereas U2 was associated with DIE compartment (A + B+C + FB; OR 5.16). No significant association was found for U3, U4, or U5.

Conclusion

CUMs are associated with endometriosis/adenomyosis and may influence lesion distribution. U2 is mainly associated with DIE, whereas U1 is primarily associated with the FA compartment. These findings support the integration of advanced 3D-TVS and the #Enzian classification in the assessment of patients with CUMs. Preoperative identification of anomaly-specific endometriotic patterns may improve diagnostic accuracy and guide minimally invasive surgical planning.

INTRODUCTION

Congenital Uterine Malformations (CUMs) prevalence ranges from 0.1% to 7% within the general population, with considerable variation attributed to differences in diagnostic methods, classification systems, and patient populations [1, 2]. Nonetheless, CUMs are reported in 4–8% of infertile women, 13.3–16.7% of those with recurrent miscarriage, and 24.5% of women experiencing both miscarriage and infertility [3–6]. Currently, three-dimensional transvaginal ultrasound (3D-TVS) is considered the gold standard for the

diagnosis of congenital uterine anomalies. Over the years, several classifications (AFS 1988, VCUAM 2005, ESHRE/ESGE 2013–2016, ASRM 2021) [7–11] and 3D-TVS parameters have been proposed to enable a precise and consistent diagnosis of these anomalies; however, a universal consensus has yet to be reached [12–15].

According to several studies CUMs can be associated to adenomyosis [16] and endometriosis, particularly in cases involving outflow obstruction and this correlation supports the retrograde menstruation theory of endometriosis pathogenesis [17–29].

TVS is also recognized now by several studies and guidelines [30] as the most reliable method for the non-invasive diagnosis of endometriosis [31–35]. At the end of 2020, the #Enzian classification was introduced as a comprehensive system for mapping endometriosis, assessing lesion location and size, adhesions, and involvement of adjacent organs. It can be used both surgically and for ultrasound evaluation. [36–40].

Therefore, an accurate non-invasive TVS evaluation can diagnose and classify CUMs as to identify and describe endometriosis lesion sites and the presence of adenomyosis.

The aim of the study is to assess the association between endometriosis/adenomyosis and CUMs and to correlate ESHRE/ESGE CUM classes [9] to the #Enzian [39] compartments in order to determine which CUM type is more frequently associated with specific endometriosis pelvic sites.

METHODS

Study Design

This retrospective study included all patients in reproductive age (range 12–45 years), with a 3D-TVS diagnosis of CUMs according to ESHRE/ESGE classification [9], referred to the Gynecological Ultrasound Unit at the University of Rome ‘Tor Vergata’ from January 2022 to December 2025.

The concurrent presence of pelvic endometriosis/adenomyosis was detected with TVS and classified according to the #Enzian compartments [39].

Inclusion criteria were age of 12–45 years, diagnosis of CUMs according to ESHRE/ESGE classification never treated surgically, complete clinical and ultrasound data and signed informed consent.

Exclusion criteria were pregnancy, reproductive tract cancer, pelvic pathologies interfering with accurate ultrasound assessment (e.g. large fibroids or pelvic masses), previous uterine or endometriosis surgery, incomplete reproductive or clinical history, lack of informed consent, suboptimal 3D images, and uncertain congenital uterine malformations. Uteri with an arcuate fundus and < 5 mm fundal indentation, classified as subsepta according to ESHRE/ESGE, were excluded to ensure sample homogeneity. [41, 42].

Clinical history and symptoms

Patient data were recorded using FileMaker Pro® 9.0, including date of birth, age at ultrasound, BMI (Body Mass Index), age at menarche, parity, menstrual characteristics, last menstrual period, and previous surgeries. Patients attempting to conceive also provided reproductive history, including previous spontaneous or assisted pregnancies, recurrent pregnancy loss (≥ 2 losses before 23 weeks), and infertility (≥ 1 year of trying to conceive in the absence of male infertility factors).

Ultrasound examination

All patients with congenital uterine malformations underwent 2D, 3D, and Power Doppler transvaginal ultrasound (TVS). Examinations were performed using Voluson E6 or E8 systems (GE Healthcare) with standardized settings and a transvaginal probe. In virginal patients, a transrectal approach was used for adequate visualization.

A conventional 2D grayscale and Power Doppler examination initially assessed the pelvis, including the uterus, endometrium, myometrium, and adnexa, documenting any abnormalities. Subsequently, 3D volumes were acquired from transverse and/or sagittal planes to optimize the coronal view. Multiple acquisitions were obtained to minimize uterine contraction artifacts, and datasets were stored for offline analysis. Uterine morphology was assessed on a standardized coronal plane, using the interstitial portions of the fallopian tubes and internal tubal ostia as reference points to improve visualization of the cervical isthmus and internal cervical orifice.

The following specific measurements were determined:

- septal width (W): the distance between the two internal tubal ostia.
- uterine fundal wall thickness (M), the distance from interostial line and the external uterine serosa.
- fundal indentation angle (α), the angle between the two endometrial layers.
- indentation length (L), the distance from the tip of the fundal indentation to the interostial line
- fundal cavity width (R0) (distance between the two internal tubal ostia)
- width of uterine cavity at the isthmic level or internal uterine orifice (Wi- corpus isthmic level cavity width)
- fundal/isthmic cavity width ratio (R0/Wi)
- External indentation: distance between two lines, one joining the two tubal ostia, the other the external profile of the two hemiuteri.

