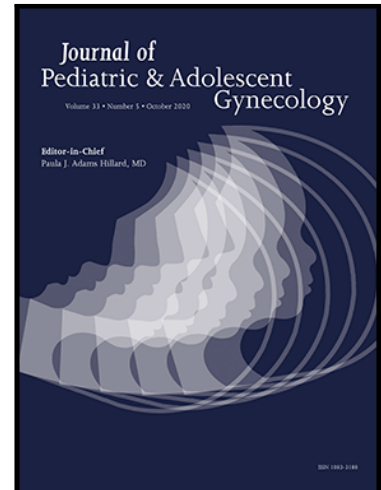


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Pain Levels of Women Diagnosed with Endometriosis: Is There a Difference in Younger Women?

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Pain Levels of Women Diagnosed with Endometriosis: Is There a Difference in Younger Women?

Running title: Young Endometriosis Patients Present Higher VAS Scores for Dysmenorrhea and Dyspareunia, with a Significant Number Already Showing Severe Endometriosis.

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Abstract

Study objective: Early diagnosis and treatment of endometriosis affecting adolescent women are important in preventing chronic pain. Our aim was to analyze the clinical characteristics and severity of symptoms in adolescent patients with endometriosis compared to older patients.

Methods: This single-center retrospective cohort study in a tertiary referral hospital analyzed women whose first consultation at the certified endometriosis center of the Bern University Hospital between January 2017 and December 2020 resulted in the clinical diagnosis of endometriosis. Patients, divided into 2 groups by age, reported Visual Analog Scale (VAS) scores for non-cyclic pelvic pain, dysmenorrhea, dyschezia, dysuria, and dyspareunia. The symptom types and severity in the two groups were compared. The young patients with endometriosis were analyzed in greater detail, comparing VAS scores and types of endometriosis.

Results: From a total of 826 patients, 144 (17.4%) patients aged ≤ 24 years old and 682 (82.6%) patients aged > 24 years old were compared. The younger patients reported significantly higher pain scores for dysmenorrhea (VAS 7.3 vs. VAS 6.6, $p= 0.015$), dyspareunia (VAS 4.6 vs. VAS 3.4, $p= 0.001$), and non-cyclic pelvic pain (VAS 4.3 vs. 3.7, $p= 0.032$) compared to the older patient collective. Similar results were found when excluding patients with hormonal treatment.

Conclusion: Young patients with clinically diagnosed endometriosis have significantly higher dysmenorrhea and dyspareunia pain levels than older patients. By acknowledging and understanding this, early diagnosis and adequate treatment can be promoted. Dyspareunia in adolescents in particular merits clinical attention.

Key words: adolescent endometriosis, pain, endometriosis, dyschezia, dysmenorrhea, dyspareunia, dysuria, non-cyclic pelvic pain, VAS scores

Introduction

Endometriosis is a gynecological condition characterized by the presence of extra uterine endometrial glands and stroma. The disease is estimated to affect approximately 10% of all women of reproductive age (1). Several symptoms are associated with endometriosis, the leading cause of chronic pelvic pain (2). In the adult population, the most common symptoms are dysmenorrhea, dyspareunia, dyschezia, and infertility (3). However, the disease occurs not only in the adult population, but also in adolescents and young women.

Endometriosis patients often report that their symptoms already occurred in adolescence (4). According to a large registry, two-thirds of women diagnosed with endometriosis in adulthood have already had symptoms before the age of 20 (5). Nevertheless, especially in young women, the diagnosis of endometriosis is delayed, even more than in older patients. In the review of Yeung et al from 2017 (6), the diagnosis was delayed in average by 12 years in adolescents. Possibly, in countries who have pushed on awareness in the young this time is reduced. Women and girls who first experienced symptoms as adolescents waited 3 times longer (around 6 years) before seeing a doctor, compared to those with symptom onset in adulthood (4); young women often have consultations with 4 or 5 different physicians before establishing the diagnosis (4,5). The majority of adolescent girls with non-cyclic chronic pelvic pain not responding to conventional medical therapy (such as oral contraceptive pills or non-steroidal anti-inflammatory drugs) have endometriosis (6–8). Still, the prevalence of endometriosis in the young population is less clear than in the adult population.

Adolescent endometriosis presents differently from adult endometriosis. The main symptoms in adolescents and young women are non-cyclic chronic pelvic pain and dysmenorrhea (6). However, little is known about pain intensity and different types of symptoms. The disease has an impact on the quality of life. It is associated with absenteeism from school and a lack of participation in daily activities (9). Compared to unaffected peers, adolescents and young women with diagnosed endometriosis reported significantly worse quality of life (10). More and earlier clinical diagnoses and an early start with treatment are important, especially in the young collective, and could possibly prevent chronic pain disorders and reduce the

negative impact of endometriosis on the quality of life of young women. To improve early diagnosis, a deeper understanding of the symptoms of young patients with endometriosis is required. This study aimed to compare types of symptoms and symptom severity by age.

Methods

This study is a monocentric cohort study. Data were collected prospectively and analyzed retrospectively. The database included all consultations in the certified endometriosis center of the Bern University Hospital with informed consent from January 2017 to December 2020.

