

The relationship between uterine prolapse and premalignant endometrial pathology

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Summary

Objective: The aim of this study was to stress the importance of performing a thorough uterine assessment before selecting an organ-sparing surgery in patients presenting with uterine prolapse and no other complaints. **Materials and Methods:** This study included a total of 111 participants who presented with pelvic organ prolapse and underwent hysterectomy for grades 3-4 uterine prolapse. The post-hysterectomy histopathology results were classified as benign (atrophic endometrium, proliferative or secretory endometrium) or pathologic (endometrial hyperplasia, endometrial polyp, adenomyosis, myoma uteri, and endometrium carcinoma). **Results:** Of the 111 patients enrolled in this study, 23 (20.2%) had endometrial hyperplasia, eight (7.2%) had endometrial polyps, 30 (27%) had uterine fibroids, and 20 (18%) had adenomyosis. **Conclusion:** There may be premalignant lesions of the endometrium in both premenopausal and postmenopausal women presenting with uterine prolapse and no other symptoms. A chronic inflammatory process resulting from the extra-vaginal location of the uterus may play a role in the development of these lesions. Further studies are needed on this subject.

Key Words: Uterine prolapse; Hysterectomy; Endometrial hyperplasia.

Introduction

Pelvic organ prolapse (POP) is defined as the herniation of the pelvic organs into the vaginal canal or externally through the canal. POP is an important condition affecting women and the prevalence has been reported as 51% in outpatient clinics [1].

POP may simultaneously occur with other pelvic floor disorders, including urinary or fecal incontinence, sexual dysfunction, and chronic pain syndromes. A history of hysterectomy, age, number of previous pregnancies, and body mass index have been described as the most important risk factors for POP development [2]. The prevalence of POP surgery has been estimated at 1.5 to 4.9/1,000 females/year [3, 4]. Patients with POP may receive a hysterectomy or have a uterus-sparing procedure, such as a vaginal sacrospinous hysteropexy, laparoscopic sacrohysteropexy, and laparoscopic ligament suspension [5].

The aim of this study was to stress the importance of uterine assessment before selecting organ-sparing surgery in women presenting with uterine prolapse even if they had no other symptoms.

Materials and Methods

This study was performed in 111 patients who presented to Sifa University Faculty of Medicine Department of Obstetrics and Gynecology clinic for POP and received a hysterectomy for grades 3-4 uterine prolapse between March 2007 and March 2014. The patients were scored according to The International Continence Society [6].

The study was retrospectively conducted by accessing and evaluating the gynecological and clinical records of these cases. The patients were divided into two groups based on the menopausal state at the time of the operation. Patients who had amenorrhea for more than one year after the last menstrual cycle were considered in menopause. Accordingly, 80 patients were classified as postmenopausal, and 31 were premenopausal (Table 1). Ninety-four patients underwent hysterectomy via the vaginal route and 17 patients via the abdominal route.

Patients with a history of hormone use were excluded. Patients with gynecological complaints other than POP were also excluded. Patients with malignant pathologies of the ovaries or cervix were also excluded. The post-hysterectomy histopathological results of the patients were assessed (Table 2). In the histopathological examination, atrophic endometrium and proliferative or secretory endometrium were classified as benign lesions, whereas endometrial hyperplasia, endometrial polyps, adenomyosis, myoma uteri, and endometrium carcinoma were classified as pathological findings (Table 2).

Along with the descriptive statistics (mean, standard deviation), a chi-square test was used to compare the mean values between premenopausal and postmenopausal patients. The results were assessed within a 95% confidence interval. A *p*-value less than 0.05 was considered statistically significant.