The diagnosis of congenital uterine malformation was made in accordance with the current parameters and classification system ESHRE/ESGE 2013. Anomalies are sorted into six major classes (U1-6), and each class is divided into sub-classes, according to increasing severity of the anatomical deviation.

For dysmorphic uteri (class U1), the uterine cavity parameters proposed in a recent study were used to better define T-, Y- and I-shaped configurations [11, 14, 15].

According to the 2013 ESHRE/ESGE classification, CUMs are divided into six major classes (U0–U6), each with subclasses reflecting increasing anatomical severity, from the least to the most severe deformity.

Among patients with CUMs, we retrospectively identified those with concomitant endometriosis, including ovarian endometriosis, adenomyosis, or deep endometriosis.

The presence of adenomyosis and all potential sites of endometriosis were systematically evaluated and documented using previously validated anatomical mapping sheets (IDEA, #Enzian, MUSA) [33, 34, 39, 43]. The pelvic cavity was examined across the anterior, lateral, and posterior compartments.

The #Enzian classification is based on the known Enzian classification for deep endometriosis 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), ovary (O), other intestinal locations (sigmoid colon, small bowel; FI), as well as adhesions, involving the tubo-ovarian unit (T), and, optionally, tubal patency.

Neither the presence of pelvic adhesions alone nor ultrasound features suggestive of superficial endometriosis, as defined in the recent addendum to the IDEA study, were considered in this study, for this reason the P compartment was not included in the analysis [38].

Statistical analysis

Descriptive statistics summarized patients' demographic and clinical characteristics. Categorical variables were expressed as counts (n) and percentages (%), while continuous variables were reported as mean ± standard deviation (SD).

The association between ESHRE uterine malformation class (U1–U5) and endometriosis/adenomyosis was assessed using the Chi-square test. Univariate binary logistic regression was then performed, with endometriosis/adenomyosis as the dependent variable and ESHRE class as the categorical independent variable. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated using one class as reference. A multivariable model was subsequently adjusted for potential confounders, including the clinical indication for ultrasound. Secondary univariate and multivariable logistic regression analyses evaluated the association between ESHRE class and specific #Enzian compartments.

Statistical significance was set at $p < 0.05$, unless otherwise specified for multiple comparisons. Analyses were performed using MedCalc Statistical Software (MedCalc Software Ltd., Ostend, Belgium).

RESULTS

Of 430 patients with an ultrasound diagnosis of CUMs referred to our Gynecological Unit between 2022 and 2025, 304 patients met the inclusion criteria. (Fig. 1).

In our study population, the mean age of patients was 32.7 ± 7.4 years (range 13–45). 86.5% of our patients were nulliparous. The most frequent indications for undergoing ultrasound examination included suspected uterine anomalies in 155 patients (50.9%), suspected endometriosis in 100 patients (32.8%), infertility in 46 patients (15.1%), recurrent pregnancy loss in 15 patients (4.9%), other indications like pelvic pain, polycystic ovary syndrome (PCOS), endometrial polyps, ovarian cyst in 40 patients (13.2%). **(**Table 1**).**

Table 1
Patients characteristics, reproductive history and indications to TVS evaluation of the 304 patients with CUMs included in this study. *(TVS: transvaginal sonography, SD: standard deviation; CUMs: Congenital Uterine Malformations)*

Patients Characteristics at TVS diagnosis (n 304)	**Mean ± SD N (%)**
AGE	32.7 (± 7.4)
BMI	22.4 (± 3.6)
MENARCHE (YEARS)	12.3 (± 1.4)
GRAVIDITY	0.6 (± 1.1)
PARITY	0.2 (± 0.5)
NULLIPARITY	263/304 (86.5%)
MULTIPARITY	41/304 (13.5%)
PRE-SEXUALLY ACTIVE	11/304 (3%)
Indication to TVS	
SUSPECTED UTERINE ANOMALIES	155/304 (50.9%)
SUSPECTED ENDOMETRIOSIS	100/304 (32.8%)
INFERTILITY	46/304 (15.1%)
RECURRENT PREGNANCY LOSS	15/304 (4.9%)
OTHER (PELVIC PAIN, PCOS, ENDOMETRIAL POLYPS, OVARIAN CYST)	40/304 (13.2%)
CONTROL	36/304 (12%)

Table 2 shows the distribution of the different classes and subclasses of CUMs according to the ESHRE/ESGE classification in our study population. Among the 304 patients diagnosed with CUMs enrolled in the study, 44 (14.5%) presented with a dysmorphic uterus (U1 according to the ESHRE classification), 193 (63.5%) with a septate uterus (U2), 30 (9.8%) with a bicorporeal uterus (U3), 35 (11.5%) were diagnosed with a unicornuate uterus (U4), and 2 (0.6%) patients were diagnosed with an aplastic uterus (U5).