All patients with a diagnosis of endometriosis (either clinically suspected, or diagnosed by examination and imaging, or confirmed by surgery) were included.

Clinical data were obtained from the hospital's internal database, collected prospectively and systematically (done as part of the certification of the center). The database included Visual Analog Scale (VAS) scores for the different types of pain (non-cyclic pelvic pain, dysmenorrhea, dyschezia, dysuria, and dyspareunia), reason for the consultation, current hormonal treatment, past surgery, examination findings, suspicion of endometriosis, recommended measures, and past pregnancies or births. The women rated the severity of their symptoms over the 4 weeks prior to the consultation using VAS scores, from 0 (no pain) to 10 (worst possible pain).

To establish a clean cohort, we selected all patients coming for the first time to the certified endometriosis center of Bern University Hospital, where the diagnosis of endometriosis was made. In this certified endometriosis center, patients are either referred to by general gynecologist due to complex cases or also patients that seek a specialists by there own.

The patient collective was divided into 2 groups according to age: (1) patients 24 years old or younger; and (2) patients 25 years old or older. We compared the types of symptoms of the 2 groups and analyzed whether or not there was a difference in the severity of the symptoms.

The same analysis was conducted for all patients with no hormonal treatment at the time of the first consultation.

A detailed analysis of the clinical parameters of the young collective was conducted. The data required for this purpose were collected retrospectively. We analyzed the women's medical histories (past surgeries, diagnostics, and type of endometriosis).

The primary outcome was a difference in the severity of the symptoms between the 2 age groups, with and without hormonal treatment. The secondary outcome was a descriptive analysis of the younger patient collective.

For this research, ethics approval was obtained from the Ethics Commission of the Canton of Bern, Switzerland (reference number: 2020-00937)

Statistics

The statistical analysis was performed using IBM SPSS Statistics (version 25.0). For patient and clinical data analyses, basic descriptive statistics were applied. To compare the characteristics between the groups, a chi-square test and ANOVA were used. A non-parametric test was used for variables not meeting the assumptions of the t-test equivalent. All tests were two-sided and *P* values were considered statistically significant when $< .05$.

Results

A total of 2583 consultations were analyzed. After the inclusion and exclusion criteria were applied, 826 women who had their first consultation at the certified endometriosis center and were diagnosed with endometriosis were included in the study (Figure 1). Patient characteristics are summarized in Table 1. The median age was 32.17 years (15-53 years) at the time of the first consultation. One hundred and forty-four (17.4%) patients were 24 years old or younger, whereas 682 (82.6%) were 25 years old or older. In 675 patients (81.7%), VAS scores were documented. Of the young women, 92.4% ($n = 133$) visited the endometriosis center because of pain. In the older collective, pain was the reason for consultation in only 69.9% ($n = 477$) of the patients. Other common reasons for consultation in the older collective were diagnostic findings ($n = 58$, 8.5%), infertility ($n = 51$, 7.4%) or second opinions ($n = 32$, 4.7%). Diagnosis was surgically confirmed in 45.0% ($n = 372$) of the

patients; the other 55.0% (n =454) had a clinical diagnosis of endometriosis. The diagnosis endometriosis was given, if the patient had the typical symptoms and/or findings in the gynecological examination including ultrasound and in some cases also an MRI. This is explicitly recommended for adolescent in the 2022 ESHRE guidelines.

A total of 489 women were not undergoing hormonal treatment at the time of the first consultation. In 39.6% (n =327) of the cases, hormonal therapy was initiated after the first consultation. In 23.4% (n =193) of the cases, surgery was recommended.

Table 2 shows the comparison of the VAS scores of the patients consulting the endometriosis center for the first time. Young patients had significantly higher pain scores for dysmenorrhea (VAS 7.3 vs. VAS 6.6, $p = 0.015$), dyspareunia (VAS 4.6 vs. VAS 3.4, $p = 0.001$), and non-cyclic pelvic pain (VAS 4.3 vs. 3.7, $p = 0.032$) (Figure 2a). The other VAS scores for dysuria and dyschezia were also slightly higher in the younger collective, but the difference was not statistically significant.

In Table 2, we also compare all patients at the first consultation without any prior hormonal treatment (N=489). Sixty-eight (13.9%) of these patients belong to the younger collective and 421 (86.1%) belong to the older collective. The younger patients had significantly higher VAS scores for dysmenorrhea (VAS 8.1 vs. 7.1, $p = 0.001$) and dyspareunia (VAS 4.8 vs. 3.3, $p = 0.002$) compared to the older collective (Figure 2b). VAS scores for dysuria, dyschezia, and non-cyclic pelvic pain were slightly higher in the younger collective, but the difference was not statistically significant.

The focus of our study stands on the young patients with endometriosis, which is why the cohort of the young women with endometriosis n=144 was analyzed in more detail.

