



## Cohort Study

# Prevalence of adenomyosis in women undergoing hysterectomy for abnormal uterine bleeding, pelvic pain or uterine prolapse – A retrospective cohort study

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## ABSTRACT

**Background:** Adenomyosis can cause symptoms like dysmenorrhea, dyspareunia, pelvic pain and bleeding disorders and is related to subfertility and obstetrical complications. The disease is probably underestimated and underdiagnosed because of difficulties in reliable clinical examination and imaging results. The age-related prevalence of adenomyosis still remains unclear. In this retrospective analysis we describe the rate of adenomyosis in two independent cohorts of patients undergoing hysterectomy for benign diseases (2011–2013 and 2015–2018) and its correlation to presurgical symptoms respectively indications for hysterectomy.

**Materials and methods:** All surgeries have been performed in the same department of minimally invasive gynecological surgery by a total of two experienced surgeons following a surgical internal standard for the indication bleeding disorder, dysmenorrhea. We analyzed the overall rate of patients with adenomyosis in both cohorts and related the histological presence of adenomyosis to presurgical symptoms. We also analyzed a subgroup of postmenopausal patients with uterine prolapse.

**Results:** In 307 patients we detected 42.0% of cases with histologically proven adenomyosis. In the group of patients with bleeding disorders and dysmenorrhea as indication for surgery we found the highest rate of adenomyosis (59.3%, cohort 1). 81.1% patients with adenomyosis (cohort 1) reported symptoms. In the subgroup of 42 postmenopausal patients, we found 23.8% of cases with adenomyosis.

**Conclusion:** Our data shows that a positive anamnesis regarding the symptoms bleeding disorders and dysmenorrhea is suspicious for adenomyosis. In hysterectomy specimen adenomyosis can be found in more than 40%. The role of adenomyosis-related symptoms requires further investigation, especially in adolescent and postmenopausal patients.

## 1. Introduction

Adenomyosis affects the central reproductive organ in the central female pelvis, has an important impact on women's health in reproductive age and can also cause symptoms or irregular imaging findings in postmenopausal women, especially when they are under hormone replacement therapy or endocrine treatment for breast cancer (Tamoxifen). Most of the patients with adenomyosis are symptomatic [1]. Typical symptoms in adenomyosis are dysmenorrhea, bleeding disorders, dyspareunia and pelvic pain. Adenomyosis can have a negative impact on fertility. It is related to higher abortion rates, reduced pregnancy rates and reduced birth rates, the success rate in assisted

reproduction is lower in patients with adenomyosis [2–7]. Adenomyosis can also be the cause for obstetrical complications like premature birth, rupture of membrane, uterine rupture and postpartum hemorrhage [8–10]. With the combination of anamnesis, clinical examination and imaging (transvaginal ultrasound and/or MRI) adenomyosis can be diagnosed and included to the treatment of patients with endometriosis [11,12]. The first diagnostic step is a complete and comprehensive anamnesis, as adenomyosis is related to typical symptoms. Adenomyosis might also be the reason for persistent symptoms after surgical interventions for peritoneal and deep endometriosis [13], as in almost 50% of deep endometriosis an additional adenomyosis can be found [14]. Various typical ultrasound patterns in adenomyosis have been

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reported in the last years: subendometrial microcysts, myometrial cysts, question mark sign, heterogenous myometrium, uterine asymmetry, hyperechoic myometrial lesions, subendometrial thickening, disruption of the junctional zone, subendometrial linear striae and uterine enlargement [15]. It remains unclear which of these ultrasound signs have the highest importance and if a certain combination of ultrasound signs is related to a reliable prediction of adenomyosis. In a 10-year meta-analysis the pooled sensitivity (83.8%) and pooled specificity (63.9%) showed a good accuracy of the transvaginal ultrasound in the hands of the skilled examiner [16]. Additional sonographic techniques like doppler-ultrasound, elastography and 3D transvaginal ultrasound can enhance the diagnostic reliability [17,18]. These diagnostic criteria might be missing in adolescents and young women [19,20]. In order to differentiate focal and diffuse adenomyosis and to presurgically localize and measure the affected uterine tissue, MR imaging is a potential diagnostic tool with high accuracy [21]. The most important diagnostic sign in MR imaging seems to be the irregularity of the junctional zone [22], followed by focal or diffuse thickening of the junctional zone, a JZ (max) to myometrial thickness ratio >40%, areas of myometrial low-signal-intensity and high-signal-intensity spots in the T2-weighted technique [23–25]. Transvaginal, hysteroscopic and laparoscopic biopsy techniques can help to determine the diagnosis by obtaining a histological proof [26]. However, the prevalence of this important benign disease is not yet known exactly. The few available data report the incidence of adenomyosis in hysterectomy specimen. In our analysis we describe the prevalence in hysterectomy specimen and relate the results to the presurgical indication and age including postmenopausal patients.