Table 2

Distribution, in our study population, of the different classes and subclasses of CUMs according to the ESHRE/ESGE classification and the respective percentage of patients affected and not affected by endometriosis/adenomyosis (statistical significance p value < 0.05). *(CUMs Congenital Uterine Malformations)*

CUMs ESHRE/ESGE CLASSIFICATION	**TOTAL PATIENTS**	**PATIENTS WITH ENDOMETRIOSIS/ ADENOMYOSIS**	**PATIENTS WITHOUT ENDOMETRIOSIS/ ADENOMYOSIS**	**p value**
	n/total patients (%)	**n/total patients with endometriosis/adenomyosis (%)**	**n/total patients without endometriosis/adenomyosis (%)**	
Total	304 (100%)	116 (38.2%)	188 (61.8%)	
U1	44/304 (14.5%)	22/116 (19.0%)	22/188 (11.7%)	0.08
U1A	17/304 (5.6%)	8/116 (6.9%)	9/188 (4.8%)	0.04
U1B	1/304 (0.3%)	0/116 (0%)	1/188 (0.5%)	0.04
U1C	26/304 (8.6%)	14/116 (12.1%)	12/188 (6.4%)	0.08
U2	193/304 (63.5%)	80/116 (69.0%)	113/188 (60.1%)	0.1
U2A	160/304 (52.6%)	69/116 (59.5%)	91/188 (48.4%)	0.06
U2B	33/304 (10.8%)	11/116 (9.5%)	22/188 (11.7%)	0.5
U3	30/304 (9.8%)	5/116 (4.3%)	25/188 (13.3%)	0.01
U3B	19/304 (6.2%)	4/116 (3.4%)	15/188 (8.0%)	0.1
U3C	11/304 (3.6%)	1/116 (0.9%)	10/188 (5.3%)	0.04
U4	35/304 (11.5%)	9/116 (7.8%)	26/188 (13.8%)	0.1
U4A	15/304 (4.9%)	3/116 (2.6%)	12/188 (6.4%)	0.1
U4B	20/304 (6.6%)	6/116 (5.2%)	14/188 (7.4%)	0.4
U5	2/304 (0.6%)	0/116 (0%)	2/188 (1.1%)	0.3

CUMs ESHRE/ESGE CLASSIFICATION	TOTAL PATIENTS	PATIENTS WITH ENDOMETRIOSIS/ ADENOMYOSIS	PATIENTS WITHOUT ENDOMETRIOSIS/ ADENOMYOSIS	p value
	n/total patients (%)	n/total patients with endometriosis/adenomyosis (%)	n/total patients without endometriosis/adenomyosis (%)	
U5A	2/304 (0.6%)	0/116 (0%)	2/188 (1.1%)	0.3
U5B	0/304 (0%)	0/116 (0%)	0/188 (0%)	/

Analyzing the presence of endometriosis/adenomyosis among the 304 patients enrolled in the study, 116 (38.2%) exhibited at least one direct ultrasound sign indicative of endometriosis/adenomyosis, while 188 (61.8%) showed no evidence of the condition. In the group of 116 patients with endometriosis/adenomyosis, U1 (dysmorphic uterus) and a U2 (septate uterus) are the most represented malformations (19% and 69% respectively) compared to bicornuate U3 (4.3%), unicornuate U4 (7.8%) or aplastic uterus U5 (0%).

The prevalence of endometriosis, furthermore, differed across ESHRE/ESGE classes, indicating that the distribution of endometriosis was not uniform among CUMs types **(**Fig. 2**)**.

When analyzing the distribution of endometriosis/adenomyosis across the individual ESHRE/ESGE classes and subclasses, a markedly higher prevalence of endometriosis is observed in U1 and U2 anomalies. Specifically, 22 out of 44 patients in the U1 class (50%) were affected by endometriosis, while in the U2 class, 80 out of 193 patients (41.5%) had a diagnosis of endometriosis/adenomyosis.

Within these two classes, the U1c and U2a subclasses showed the highest prevalence rates, with 54% and 43.2% of patients affected by endometriosis, respectively. In contrast, the prevalence of endometriosis was considerably lower among patients with U3 (bicorporeal uterus) and U4 (hemi-uterus) anomalies, at 16.7% and 25.7%, respectively. No cases of endometriosis were reported among the two patients classified as U5 (aplasia). **(Supplementary Table).**

To identify which CUM had a higher correlation with endometriosis/adenomyosis in our study population, we compared the CUM ESHRE/ESGE groups and the respective percentages of patients with endometriosis/adenomyosis. This analysis revealed that, in our study population, the CUM with the lowest association with endometriosis/adenomyosis was the U3 malformation (OR 0.29, CI 0.11–0.79) as compared to U1 (OR 1.77, CI 0.93–3.36), U2 (OR 1.47, CI 0.90–2.40), U4 (OR 0.52, CI 0.24–1.16) and U5 (OR 0.32, CI 0.01–6.73) **(**Fig. 3**).**

Taking class U3 as the reference category, a univariate binary logistic regression was performed to quantify the association between ESHRE/ESGE classification and the presence of endometriosis/adenomyosis. This analysis showed a significant association between U1 (OR = 5.00; 95% CI 1.62–15.44, p 0.005) and U2 (OR =

3.54; 95% CI 1.30–9.64, p 0.01) with endometriosis/adenomyosis. U4 and U5 instead, don't show statistically significant differences.