The youngest patient in this collective was 15 years old at the time of the first consultation. In the first consultations of the young women, hormonal treatment was initiated or continued in 123 (85.4%) women. Of these young patients, 36.8% (n = 53) had a minimum of 1 surgery; 31 already had undergone an operation prior to the first consultation in the certified endometriosis center. In 22 patients, surgery was recommended and carried out. In 34 young

patients, the revised American Society for Reproductive Medicine (rASRM) score was recorded: 21 (61.8%) patients had a score of I, 5 (14.7%) patients had a score of II, 6 (17.6%) patients had a score of III, and 2 (5.9%) patients had a score of IV.

Looking at the type of endometriosis clinically, we saw the following distribution diagnosed by sonography, MRI, or/and confirmed by surgery: 21 of the 144 young women were diagnosed with deep infiltrating endometriosis; in 16 patients, the deep infiltrating endometriosis was diagnosed by MRI or surgery, and in 5 patients the diagnosis was provided by clinical and sonographic examination (for these 5 patients no further diagnostic was needed, and no surgery was performed). A total of 38 young patients (26.4%) had adenomyosis diagnosed by sonography or MRI. Thirteen (9%) young women had ovarian endometriosis diagnosed by MRI or by sonography.

Three of the young women had already been pregnant at least once; all 3 had at least one abortion.

Deeper Analysis of the Young Cohort

Comparison of the symptoms presented at the first consultation with the different forms of endometriosis in the young collective revealed a significant difference in only two categories of symptoms (Table 3). We found that young women with adenomyosis reported significantly higher VAS scores for dysuria (2.5 vs. 1.7, $p = 0.031$) compared with the young women with other forms of endometriosis. The young women with an earlier stage of endometriosis (rASRM stages I or II) reported significantly higher VAS scores for dyspareunia (5.1 vs. 1.6, $P = 0.018$) compared to the young women with a severe stage of endometriosis (rASRM stage III or rASRM stage IV).

Discussion

The primary finding of this study is a difference in the severity of the symptoms between the 2 age groups, both with and without hormonal treatment. The secondary outcome was a descriptive analysis of the young patient group.

Research focusing on the adolescent population is rare. A large survey demonstrated that young girls often begin to suffer from endometriosis in their adolescence, with 70% of the patients reporting symptoms before age 20 and nearly 40% before age 15 (11). Indirect evidence gathered by the ACOG in 2005 suggests widespread occurrence of endometriosis in adolescence, since in approximately 60% of adult patients with endometriosis, symptoms had already started before 20 years of age (12).

However, since early identification and treatment of endometriosis may help resolve pain, prevent disease progression and organ damage, and preserve fertility (13), we should pursue the diagnosis of endometriosis in adolescent girls and women.

Given the lack of non-invasive diagnostic tests, symptoms present in adolescent females are probably the most reliable predictors of endometriosis.

According to a review by Chapron et al. (14), the main signs of endometriosis in young women are prolonged use of non-steroidal, anti-inflammatory drugs, family history of endometriosis, frequent absenteeism from school or work during menstruation, and prescription of combined contraceptives before 18 years of age to treat severe primary dysmenorrhea.

In this study, we found that younger patients came to the endometriosis center with significantly higher VAS scores for dysmenorrhea, dyspareunia, and non-cyclic pelvic pain, compared to the older collective. Many studies demonstrate that the severity of a case of endometriosis does not correlate with the pain severity; however, there seems to be an age difference factor that has not been documented this clearly before. The question is whether the endometriosis itself is different in younger age or whether it is due to the pain perception in younger women. Moreover, if young women have so much pain, why is it still considered

normal by family doctors or even specialists? Possible reasons for the delay in diagnosis are ignorance of pain as a possible sign of endometriosis in adolescent women and the lack of knowledge and experience of the adolescents themselves, not knowing how to advocate for their own diagnosis and treatment. Di Vasta et al. (15) assumed that delays frequently occurred between the presentation of symptoms to a clinician and the referral to a gynecologist, often including visits with non-gynecologic specialists and misdiagnoses. Greene et al. (4) noticed that adolescents with pelvic pain may present a diagnostic challenge, because they describe non-cyclic pain as well as cyclic pain and may present with an array of confounding symptoms. This cross-sectional study of 4746 women showed that girls with onset of symptoms in adolescence were significantly more often told nothing was wrong, compared to those whose symptoms began when they were adults. More than half of the respondents (59.6%) reported that they were not taken seriously by their physicians overall, and each step of the diagnostic process took longer for the adolescent-onset group. Therefore, we can postulate that dysmenorrhea may have a bigger impact in adolescent women: a higher pain level than in the older collective. If a possible delay in diagnosis and possible under treatment once a diagnosis has been established lead to a higher pain level, the consequences can have a high impact on the course of the disease.

The significantly higher pain scores for dyspareunia in adolescent girls compared to the older patient collective should also be discussed. Dyspareunia is an important indicator of possible endometriosis. In the study of Martire et al. (16), dyspareunia reached a prevalence of 33% for all forms of endometriosis, 25% for deep-infiltrating endometriosis and endometriomas, and 12.5% for adenomyosis. Many adult women with endometriosis experience pain during intercourse or in the 24 hours following penetrative sex. Schneider et al. (17) found that young adults with endometriosis were nearly twice as likely to experience dyspareunia (79%) than controls without known endometriosis (40%). The prevalence of dyspareunia in adolescent and young adult women was high, with over three quarters of participants in their sample experiencing pain from sexual intercourse. A longitudinal cohort study highlighted

that the impact of dyspareunia on both relationships and social functioning during adolescence and young adulthood could be particularly distressing and impact negatively self-image as well as overall health (17). Pain during sexual intercourse may confer a great additional burden, beyond other symptoms.