Table 1. — *Demographic characteristics.*

	Postmenopausal	Premenopausal
Age (years)	60.2 ± 11.3 (min-max 44-81)	45.8 ± 5.6 (min-max: 41-52)
Multiparity (%)	77 (97.5%)	31 (100%)
Nulliparity (%)	3 (2.5%)	0
Weight (kg)	69.7	71.4
Body mass index (kg/m ²)	27.7	27.9
Total	80	31

Table 2. — *Histopathological results after hysterectomy.*

Number (%)	111 (100)
Benign histopathological result	30 (27.2)
Senile cystic atrophy	8 (7.2)
Proliferative or secretory endometrium	22 (20)
Pathological histopathological result	81 (72)
Endometrial hyperplasia	23 (20.2)
Simple	21 (18.9)
Simple with atypia	1 (0.9)
Complex	-
Complex with atypia	1 (0.9)
Endometrial polyp	8 (7.2)
Simple	7 (6.3)
Hyperplastic	1 (0.9)
Uterine fibroid	30 (27)
Adenomyosis	20 (18)
Endometrial carcinoma	-

Results

The mean age of the 111 patients enrolled in the study was 53.8 ± 11.83 (min-max: 41-81) years. The mean ages of the premenopausal and postmenopausal women were 45.8 ± 5.6 (min-max: 41-52) and 60.2 ± 11.3 (min-max 44-81) years, respectively (Table 1). The mean body mass index and the previous number of births in the study population are summarized (Table 1). Twenty-two of 30 patients with a benign post-operative histopathology (senile cystic atrophy or proliferative or secretory endometrium) were postmenopausal prior to the operation, and the remaining eight patients were premenopausal (Table 3).

Fifty-eight of 81 patients with a pathological post-operative histopathological diagnosis (endometrial hyperplasia, endometrial polyp, myoma uteri, adenomyosis, or endometrial cancer) were postmenopausal prior to the operation, while 23 patients were premenopausal (Table 3).

Discussion

Pelvic floor insufficiency is an important health issue among middle to advanced-age women. With the prolongation of the average life expectancy and a desire to live a high quality life, this condition has become increasingly

Table 3. — *Classification of the histopathological examination of the hysterectomy materials according to the menopausal state.*

	Post-menopausal	Pre-menopausal	p-value
Number (%)	80	31	
Benign histopathological result	22 (27.5)	8 (25.8)	0.09
Senile cystic atrophy	5 (6.25)	3 (9.7)	0.06
Proliferative or secretory endometrium	17 (21.25)	5 (16.2)	0.08
Pathological histopathological result	58 (72.5)	23 (74.2)	0.06
Endometrial hyperplasia	16 (20)	7 (22.6)	0.06
Simple	14 (17.5)	7 (22.6)	
Simple with atypia	1 (1.25)	-	
Complex	-	-	
Complex with atypia	1 (1.25)	-	
Endometrial polyp	7 (8.75)	1 (3.2)	0.06
Simple	6 (7.5)	1 (3.2)	
Hyperplastic	1 (1.25)	-	
Uterine fibroid	22 (27.5)	8 (25.8)	0.08
Adenomyosis	13 (16.25)	7 (22.6)	0.06
Endometrial carcinoma	-	-	

more common in gynecology practices. POP is a prevalent condition in the female population, and 11% of women receive surgery for this condition by the time they are 80 years old [7]. Advanced age, delivering a large baby, menopause, and a previous hysterectomy or pelvic prolapse surgery are strong etiological factors for severe POP [8-10].

Uterine prolapse surgery can be performed via abdominal, vaginal, or laparoscopic routes. Although a vaginal hysterectomy is the standard approach, symptomatic uterovaginal prolapse therapy is a special technique for women desiring a uterine-sparing approach. Increasingly more women desire to avoid a hysterectomy. Uterine-sparing surgical operations, such as vaginal sacrospinous hysteropexy, laparoscopic sacrohysteropexy, and laparoscopic uterosacral ligament suspension, may be used in women that do not desire a hysterectomy. However, some unexpected uterine pathologies may be encountered in asymptomatic women with uterine prolapses. Mahajan *et al.* reported that premalignant lesions can be detected in patients with no pathological symptoms [11]. Therefore, they suggested performing a pap smear and a careful pelvic examination preoperatively. Frick *et al.* reported that post-operative histopathological examination of uterine tissue after a hysterectomy revealed a high likelihood of premalignant and malignant endometrial pathologies in postmenopausal patients with vaginal bleeding [12].