Specifically, women with U1 malformations had higher odds of endometriosis (OR = 5.00; 95% CI 1.62–15.44; p = 0.005). Multivariate logistic regression analysis confirms the statistical significance also after adjustment for indication of suspected endometriosis (aOR = 4.89; 95% CI 1.54–15.50; p = 0.007) and for indication of suspected uterine malformation (aOR = 4.58; 95% CI 1.46–14.3; p = 0.008). Similarly, class U2 was associated with increased odds of endometriosis (OR = 3.54; 95% CI 1.30–9.64; p = 0.01), which also remained significant in multivariable analyses adjusted for indication of suspected endometriosis (aOR = 2.83; 95% CI 1.01–7.9; p = 0.04) and for indication of suspected malformation (aOR = 2.85; 95% CI 1.03–7.9; p = 0.04) **(**Table 3**).**

Table 3

Univariate binary and multivariate logistic regression analysis to quantify the association between CUMs ESHRE/ESGE classification and the presence of endometriosis/adenomyosis, taking U3 class as a reference category. *(OR: Odds Ratio, aOR: Adjusted Odds Ratio, 95% CI: Confidence Intervals, CUMs: Congenital Uterine Malformations)*

CUMs ESHRE/ESGE CLASS	**UNIVARIATE BINARY LOGISTIC REGRESSION ANALYSIS**			**MULTIVARIATE LOGISTIC REGRESSION ANALYSIS (ADJUSTED FOR INDICATION OF SUSPECTED UTERINE MALFORMATION)**			**MULTIVARIATE LOGISTIC REGRESSION ANALYSIS (ADJUSTED FOR INDICATION OF SUSPECTED ENDOMETRIOSIS)**		
	OR	**95% CI**	**p value**	**aOR**	**95%CI**	**p value**	**aOR**	**95%CI**	**p value**
U1	5.00	1.62–15.44	0.005 *	4.58	1.46–14.3	0.008 *	4.89	1.54–15.5	0.007 *
U2	3.54	1.30–9.64	0.01 †	2.85	1.03–7.9	0.04 †	2.83	1.01–7.9	0.04 †
U4	1.73	0.52–5.88	0.38	1.71	0.5–5.9	0.4	1.69	0.48–5.9	0.4
U5	0.00	/	0.99	0.00	/	0.99	0.00	/	0.99

***** *Significant association between endometriosis/adenomyosis and U1 (OR = 5.00; 95% CI 1.62–15.44, p 0.005). Multivariate logistic regression analysis confirms the statistical significance also after adjustment for indication of suspected endometriosis and for indication of suspected uterine malformation*

† Significant association between endometriosis/adenomyosis and U2 (OR = 3.54; 95% CI 1.30–9.64, p 0.01). Multivariate logistic regression analysis confirms the statistical significance also after adjustment for indication of suspected endometriosis and for indication of suspected uterine malformation

Subsequently, a univariate logistic regression was performed to assess the association between ESHRE classification and the different #ENZIAN compartments (Table 4).

Table 4

Univariate logistic regression to assess the association between CUMs ESHRE/ESGE classes and the different #ENZIAN compartments. *(OR: Odds Ratio, aOR: Adjusted Odds Ratio, 95%CI: Confidence Intervals, NA: Not Applicable, CUMs: Congenital Uterine Malformations)*

CUMs ESHRE/ESGE CLASSES **WITH ENDOMETRIOSIS/** **ADENOMYOSIS**	**O**	**T**	**FA**	**A**	**B**	**C**	**FB**	**DIE TOT** **(A + B+C + FB)**
U1 (n = 22)	3/22 (14%) OR 2.12 (0.21–21.4)	4/22 (18%) OR NA	16/22 (73%) OR 8.00 (1.68–38.09) *	4/22 (18%) OR 1.4 (0.24–8.18)	7/22 (32%) OR NA	3/22 (14%) OR NA	0	10/22 (45%) OR 4.11 (0.83–20.36)
U2 (n = 80)	6/80 (8%) OR 0.93 (0.11–8.01)	19/80 (24%) OR NA	37/80 (46%) OR 3.32 (0.76–14.6)	11/80 (14%) OR 0.85 (0.18–4.02)	46/80 (58%) OR NA	7/80 (9%) OR NA	2/80 (2.5%) OR NA	52/80 (65%) OR 5.16 (1.19–22.4) †
U4 (n = 9)	0	0	8/9 (89%) OR 4.14 (0.81–21.3)	0	1/9 (11%) OR NA	0	0	1/9 (11%) OR 0.4 (0.03–4.78)
U5 (n = 0)	0	0	0	0	0	0	0	0

***** *Significant association between U1 and FA compartment OR = 8.00 (95%CI 1.68–38.09) [aOR (suspected endometriosis) = 7.73 (95% CI 1.61–36.99) and aOR (suspected malformation) = 7.46 (95% CI 1.56–35.70)]*

† *Significant association between U2 and deep infiltrating endometriosis (DIE) OR = 5.16 (95%CI 1.19–22.4) [aOR (suspected endometriosis) = 4.03 (95% CI 0.90–18.01) and aOR (suspected malformation) = 4.51 (95% CI 1.02–19.88)]*

U1 was associated with the FA compartment, showing an OR = 8.00 (95% CI 1.68–38.09, p = 0.02), also after adjustment for indication of suspected endometriosis or suspected uterine malformation [aOR = 7.73 (95% CI 1.61–36.99) and aOR = 7.46 (95% CI 1.56–35.70), respectively].