## 2. Aim of the study

To describe the prevalence of adenomyosis in hysterectomy specimen in patients with benign symptomatic diseases and its relation to the respective indication for hysterectomy.

## 3. Material and methods

All surgeries have been carried out by three skilled gynecological surgeons following the same internal standard procedures in a department of gynecology in a German public hospital. In both cohorts, all patients signed an informed consent. Cohort 1 included total laparoscopic hysterectomies, laparoscopic subtotal hysterectomies, vaginal hysterectomies assisted by laparoscopy and vaginal hysterectomies. Cohort 2 only included laparoscopic supracervical hysterectomies. The work has been reported in line with the STROCCS criteria [27]. The study has been retrospectively registered in Research Registry under the UIN 7619.

<https://www.researchregistry.com/browse-the-registry#home/registrationdetails/62002bb120a3a0001e151e1c/>

### 3.1. Cohort 1

Retrospective single center analysis including 153 laparoscopic hysterectomies in benign uterine pathologies from 2011 to 2013. We included total laparoscopic hysterectomies, laparoscopic subtotal hysterectomies, vaginal hysterectomies assisted by laparoscopy and vaginal hysterectomies. We did not include abdominal hysterectomies as we did not realize any open procedures for benign diseases in that period. We excluded all cases suspicious for uterine malignancy or with histological proven malignancy. All hysterectomy specimen underwent standard pathological examination. We analyzed the incidence of adenomyosis in this cohort by histological proof of adenomyosis by the pathologist. Within the included patients we found one case of occult endometrial cancer in an endometrial hyperplasia related to adenomyosis and one case of endometrial hyperplasia with irregular cells. In this cohort we included patients with the indications bleeding disorders,

dysmenorrhea, the combination of both and we also included patients with hysterectomies for the indication uterine descensus or prolapse in a subgroup of postmenopausal women ( $n = 42$ ). The mean age in this cohort therefore was 54.9 years. The mean uterine weight was 186.9 g (with a minimum weight of 20 g and a maximum weight of 1565 g). The mean duration of the surgical procedure was 109.2 min (Table 1).

### 3.2. Cohort 2

Retrospective single center analysis including 154 laparoscopic supracervical hysterectomies from 2015 to 2018. In this cohort, we included all patients with indication for laparoscopic supracervical hysterectomies for benign pathologies. In this cohort we did not collect the data on indication for hysterectomy. Thus, this analysis is limited to cohort 1. The uterine tissue has been evaluated by our pathological institute. No occult malignancy has been revealed by histological examination.

## 4. Results

In 307 patients who underwent hysterectomy in two independent analysis from 2011 to 2013 (cohort 1) and 2015–2018 (cohort 2) the histological examination revealed a total of 129 cases of adenomyosis (42.0%). The main indication for hysterectomy in both groups have been bleeding disorders without or in combination with dysmenorrhea. The mean age in cohort 1 was higher due to the fact of inclusion of postmenopausal women with the indication of pelvic floor defect (Figs. 1–3).

### 4.1. Cohort 1

In this cohort of 153 patients who underwent hysterectomy for the indications dysmenorrhoea, bleeding disorders, the combination of both and uterine descensus or prolapse we found 53 cases of adenomyosis (53/153) (34.6%). Without the subgroup of patients with the indication uterine descensus or prolapse (postmenopausal patients), adenomyosis was found in 43/111 cases (38.7%). In 40/53 (75.5%) of the patients with adenomyosis an additional uterine myomatosis was diagnosed by histological examination. The mean age of all patients included was 54.9 years (29–88 years). We analyzed the incidence of adenomyosis in relation to the indication for hysterectomy (Table 2). 48.4% of the included patients presented with bleedings disorders as main indication for hysterectomy, while 17.7% presented with bleeding disorders and dysmenorrhea and 6.5% indicated pain as the main symptom. In the subgroup of patients with a combination of both symptoms (bleedings disorders and dysmenorrhea), adenomyosis was diagnosed in 59.3% of cases. Analyzing the symptoms caused by adenomyosis, the data shows that 43/53 (81.1%) patients with adenomyosis were symptomatic, reporting bleeding disorders, dysmenorrhea or a combination of both. Additional endometriosis was found in 11% of the patients with adenomyosis.