However, dyspareunia does not appear to be an uncommon symptom of adolescent girls including those without diagnosed endometriosis. Landry et al. (18) found that dyspareunia was reported by 1 in 5 girls in a cross-sectional study within a large adolescent sample. The dyspareunia reported was mostly primary chronic (6 months or more) and at the vaginal opening.

Acyclic pain seems to be more common in adolescents than in adults (6). In our study, non-cyclic pelvic pain was also significantly higher in the adolescent group compared to the adults.

Similar results regarding the degree of pain were found in the cross-sectional study of Di Vasta and colleagues (15). They also compared symptoms of endometriosis in surgically diagnosed adolescent and adult women. Most participants (93%) experienced moderate menstrual (pain usually requiring medication) to severe menstrual pain (pain requiring medications and bed rest), without an appreciable difference between the age groups. They concluded that pelvic pain could be severe already at a young age: one-half of those diagnosed as adolescents reported pain starting with their very first period, compared to one third of adults, which has a great negative impact on the quality of life.

According to the literature, women with a history of early dysmenorrhea are more likely to have and to develop endometriosis than women who never or rarely experienced pain during menstruation; the risk even increases with the amount of reported pain (19,20). The fact that the pain level does not correlate with the severity of the endometriosis (rASRM stage) is known and is also reflected in our analysis on the forms of endometriosis in the young (3,21).

We explored whether there was any correlation in our collective between symptoms and the type of endometriosis. We found that young women with adenomyosis reported significantly higher VAS scores for dysuria compared to the young women with other forms of endometriosis, and 21 (14.6%) of the 144 young women had a diagnosis of deep infiltrating endometriosis. Deep infiltrating endometriosis or an advanced stage of the disease (rASRM III or IV) can be detected already in young women. This is in line with previously published articles (22–24). Vicino et al. (25) found no difference in stages of surgically treated endometriosis between adolescents aged 18 years and younger compared to patients 19 years old or older, while the two groups showed severe endometriosis in 75% and 66% of cases respectively. He concluded that even in adolescence, the risk of severe endometriosis needs to be taken into account. The analysis of our young cohort, with clinically diagnosed deep infiltrating endometriosis, confirms this statement.

In young women in our cohort, significantly fewer surgeries were performed or were recommended. However, 21.5% of our adolescents had a surgically confirmed diagnosis (including cases before the first consultation) already at this young age. The 2022 ESHRE guidelines recommend that the diagnosis of endometriosis and an empirical treatment should be given when clinical signs are clear enough, without a prior diagnostic laparoscopy (26). An accurate clinical and imaging evaluation can be much more effective, along with its being noninvasive for the patient, allowing both early diagnosis and adequate clinical management, with surgery justified only for intractable cases (16).

Limitations of our study are that data, especially for certification, were collected prospectively, while findings such as information from endometriosis forms and other clinical data were added retrospectively. Due to the different age range, the numbers between the 2 groups (older and younger) differ and therefore do not represent two similar cohorts.

A major strength of the study is that we obtained VAS scores directly from the patients, however, further detailed description of the pain experienced, pain timeline, and pain altering diagnosis, such as psychiatric disease etc., are not evaluated.

Another major strength of this study is that it is the first study, to our knowledge, that compares, using VAS scores, symptoms of adolescents with symptoms of adults; this is important to understand the degree of suffering even at a young age.

Conclusions

Young patients with clinically diagnosed endometriosis have significantly higher dysmenorrhea and dyspareunia pain levels than older patients. By acknowledging and understanding this, early diagnosis and adequate treatment can be promoted.

Dyspareunia in adolescents in particular merits clinical attention and further research. Dyspareunia remains greatly under investigated, especially in the adolescent population, where sexual activity generally first occurs.

Endometriosis in young women presents more often with non-cyclic pelvic pain. This finding is important, because it makes the diagnosis of endometriosis more challenging and possibly could be a risk factor for the development of chronic pelvic pain.