U2 showed a significant association with deep infiltrating endometriosis (DIE = A + B + C+FB) (OR = 5.16; 95% CI 1.19–22.4, p = 0.03), also after adjustment for indication of suspected endometriosis or suspected uterine malformation [aOR = 4.03 (95% CI 0.90–18.01) and aOR = 4.51 (95% CI 1.02–19.88), respectively].

No other specific associations were observed between other ESHRE/ESGE classes and the remaining #ENZIAN compartments (Fig. 4).

DISCUSSION

This study is the first to investigate the relationship between CUMs, classified according to the ESHRE/ESGE system, and the presence, extent, and anatomical distribution of endometriosis/adenomyosis using the #Enzian classification. Our findings show a significant association between specific uterine malformations and endometriosis/adenomyosis, particularly in dysmorphic (U1) and septate (U2) uteri. Different CUM classes were also associated with distinct disease phenotypes, suggesting that uterine morphology may influence both the development and anatomical distribution of endometriosis.

The association between CUMs and endometriosis/adenomyosis remains controversial and has long been investigated for its potential role in endometriosis pathogenesis. Several studies have reported a higher prevalence of endometriosis in women with uterine anomalies, particularly those causing impaired menstrual outflow, supporting retrograde menstruation as a key pathogenic mechanism [16, 20–23, 25, 27, 29]. However, the association between endometriosis and non-obstructive anomalies has also been consistently reported, indicating that retrograde menstruation alone is unlikely to fully explain the development of the disease.

In this context, Leyendecker et al. [21] proposed that abnormal uterine contractility, characteristic of U2 anomalies, may promote retrograde menstruation and facilitate ectopic implantation of endometrial tissue, particularly in the retrocervical and parametrial regions. Similarly, Nawroth et al. [23] suggested that uterine dysperistalsis may represent an important mechanical factor linking septate uteri and endometriosis, independently of outflow obstruction. According to this hypothesis, congenital uterine anomalies may disrupt physiological uterine peristalsis and create a uterine environment favouring the establishment and progression of endometriotic lesions [20, 21]. Additional support for a relationship between CUMs and endometriosis was provided by Matalliotakis et al. [22], who reported a higher prevalence of uterine anomalies among women with endometriosis compared with controls. In their study, septate uterus was the most frequent anomaly identified, followed by didelphic, unicornuate, and bicornuate uteri. Interestingly, a substantial proportion of affected women also reported a family history of endometriosis, suggesting that genetic susceptibility may contribute to the observed association.

Nevertheless, the relationship between specific CUM classes and disease severity remains unclear. Boujenah et al. [4] reported that the prevalence and severity of endometriosis were not associated with a particular class of uterine anomaly. Instead, moderate-to-severe disease, including ovarian endometrioma and deep endometriosis, appeared to be more frequent in women with infertility. Similarly, Pitot et al. [25] highlighted the potential contribution of infertility to endometriosis severity in women with uterine malformations. Taken together, these observations support the concept that multiple mechanisms, including retrograde menstruation, uterine dysperistalsis, impaired reproductive function, and possibly genetic predisposition, may interact in the pathogenesis of endometriosis associated with CUMs.

In our cohort, U1 and U2 uteri showed the strongest associations with endometriosis/adenomyosis, with U1c and U2a showing the highest prevalence among individual subclasses. The higher prevalence in U2a uteri may reflect altered uterine contractility and greater disruption of uterine peristalsis compared with complete septate uteri (U2b). The association with U1c suggests that dysmorphic uterine cavities may involve abnormal contractility and junctional zone dysfunction, potentially facilitating retrograde menstruation and promoting endometriotic and adenomyotic lesions. Clinically, women with these malformations may represent a higher-risk subgroup and could benefit from more comprehensive diagnostic assessment. The association between U1 and U2 uteri and endometriosis/adenomyosis was confirmed in both univariate and multivariable analyses. Importantly, it remained significant after adjusting for referral indications, including suspected endometriosis or uterine malformation, supporting the robustness of these findings and reducing the likelihood of referral bias.

A further strength of this study is the assessment of disease distribution according to individual #Enzian compartments, revealing distinct associations between uterine malformations and disease phenotypes. Dysmorphic U1 uteri were significantly associated with adenomyosis (FA compartment), whereas septate U2 uteri were associated with deep endometriosis. Although the underlying mechanisms remain unclear, these findings may reflect different effects of altered uterine architecture and contractility. The association between U1 and adenomyosis may support a role for abnormal uterine peristalsis and junctional zone dysfunction in myometrial involvement, while the association between U2 and deep endometriosis may suggest that altered uterine dynamics favour pelvic implantation and progression of endometriotic lesions. Overall, specific uterine phenotypes may predispose to distinct manifestations of endometriosis/adenomyosis.

Despite the well-established relationship between endometriosis and ovarian involvement, no significant differences in the #Enzian ovarian compartment were observed among the various uterine malformation classes. This finding may indicate that ovarian endometriosis is influenced to a greater extent by systemic, genetic, hormonal, or immunological factors than by uterine morphology itself, as previously suggested by Vercellini et al. [28].

Patients with uterine aplasia (U5) did not present with endometriosis/adenomyosis in our cohort. Although the number of cases was limited, this observation is biologically plausible given the absence of functional endometrial tissue and the consequent lack of retrograde menstruation, which remains one of the principal mechanisms implicated in endometriosis development.