### 4.2. Subgroup of hysterectomies with indication “bleeding disorder” ( $n = 74$ )

The mean age in this subgroup was 50.2 years. The mean uterine weight was 272.9 g and the mean surgical time 119.9 min. In most of the patients in this subgroup uterine fibroids were the main pathological finding. Pathology also revealed adenomyosis in 25 patients in this

**Table 1**  
General information on patients of cohort 1 and 2.

Cohort	total number of patients	median age of patients	mean uterine weight	mean surgical time
1	153	54.9 years	186.9 g	109.2 min
2	154	44.5 years	172.8 g	103.5 min

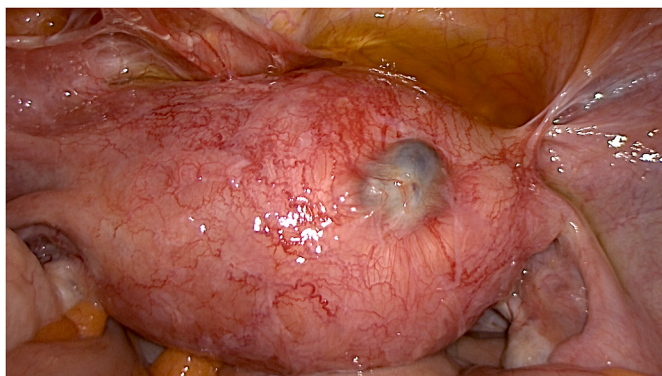


Fig. 1. Laparoscopic appearance of adenomyotic uterus with subserous cystic adenomyosis and hypervascularization.

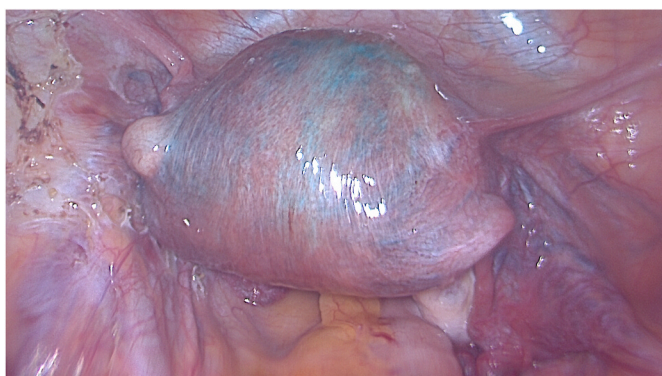


Fig. 2. Laparoscopic blue sign in adenomyosis during test of fallopian tube permeability with blue dye. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

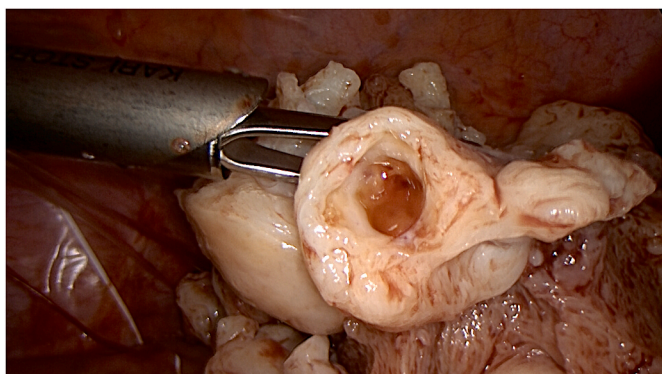


Fig. 3. Adenomyotic uterine tissue during laparoscopic subtotal hysterectomy with laparoscopic in-bag morcellation.

group (25/74) (33.8%). In 23/25 (92.0%) cases of patients with adenomyosis and the symptom bleeding disorder we found additional uterine myomatosis.

**Table 2**  
Indications for hysterectomy in cohort 1 and relation to adenomyosis. N = 153.

	Bleeding disorders	Dysmenorrhea	Bleeding disorders and dysmenorrhea	Uterine deszenus
Indication for hysterectomy	74/153 (48.4%)	10/153 (6.5%)	27/153 (17.7%)	42/153 (27.5%)
Adenomyosis	25/74 (33.8%)	2/10(20.0%)	16/27 (59.3%)	10/42 (23.8%)

4.3. Subgroup of hysterectomies with indication “dysmenorrhea” (n = 10)

The mean age in this subgroup was 48.1 years. The mean uterine weight was 185.7 g and the mean surgical time 126.0 min. Pathology revealed 2 cases of adenomyosis in this group (2/10) (20.0%).