The present authors also detected other pathological histopathological findings, including myoma uteri (n=22; 27.5%), adenomyosis (n=13; 16.25%), endometrial hyperplasia (n=16; 20%), and endometrial polyps (n=7; 8.75%) in postmenopausal patients. In the premenopausal

patients, the pathological findings were as follows: 25.8% myoma uteri (n=8), 22.6% adenomyosis (n=7), 22.6% endometrial hyperplasia (n=7), and 3.2% endometrial polyp (n=1). There were no significant differences between the premenopausal and postmenopausal women ($p > 0.05$). In a study of 68 asymptomatic women, Mingels *et al.* found that the rates of simple endometrial hyperplasia, complex hyperplasia, hyperplasia with simple atypia, hyperplasia with complex atypia, and endometrioid endometrial carcinoma were 15%, 2%, 3%, 3%, and 3%, respectively [13]. In contrast, the present study found that the rates of endometrial hyperplasia without simple atypia, endometrial hyperplasia with simple atypia, and endometrial hyperplasia with complex atypia were 18.9%, 0.9%, and 0.9%, respectively. Furthermore, they did not detect any cases of endometrial carcinoma. Mingels *et al.* encountered more clinically significant endometrial pathologies than the present study.

It is already known that estrogen levels have a positive correlation with myoma uteri, adenomyosis, endometrial hyperplasia, and endometrial polyps [14-17]. Serum estrogen levels have been reported to be lower in patients with uterine prolapse [5,18]. However, previous studies have shown that some uterine pathologies have a positive correlation with estrogen levels in patients with uterine prolapse, as demonstrated in the present study. This suggests that the present findings may be the result of a locally increased uterine estrogen level rather than the circulating estrogen level. Epidemiological studies have shown that there may be a positive relationship between local tissue inflammation and the development of endometrial carcinoma [19,20]. Increased levels of cytokines and free radicals during this inflammatory process give rise to tissue estrogen production, which facilitates the emergence and development of premalignant and malignant endometrial diseases [19,20]. Externalization of the cervix in grades 3 to 4 uterine prolapse may render the endometrium more susceptible to infections. In addition, endometrial tissue protruding from the vagina may be more exposed to mechanical trauma. The resulting chronic inflammatory process may lead to premalignant and malignant endometrial lesions through the local effects of free radicals and cytokines. These factors may explain the unexpected endometrial alterations in patients with uterine prolapse in the present study as well as in previous studies. The possibility of premalignant and malignant endometrial pathologies should not be overlooked in asymptomatic patients [13]. In patients destined for uterine prolapse surgery, it is essential to assess the uterus and ovaries and perform a Thin Prep Pap test. Transvaginal ultrasonography can be used for endometrial evaluation [21].

The first limitation of the present study was the relatively small sample size. The second limitation is the study's retrospective nature and the lack of data regarding preopera-

tive blood estrogen levels. However, a systemic estrogen insufficiency may be a predisposing factor for uterine prolapse [18, 22]. The authors believe that this study is important because it stresses the importance of the relationship between premalignant endometrial changes, which are known to be related to estrogen levels, and the inflammatory process. As uterine-sparing surgical techniques advance more with each passing day, additional studies are needed to further understand this subject.

Conclusion

Premenopausal and postmenopausal patients with uterine prolapse and with negative gynecological complaint have a risk of premalignant lesions in the endometrium. The present authors found a high number of women with endometrial pathology in especially the postmenopausal group. It is essential to assess the endometrium before selecting an organ-sparing surgery in premenopausal and postmenopausal patients with uterine prolapse. The entire uterine tissue should be sent for histopathological examination after the hysterectomy is performed. Patients may have premalignant lesions in the endometrium even if their only gynecological complaint is uterine prolapse. A chronic inflammatory process due to the external location of the uterus may play a role in the development of these lesions. Additional studies are needed in this field.

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