Strengths of this study include its large cohort, standardized ultrasound criteria, and combined use of the ESHRE/ESGE and #Enzian classifications, enabling detailed characterization of uterine morphology and endometriosis phenotype. Limitations include the retrospective single-centre design and potential selection bias, as well as possible overestimation of disease prevalence due to the tertiary referral setting. The small number of patients in some malformation subclasses, particularly U5, also limits subgroup analysis.

In conclusion, dysmorphic (U1) and septate (U2) uteri are associated with increased prevalence of endometriosis/adenomyosis and distinct #Enzian disease patterns. These findings support a potential role for altered uterine morphology and contractility in disease pathogenesis. Prospective studies are needed to

clarify the underlying mechanisms and assess whether identifying specific uterine malformations could facilitate earlier diagnosis and more personalized management.

Conclusions

This study clearly highlighted that some CUMs are more strongly associated with endometriosis than others, particularly U1c and U2a. Specifically, malformations such as U1 and U2 carry a 5-fold and 3.5-fold increased risk, respectively, of concomitant endometriosis/adenomyosis compared with other malformations. Furthermore, it was shown that U1 and U2 are not only more frequently associated with endometriosis but also involve specific #Enzian compartments (FA and DIE = A + B + C+FB).

Clinically, these data advocate for the integration of advanced 3D-TVS and the #Enzian classification framework in the evaluation of patients with CUMs; these data underscore the importance of performing a thorough pelvic staging for the potential presence of associated endometriotic disease at the time of TVS or hysteroscopic diagnosis of a uterine malformation, in order to ensure proper and comprehensive management of the patient.

Future prospective studies are warranted to elucidate the causal mechanisms linking CUMs and endometriosis/adenomyosis, and to assess whether surgical correction of anomalies such as U2 and U1 may mitigate endometriotic progression or symptom severity.

Declarations

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Declaration of competing interest

The authors have no proprietary, financial, professional or other personal interest of any nature in any product, service or company. The authors alone are responsible for the content and writing of the paper.

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Institutional review board approval was obtained (No.143/19) and informed consent to data utilization was signed by all included patients, or, in the case of minors, informed consent was signed by the parents or legal guardians.

Author Contribution

All authors have contributed to this paper. All authors contributed to the study conception and design. C.E., G.M., F.I, E.N, C.R., A.S., S.V., A.E.: study conceptualization and protocol planning and design, supervision. G.M., F.I., D.F., M. A., E.N., C.R.: clinical data search, collection and analysis. C.E., G.M., F.I., D.F: formal

analysis. C.E., G.M., M.A., F.I.: manuscript writing/editing. All authors read and approved of the final manuscript.

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Data Availability

All data supporting the findings of this study are available within the paper and its Supplementary Information.