4.4. Subgroup of hysterectomies with indication “bleeding disorder and dysmenorrhea” (n = 27)

The mean age in this subgroup was 47.2 years. The mean uterine weight was 168.9 g and the mean surgical time 98.7 min. Pathology revealed 16 cases of adenomyosis in this group (16/27) (59.3%). In 11/16 (68.8%) cases of adenomyosis in this group we found additional uterine myomatosis.

4.5. Subgroup of hysterectomies with indication “uterine deszenus” (n = 42)

27.5% of the patients in cohort 1 required hysterectomy for pelvic floor defect. The mean age in this subgroup was 68.5 years. All patients in this subgroup were postmenopausal at the moment of surgery. The mean uterine weight was 52.2 g and the mean surgical time 94.5 min. Pathology revealed 10 cases of postmenopausal adenomyosis in this group (10/42) (23.8%).

4.6. Cohort 2

In this cohort of 154 patients who underwent laparoscopic supra-cervical hysterectomy for benign uterine pathologies, the histopathological examination revealed adenomyosis in almost every second patient (76/154; 49.4%) and uterine myomatosis in 68.2% (105/154) of the patients. In 36/76 patients, pathology reported a combination of adenomyosis and uterine myomatosis (47.4%). In 5 patients a disseminated uterine leiomyomatosis was found (3.25%) and in 4 patients any pathology was detected (2.6%). No occult malignant lesions were found in the extracted tissue (0/154).

4.7. Prediction of adenomyosis by presurgical transvaginal ultrasound

In 56/76 patients of cohort 2 we predicted adenomyosis by transvaginal 2D ultrasound examination using the sonographic patterns subendometrial microcysts, myometrial cysts, question mark sign, heterogenous myometrium, uterine asymmetry, hyperechoic myometrial lesions, subendometrial thickening, disrapture of junctional zone, subendometrial linear striae and uterine enlargement. This is a prediction rate of 73.7%. There was no false positive prediction, but 20/76 cases with adenomyosis have not been detected or suspected before surgery (Figs. 4–6).

As the ultrasound prediction of adenomyosis was not the aim of the study group in cohort 2, we cannot present more detailed data on the combination of ultrasound signs in each case. From 2011 to 2013 we did not yet include presurgical transvaginal sonography prediction of adenomyosis to our standard ultrasound protocol.

5. Discussion

Our data shows that the rate of adenomyosis in patients with indication for hysterectomy is high (42%) and that adenomyosis plays an



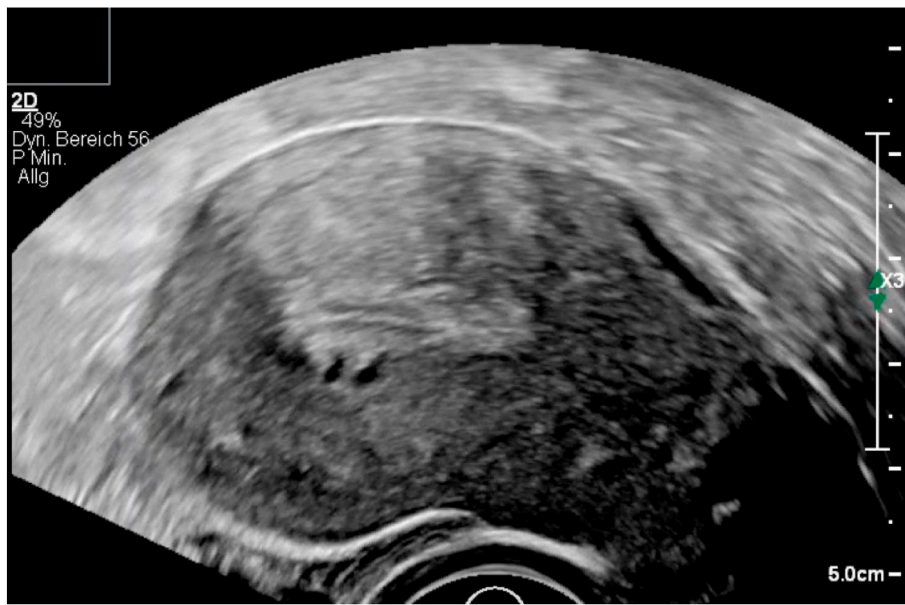


Fig. 4. Transvaginal ultrasound in adenomyotic uterus with subendometrial cysts, hyperechoic spots, irregular myometrium.