Conflict of interest

Author 1: nothing to disclose

Author 2: nothing to disclose

Author 3: nothing to disclose

Author 4: Grants or contracts from any entity:

- foundation for clinical-experimental cancer research: Grant for DESI and for ctDNA
- SAKK/Dr. Paul Janssen Fellowship for ctDN
- SNF exchange for ctDNA

Author 5: nothing to disclose

Author 6: nothing to disclose

Author 7: nothing to disclose

Author 8: Consulting fees:

- Bayer

Participation on a Data Safety Monitoring Board or Advisory Board:

- MSD 2020

References

1. Shafir AL, Farland L V., Shah DK, Harris HR, Kvaskoff M, Zondervan K, et al. Risk for and consequences of endometriosis: A critical epidemiologic review. *Best Pract Res Clin Obstet Gynaecol* [Internet]. 2018;51:1–15. Available from: <https://doi.org/10.1016/j.bpobgyn.2018.06.001>
2. Sieberg CB, Lunde CE, Borsook D. Endometriosis and pain in the adolescent- striking early to limit suffering: A narrative review. *Neurosci Biobehav Rev* [Internet]. 2020;108(August 2019):866–76. Available from: <https://doi.org/10.1016/j.neubiorev.2019.12.004>
3. Zondervan K. Review Article: Endometriosis. *N Engl J Med*. 2020;382(3):1244–56.
4. Greene R, Stratton P, Cleary SD, Ballweg M Lou, Sinaii N. Diagnostic experience among 4,334 women reporting surgically diagnosed endometriosis. *Fertil Steril* [Internet]. 2009;91(1):32–9. Available from: <http://dx.doi.org/10.1016/j.fertnstert.2007.11.020>
5. Ballweg M Lou. Big picture of endometriosis helps provide guidance on approach to teens: Comparative historical data show endo starting younger, is more severe. *J Pediatr Adolesc Gynecol*. 2003;16(3 SUPPL.):21–6.
6. Yeung P, Gupta S, Gieg S. Endometriosis in adolescents: A systematic review. *J Endometr Pelvic Pain Disord*. 2017;9(1):17–29.
7. Saridoğan E. Adolescent endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2017;209:46–9.
8. Gerancher KR. Acog committee opinion. *Obstet Gynecol*. 2018;132(760):249–58.
9. Stuparich MA, Donnellan NM, Sanfilippo JS. Endometriosis in the Adolescent Patient. *Semin Reprod Med*. 2017;35(1):102–9.
10. Gallagher JS, DiVasta AD, Vitonis AF, Sarda V, Laufer MR, Missmer SA. The Impact of Endometriosis on Quality of Life in Adolescents. *J Adolesc Heal* [Internet]. 2018;63(6):766–72. Available from: <https://doi.org/10.1016/j.jadohealth.2018.06.027>
11. Sinaii N, Cleary SD, Ballweg ML, Nieman LK, Stratton P. High rates of autoimmune and endocrine disorders, fibromyalgia, chronic fatigue syndrome and atopic diseases among women with endometriosis: A survey analysis. *Hum Reprod*. 2002;17(10):2715–24.
12. Gerancher KR. ACOG Committee Opinion #309. *Obstet Gynecol*. 2005;105(2):453–4.
13. Laufer MR. Current approaches to optimizing the treatment of endometriosis in adolescents. *Gynecol Obstet Invest*. 2008;66(SUPPL. 1):19–27.
14. Chapron C, Lafay-Pillet MC, Monceau E, Borghese B, Ngô C, Souza C, et al. Questioning patients about their adolescent history can identify markers associated with deep infiltrating endometriosis. *Fertil Steril*. 2011;95(3):877–81.
15. DiVasta AD, Vitonis AF, Laufer MR, Missmer SA. Spectrum of symptoms in women diagnosed with endometriosis during adolescence vs adulthood. *Am J Obstet Gynecol* [Internet]. 2018;218(3):324.e1-324.e11. Available from: <https://doi.org/10.1016/j.ajog.2017.12.007>
16. Martire FG, Lazzeri L, Conway F, Siciliano T, Pietropolli A, Piccione E, et al. Adolescence and endometriosis: symptoms, ultrasound signs and early diagnosis. *Fertil Steril* [Internet]. 2020;114(5):1049–57. Available from:

<https://doi.org/10.1016/j.fertnstert.2020.06.012>

17. Schneider MP, Vitonis AF, Fadayomi AB, Charlton BM, Missmer SA, DiVasta AD. Quality of Life in Adolescent and Young Adult Women With Dyspareunia and Endometriosis. *J Adolesc Heal* [Internet]. 2020;67(4):557–61. Available from: <https://doi.org/10.1016/j.jadohealth.2020.02.024>
18. Landry T, Bergeron S. Biopsychosocial factors associated with dyspareunia in a community sample of adolescent girls. *Arch Sex Behav*. 2011;40(5):877–89.
19. Fauconnier A, Chapron C. Endometriosis and pelvic pain: Epidemiological evidence of the relationship and implications. *Hum Reprod Update*. 2005;11(6):595–606.
20. Treloar SA, Bell TA, Nagle CM, Purdie DM, Green AC. Early menstrual characteristics associated with subsequent diagnosis of endometriosis. *Am J Obstet Gynecol* [Internet]. 2010;202(6):534.e1-534.e6. Available from: <http://dx.doi.org/10.1016/j.ajog.2009.10.857>
21. Johnson NP, Hummelshoj L, Adamson GD, Keckstein J, Taylor HS, Abrao MS, et al. World endometriosis society consensus on the classification of endometriosis. *Hum Reprod*. 2017;32(2):315–24.
22. Dun EC, Kho KA, Morozov V V., Kearney S, Zurawin JL, Nezhat CH. Endometriosis in adolescents. *J Soc Laparoendosc Surg*. 2015;19(2).
23. Smorgick N, As-Sanie S, Marsh CA, Smith YR, Quint EH. Advanced Stage Endometriosis in Adolescents and Young Women. *J Pediatr Adolesc Gynecol* [Internet]. 2014;27(6):320–3. Available from: <http://dx.doi.org/10.1016/j.jpag.2013.12.010>
24. Audebert A, Lecointre L, Afors K, Koch A, Wattiez A, Akladios C. Adolescent endometriosis: Report of a series of 55 cases with a focus on clinical presentation and long-term issues. *J Minim Invasive Gynecol* [Internet]. 2015;22(5):834–40. Available from: <http://dx.doi.org/10.1016/j.jmig.2015.04.001>
25. Vicino M, Parazzini F, Cipriani S, Frontino G. Endometriosis in young women: The experience of GISE. *J Pediatr Adolesc Gynecol* [Internet]. 2010;23(4):223–5. Available from: <http://dx.doi.org/10.1016/j.jpag.2009.12.002>
26. Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, et al. ESHRE guideline: endometriosis. *Hum Reprod Open*. 2022;1–26.