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Figures

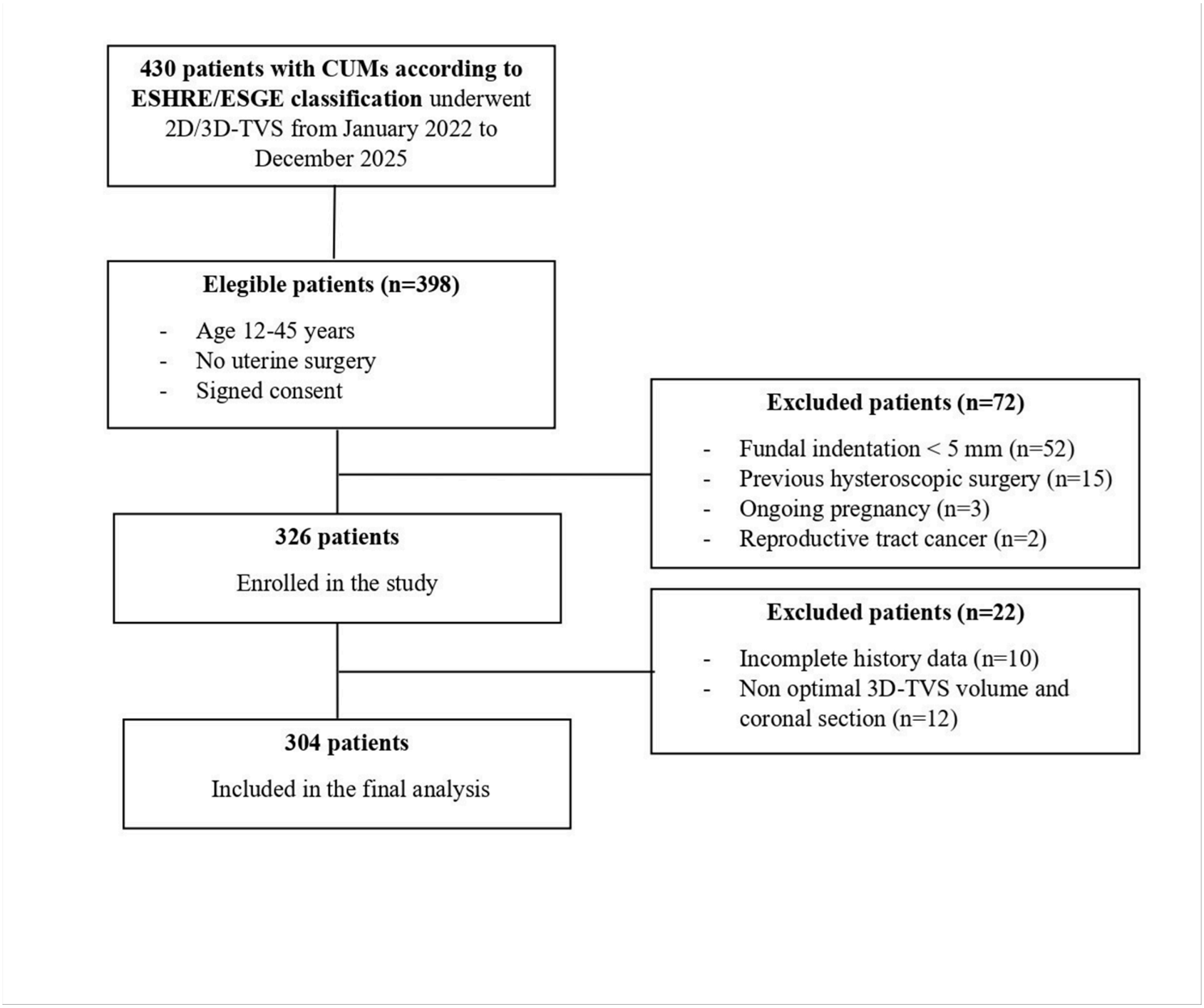


Figure 1

Design of the study

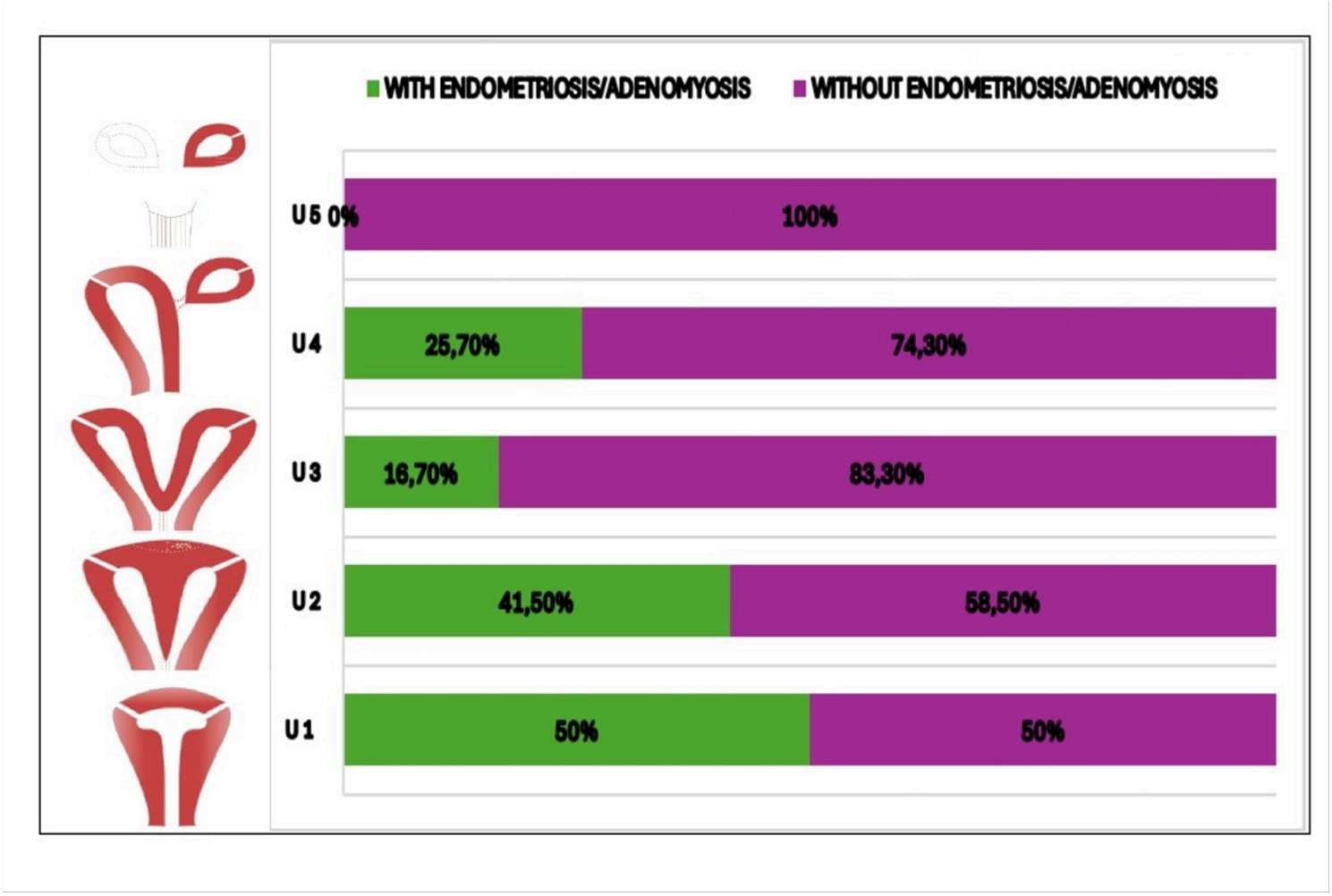
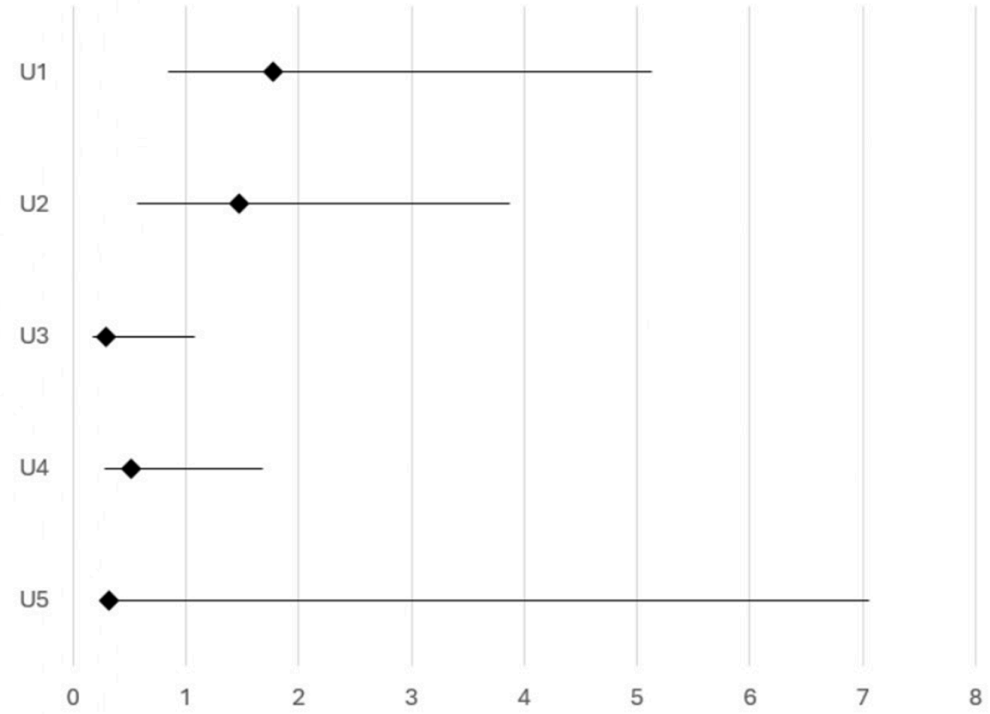