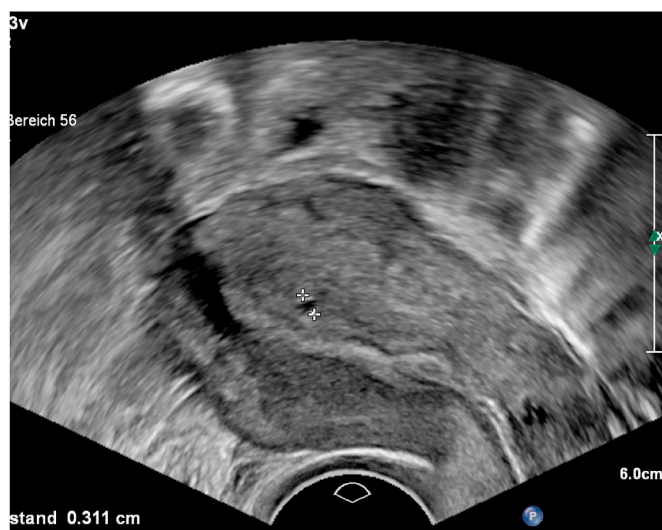


Fig. 5. Subendometrial microcysts in uterus with adenomyosis.



Fig. 6. Myometrial cystic lesion in uterus with adenomyosis.

important role as a factor for uterine symptomatology leading to hysterectomy in women older than 40 years. The rate of adenomyosis is higher in cohort 2 compared to cohort 1. The reason for this difference might be the analyzed surgical approach. Laparoscopic subtotal hysterectomy with laparoscopic in-bag morcellation plays an important role in the treatment of symptomatic adenomyosis in our department. But also in cohort 1, excluding the postmenopausal patients, the rate of histologically proven adenomyosis reaches 38.7%. However, these rates do not represent the overall prevalence of adenomyosis in the female population at fertile age as the factor hysterectomy is a bias per se. In a recent large cohort-study Yu et al. described an overall adenomyosis incidence of 28.9 per 10.000 woman-years. The incidence was highest for women aged 41–45 years [28]. Taking a closer look at the symptoms, our results support the available data. In a retrospective analysis, Chen et al. reported a rate of 71.8% of the patients with adenomyosis having symptoms [29]. Our data shows that approximately 80% of patients (cohort 1) present with symptoms. The combination of bleeding disorders and dysmenorrhea might be a predictor for the presence of

adenomyosis, as in this subgroup the rate of adenomyosis was the highest in this data collection. The probability of presence of adenomyosis in patients with dysmenorrhea, and/or bleeding disorders is higher in comparison to asymptomatic patients. Li et al. recently reported a positive relation of history of cesarian section and dysmenorrhea in patients with adenomyosis [30]. Zannoni et al. described dysmenorrhea and also dyspareunia as risk factors for adenomyosis in young women [31]. Interestingly, the rate of patients with dysmenorrhea alone was relatively low in the present cohorts. A detailed anamnesis considering all typical symptoms of adenomyosis is indispensable and can easily lead to the right diagnostic decisions in order to detect adenomyosis such as transvaginal ultrasound considering the described sonographic patterns. The evaluation of additional symptoms in future studies in patients with adenomyosis like brownish irregular spotting or dyspareunia could be useful. As the biopsy techniques are not reliable enough [26], it will be difficult to design a study on the incidence of adenomyosis in adolescents and women between 20 and 35 years of age, unless a highly sensitive imaging technique is able to detect adenomyosis without a relevant false-positive or false-negative failure rate in

these patient groups. In 2010, Dietrich stated that adenomyosis may be present during adolescence and she concluded that treatment should aim to preserve patients' fertility [32]. Juvenile cystic adenomyotic lesions in adolescents and its surgical and medical treatment has been described in various publications [33–35]. However, the role of adenomyosis in adolescents with dysmenorrhea remains unclear. Zannoni et al. reported a prevalence of 46% of adenomyosis in young women (14–24 years) in a cross-sectional study including patients with a history of pelvic pain. Young women showed a higher incidence than adolescents [30]. In a retrospective observational study, Exacoustos et al. described ultrasound features and correlation to symptoms in 43 adolescents (12–20 years) with adenomyosis. Dysmenorrhea, dyspareunia, heavy menstrual bleeding were the most reported symptoms. These results underline that adenomyosis is not just a pathology of adult life [36]. Medical and surgical treatment options of adenomyosis are able to reduce symptoms and can have a positive effect on fertility outcome [37–40]. Which treatment of adenomyosis in adolescents and young women would be the right choice and if early diagnosis and treatment of adenomyosis can prevent symptoms and worsening of the disease in fertile life can't be answered.