Figure and Table Legend

Figure 1: Flowchart of the study cohort, shows the inclusion and exclusion criteria

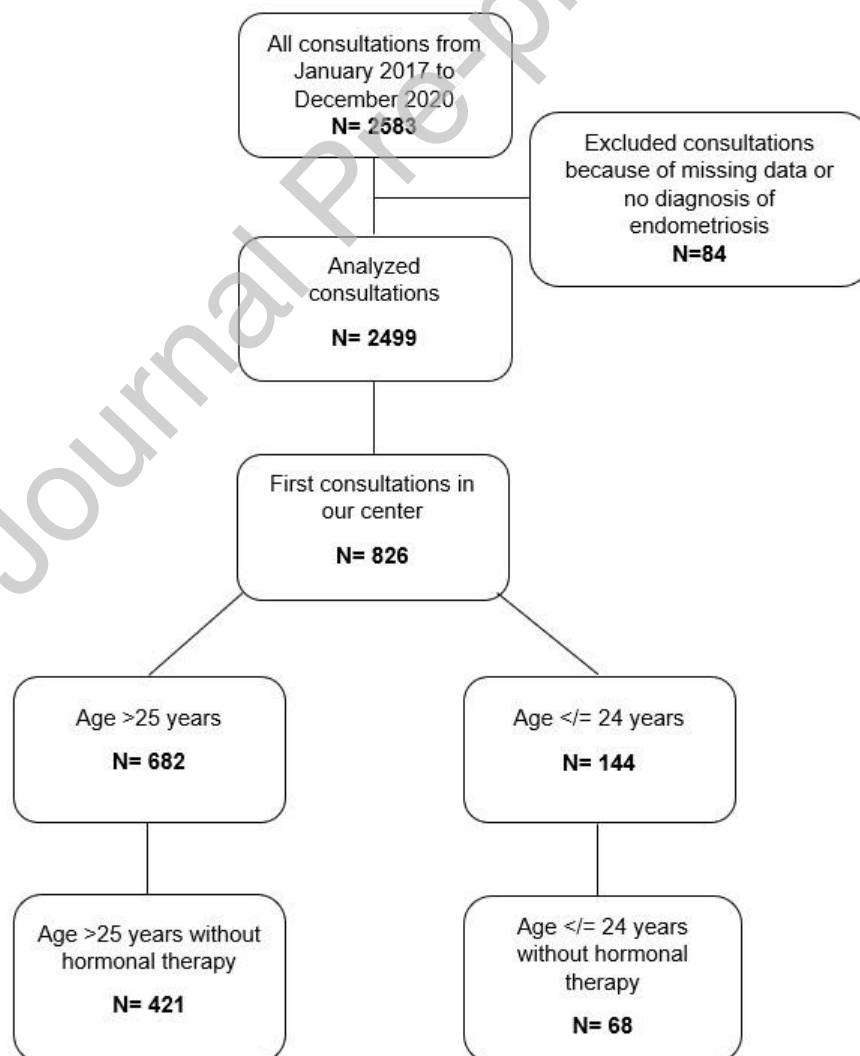
Table 1: Patient characteristics (diagnosis and therapy, pregnancy status, and history of reproductive medicine) comparing the two different age groups

Table 2: Comparison of the VAS scores of the patients consulting the endometriosis center for the first time with and without hormonal treatment

Figure 2a: Comparison of the VAS scores for dysmenorrhea, non-cyclic pelvic pain, and dyspareunia in the younger (aged ≤ 24 years old) and in the older collective (aged >24 years old) for all first consultations

Figure 2b: Comparison of the VAS scores for dysmenorrhea and dyspareunia in the younger (aged ≤ 24 years old) and in the older collective (aged >24 years old) for the first consultations without hormonal treatment

Table 3: Comparison the different forms of endometriosis and the VAS scores in the young collective (aged ≤ 24 years old)