Figure 2

Distribution of the percentage endometriosis/adenomyosis in the different CUMs ESHRE/ESGE classes



ESHRE/ESGE CLASS	OR	95%CI	p value
U1 (n=44)	1.77	0.93-3.36	0.08
U2 (n=193)	1.47	0.90-2.40	0.1
U3 (n=30)	**0.29** *	0.11-0.79	0.01
U4 (n=35)	0.52	0.24-1.16	0.1
U5 (n=2)	0.32	0.01-6.73	0.46

Figure 3

Comparison between all CUMs ESHRE/ESGE classes and the respective percentages of endometriosis/adenomyosis to identify the malformation that most correlates with endometriosis. U3 is the CUM with the lowest correlation with endometriosis/adenomyosis

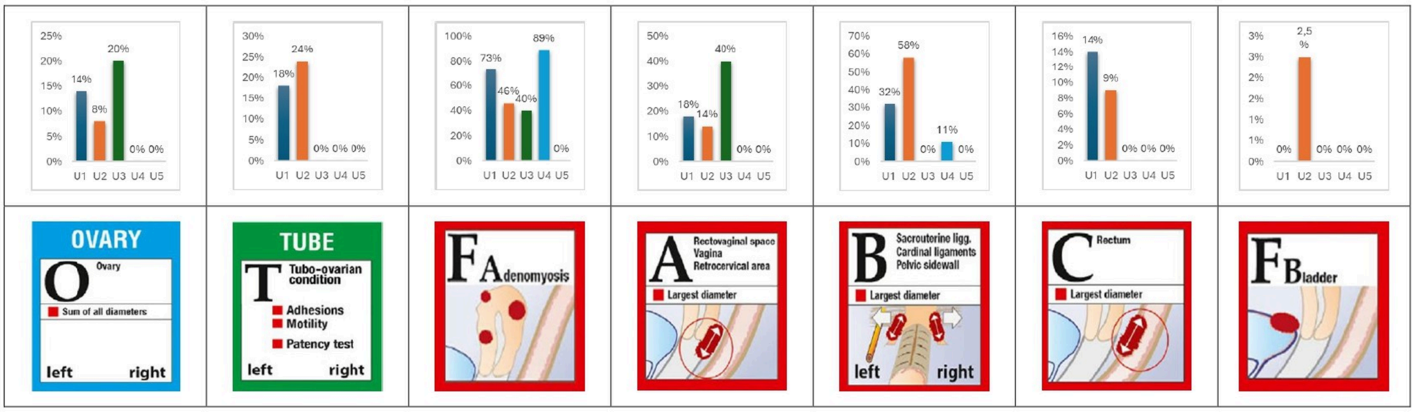


Figure 4

Association between CUMs ESHRE/ESGE classes and presence of endometriosis/adenomyosis in all pelvic compartments according to #ENZIAN classification

Supplementary Files

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- SupplementaryTable.docx