Our data shows a relatively high coexistence of adenomyosis and fibroids in 58.9% of adenomyosis cases. Previous publications reported a rate of 47.6% of co-occurrence of adenomyosis and fibroids [28]. In ultrasound diagnosis of adenomyosis this fact plays an important role, as the presence of fibroids might be the reason for false-positive prediction by transvaginal ultrasound when the examiner focuses on general ultrasound patterns like uterine enlargement, asymmetry and heterogeneous myometrium. In these combined cases, doppler ultrasound is a helpful tool in order to differentiate adenomyosis from fibroids, as fibroids usually show a circular vascularization while adenomyosis presents with central vascularization.

In cohort 1 the pathological examination revealed adenomyosis in 23.8% of hysterectomy specimen in postmenopausal patients. This might be of importance in patients using hormone replacement therapy or endocrine treatment of breast cancer [41]. These treatments are able to cause an activation of the adenomyotic lesions with irregular myometrial findings in transvaginal ultrasound. Several publications show that adenomyosis and endometrial cancer can co-exist and endometrial cancer can arise in adenomyotic lesions [42–44]. Hermens et al. described an increased incidence of endometrial cancer in patients with endometriosis and adenomyosis in a large retrospective cohort study [45]. Adenomyosis as an estrogen-dependent disease might be a potential risk factor for myometrial or endometrial neoplasms. In clinical and sonographic examination, the differentiation between adenomyosis, endometrial cancer arising in adenomyosis and endometrial cancer coexisting with adenomyosis might be difficult in postmenopausal patients. The risk of transformation of adenomyosis probably should be discussed as an indication for hysterectomy in this subgroup. However, another recent systematic review does not support an association between adenomyosis and endometrial cancer [46].

The data of our analysis is limited to patients with an indication for hysterectomy. Women with ongoing family planning (adolescents (12–19), young women (20–40)) are not considered in this data collection. Nevertheless, our data adds to the existing literature and shows that adenomyosis plays an important role causing uterine changes including symptoms like bleeding disorders and dysmenorrhea and may probably lead to subfertility, obstetrical complications and finally to organ loss. The high prevalence in these cohorts is alarming as it shows that adenomyosis plays an important role in uterine pathology. Reliable diagnostic tools are needed in order to detect adenomyosis as early as possible. The group of postmenopausal patients with adenomyosis also require further investigations as the role of adenomyosis in the development of endometrial cancer is not yet fully understood. Finally, a consensus on adenomyosis classification would be useful in order to differentiate different types of adenomyosis and correlate them to symptoms, severity and therapeutical approach and make further

investigations comparable.

## 6. Conclusion

In patients undergoing hysterectomy for uterine symptomatology adenomyosis can be found in approximately 40% of cases. In women with uterine bleeding disorders and dysmenorrhea adenomyosis should be suspected. Further investigations are needed in order to evaluate the incidence and impact of adenomyosis in adolescents, young women and postmenopausal women.

## Ethical approval

The internal ethics board decided that an approval is not necessary due to the retrospective data collection design of the study.

## Sources of funding

There is no funding.

## Author contribution

Both authors contributed equally to the study design, the data analysis and the writing. HK was mainly responsible for the data collection.

## Research registration Unique Identifying number (UIN)

Name of the registry: Research Registry.

Unique Identifying number or registration ID: 7619.

Hyperlink to your specific registration (must be publicly accessible and will be checked): <https://researchregistry.knack.com/research-registry#home/registrationdetails/62002bb120a3a0001e151e1c/>

## Guarantor

HK.

## Ethics approval

The local IRB decided that the manuscript does not require ethics approval as it is a retrospective data collection (April 20, 2020).

## Data availability

The clinical data used to support the findings of this study are stored at Clinic of Gynecology, Obstetrics and Gynecological Oncology, Bethesda Hospital Duisburg, Academic Teaching Hospital, Duisburg, Germany and are available from corresponding author upon request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

The authors have no conflict of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103809>.

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