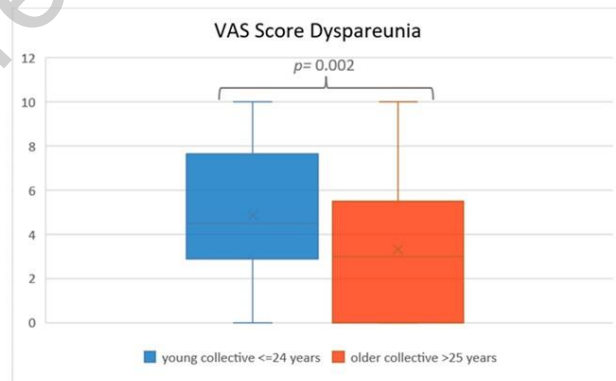
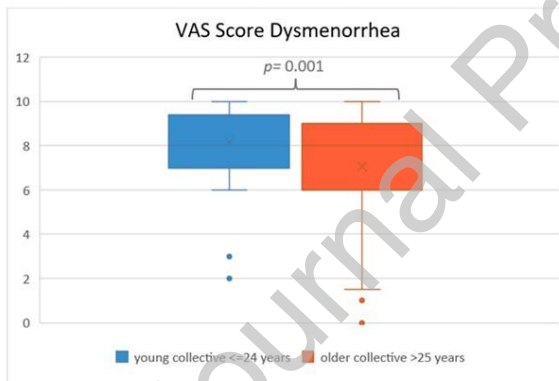
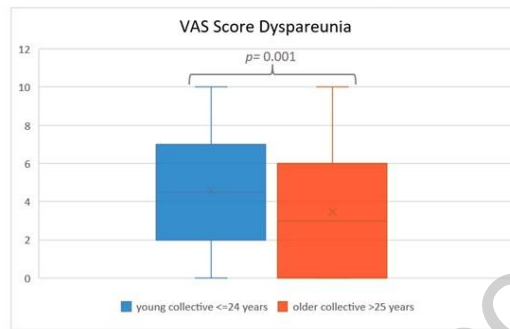
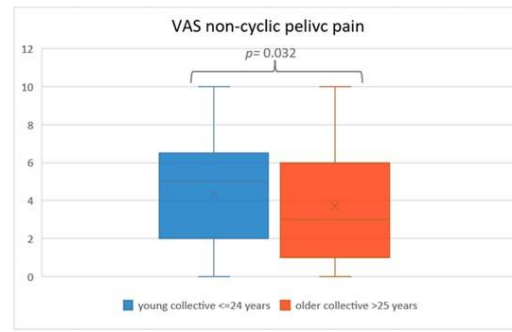
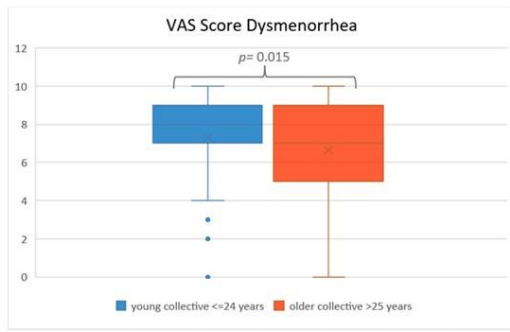


Table 1: Patient characteristics

	Total N= 826	Age <= 24 years N= 144	Age >=25 years N= 682	p-value
Diagnosis and therapy				
Clinically confirmed diagnoses	816	144 (100.0%)	672 (98.5%)	p = 0.144
Non-clinical diagnosis	10	0 (0.0%)	10 (1.5%)	
Diagnosis Total	826	144	682	
Surgically confirmed diagnoses	372	31 (21.5%)	341 (50.0%)	p = 0.000
No surgery	454	113 (78.5%)	341 (50.0%)	
Surgery recommended	193	22 (15.3%)	171 (25.1%)	p = 0.001
No surgery recommended	633	122 (84.7%)	511 (74.9%)	
Start with hormonal treatment	327	79 (54.9%)	248 (36.4%)	p = 0.000
No changes of the hormonal therapy	499	65 (45.1%)	434 (63.6%)	
Pregnancy status				
Gravida>0	224/769	3 (2.2%)	221 (34.9%)	p = 0.000
G0	545/769	132 (97.8%)	413 (65.1%)	
Para>0	177/768	0 (0.0%)	177 (28.0%)	p = 0.000
P0	591/768	135 (100.0%)	456 (72.0%)	
Abort>0	92/767	3 (2.2%)	89 (14.1%)	p = 0.000
A0	675/767	132 (97.8%)	543 (85.9%)	
Current desire for pregnancy	167/744	2 (1.6%)	165 (26.8%)	p = 0.000
No current pregnancy desire	577/744	127 (98.4%)	450 (73.2%)	
Currently infertility >12 months	107/742	1 (0.8%)	106 (17.3%)	p = 0.000
No infertility	635/742	128 (99.2%)	507 (82.7%)	
History of reproductive medicine				
Reproduction medicine performed	55	1 (1.0%)	54 (13.8%)	p = 0.000
No reproduction medicine performed	436	98 (99.0%)	338 (86.2%)	
(Total) Missing	(491) 335	(99) 45	(392) 290	

Table 2: Comparing VAS Scores

All patients coming for their first consultation N= 675			
VAS dysmenorrhea	Age <=24 years	7.3 (SD=2.6, CI 6.8 – 7.8)	p = 0.015
	Age >=25 years	6.6 (SD=2.7, CI 6.4 – 6.9)	
VAS non-cyclic pelvic pain	Age <=24 years	4.3 (SD=2.8, CI 3.8 – 4.8)	p = 0.032
	Age >=25 years	3.7 (SD=2.8, CI 3.5 – 4.0)	
VAS dyschezia	Age <=24 years	3.0 (SD=2.9, CI 2.4 – 3.5)	p = 0.474
	Age >=25 years	2.7 (SD=3.0, CI 2.5 – 3.0)	
VAS dysuria	Age <=24 years	1.7 (SD=2.6, CI 1.2 – 2.2)	p = 0.668
	Age >=25 years	1.6 (SD=2.5, CI 1.4 – 1.8)	
VAS dyspareunia	Age <=24 years	4.6 (SD=3.2, CI 4.0 – 5.2)	p = 0.001
	Age >=25 years	3.4 (SD=3.0, CI 3.2 – 3.7)	
Patients without hormonal treatment by the first consultation N=489			
VAS dysmenorrhea	Age <=24 years	8.1 (SD=1.8, CI 7.7 – 8.6)	p = 0.001
	Age >=25 years	7.0 (SD=2.3, CI 6.8 – 7.3)	
VAS non-cyclic pelvic pain	Age <=24 years	4.2 (SD=2.9, CI 3.4 – 4.9)	p = 0.066
	Age >=25 years	3.5 (SD=2.7, CI 3.2 – 3.7)	
VAS dyschezia	Age <=24 years	3.0 (SD=2.8, CI 2.2 – 3.7)	p = 0.432
	Age >=25 years	2.6 (SD=2.9, CI 2.3 – 2.9)	
VAS dysuria	Age <=24 years	1.7 (SD=2.6, CI 1.0 – 2.4)	p = 0.428
	Age >=25 years	1.4 (SD=2.4, CI 1.2 – 1.7)	
VAS dyspareunia	Age <=24 years	4.8 (SD=3.1, CI 3.9 – 5.8)	p = 0.002
	Age >=25 years	3.3 (SD=2.9, CI 3.0 – 3.6)	

Table 3: Forms of Endometriosis in the young collective (age ≤ 24 years)

	VAS dysmenorrhea	VAS non- cyclic pelvic pain	VAS dyschezia	VAS dysuria	VAS dyspareunia
Total N=144					
Deep infiltrating endometriosis N=21	7.3 (SD= 3.2, CI 5.8 – 8.7, <i>p</i> = 0.917)	5.0 (SD= 2.8, CI 3.6 – 6.3, <i>p</i> = 0.277)	3.7 (SD= 2.9, CI 2.3 – 5.1, <i>p</i> = 0.232)	2.3 (SD= 2.6, CI 1.0 – 3.5, <i>p</i> = 0.293)	5.0 (SD= 3.7, CI 3.2 – 6.8, <i>p</i> = 0.553)
Ovarian endometriosis N=13	6.6 (SD= 2.4, CI 4.8 – 8.4, <i>p</i> = 0.398)	4.0 (SD= 3.1, CI 1.8 – 6.2, <i>p</i> = 0.712)	2.0 (SD= 3.2, CI -.37 – 4.3, <i>p</i> = 0.244)	2.2 (SD= 3.0, CI 0.02 – 4.3, <i>p</i> = 0.558)	3.0 (SD= 3.7, CI 0.3 – 5.7, <i>p</i> = 0.100)
Adenomyosis N=38	7.6 (SD= 1.9, CI 7.0 – 8.3, <i>p</i> = 0.378)	4.4 (SD= 3.0, CI 3.4 – 5.5, <i>p</i> = 0.782)	3.3 (SD= 2.9, CI 2.3 – 4.3, <i>p</i> = 0.443)	2.5 (SD= 3.1, CI 1.4 – 3.7 <i>p</i> = 0.031)	5.1 (SD= 3.1, CI 3.9 – 6.4 <i>p</i> = 0.318)
rASF °I and °II N=26	6.9 (SD= 3.1, CI 5.5 – 8.2)	5.5 (SD= 2.8, CI 4.3 – 6.7)	3.1 (SD= 2.5, CI 2.0 – 4.2)	1.3 (SD= 2.0, CI .448 – 2.2)	5.1 (SD= 3.5, CI 3.3 – 6.8)
rASF °III and °IV N=8	6.1 (SD= 3.2, CI 3.2 – 9.1, <i>p</i> = 0.595)	3.8 (SD= 2.5, CI 1.7 – 5.8, <i>p</i> = 0.136)	2.5 (SD= 3.6, CI -.54 – 5.5, <i>p</i> = 0.605)	1.4 (SD= 2.7, CI -.79 – 3.7, <i>p</i> = 0.882)	1.6 (SD= 2.3, CI -.27 – 3.5, <i>p</i> = 0.018)