

Vaginal hysterectomy for uterovaginal prolapse: what is the incidence of concurrent gynecological malignancy?

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Abstract

Introduction and hypothesis Vaginal hysterectomy (VH) is a commonly performed procedure for the operative treatment of uterovaginal prolapse (UVP). The reported incidence of unexpected gynecological cancer in cases of VH for UVP ranges between 0.3 and 0.8 %. Aim of the study is to assess the incidence of malignant and premalignant gynecological histopathological findings among women who underwent a VH for UVP and had a normal preoperative workup.

Methods The histopathology reports of women who underwent VH for the treatment of UVP were retrospectively assessed. All women had a history of normal cervical smear tests and a normal preoperative transvaginal scan. Patients with a history of a premalignant or malignant gynecological pathological condition and women with abnormal uterine bleeding were excluded.

Results Overall, 14 out of 333 women who underwent VH (4.2 %) were found to have abnormal histopathological findings of the uterus. Among them, there were 9 cases of endometrial hyperplasia of any type (2.7 %), 1 case of cervical cancer (0.3 %), 1 case of cervical intraepithelial neoplasia (CIN) III (0.3 %), and 3 cases of CINI (0.9 %). No cases of endometrial cancer were detected. Among women who underwent salpingo-oophorectomy ($n=86$) three simple serous cysts (3.5 %) were found, with no cases of ovarian cancer.

Conclusions The incidence of unexpected premalignant or malignant gynecological pathological conditions among

asymptomatic women who underwent VH, with a history of normal cervical smear tests and normal preoperative TVS, was low but not negligible. This information should be included in the preoperative counseling of women planning to undergo surgery for UVP.

Keywords Vaginal hysterectomy · Uterovaginal prolapse · Risk of malignancy · Asymptomatic · Greek

Abbreviations

AUB	Abnormal uterine bleeding
BSO	Bilateral salpingo-oophorectomy
ET	Endometrial thickness
HGSIL	High-grade squamous intraepithelial lesion
HRT	Hormone replacement therapy
LGSIL	Low-grade squamous intraepithelial lesion
MUS	Midurethral slings
POP	Pelvic organ prolapse
PV	Per vaginam
SERMs	Selective estrogen receptor modulators
SSF	Sacrospinous fixation
TVS	Transvaginal scan
USL	Uterosacral ligament
UVP	Uterovaginal prolapse
VALS	Vaginal assisted laparoscopic sacrocolpopexy
VH	Vaginal hysterectomy

Introduction

Pelvic organ prolapse (POP) is estimated to affect nearly half of all women over 50 years of age [1] and may have a negative impact on the patient's quality of life, daily activities, social relationships, and emotions [2]. Vaginal hysterectomy (VH) is

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the most commonly performed procedure for the operative treatment of uterovaginal prolapse (UVP) and is usually combined with other reconstructive procedures of the pelvic floor.

During the last decade there has not only been a growing number of requests from patients, but also an increasing amount interest among gynecologists in procedures involving the preservation of the uterus. This is based on the belief that the prolapse of the uterus is the result and not the cause of POP and that hysterectomy-associated pelvic floor dissection might increase complications. On the other hand, there is always a concern regarding undiagnosed or future pathological conditions, such as cancer, if the uterus is not removed. In any case, the choice of the procedure depends on the evaluation of various factors, such as the patient's past medical history and current health status, the experience of the surgeon, the availability of materials, the cost of the proposed treatment, and ultimately the patient's preferences. Whenever a conservative approach such as a uterus-sparing procedure is elected, a thorough preoperative assessment should exclude the presence of any precancerous or cancerous pathological conditions of the uterus.

In the literature there are only a few reports of unanticipated gynecological cancer in cases of hysterectomy for POP with an incidence between 0.3 and 0.8 % [3–5]. However, these studies were based on different populations, within different health care systems, and following different preoperative patient workup. In the present study we aim to assess the incidence of a malignant and/or premalignant gynecological pathological condition in women undergoing VH for UVP, who were otherwise asymptomatic, with normal cervical screening, and who had undergone a normal transvaginal ultrasound scan (TVS).

Materials and methods

This is a retrospective study of patients who underwent VH for UVP between 2008 and 2013, in a tertiary referral urogynecology unit. Ethical approval and consent for this study were given by the Institutional Review Board (date of issue 02 April 2014; registration no: 186). The cases were identified from the hospital's registry of operative procedures. All procedures were performed or supervised by the authors TG and SA. The patient's medical notes were retrieved from the hospital's archives. Clinical details, such as age, medical history, gynecological history, including history of PAP smear tests, abnormal per vaginal (PV) bleeding, and gynecological examination were recorded. Postmenopausal status was defined as greater than or equal to 12 months. A TVS is routinely performed in all women before surgery for UVP.

In the present study we included women presenting with UVP with a history of normal smear test results within the previous 3 years and a normal preoperative TVS. Women

aged 65 and over who had had normal smear tests up to the age of 65 were also included. Patients with a history of endometrial, cervical and/or adnexal precancerous or cancerous pathological conditions were excluded. We also excluded all patients who presented concomitant abnormal gynecological clinical examination and/or abnormal uterine bleeding (AUB), such as menorrhagia or postmenopausal bleeding, and women who were on hormone replacement therapy (HRT) or on selective estrogen receptor modulators (SERMs). Postmenopausal women who were found to have an endometrial thickness (ET) of ≥ 8 mm on TVS and premenopausal women with abnormal endometrium, irrespective of the ET, were not included. Lastly, we excluded all subjects with a TVS report stating an ovarian morphology other than normal.

In all cases a vaginal hysterectomy was performed. The vaginal vault was suspended either transvaginally with high uterosacral ligament suspension, sacrospinous fixation, vaginal mesh, or laparoscopically (vaginally assisted laparoscopic sacrocolpopexy, [VALS]) [6]. Women wishing to have their ovaries removed underwent bilateral salpingo-oophorectomy (BSO), either transvaginally or laparoscopically. A midurethral sling (MUS) was placed in cases of coexisting stress urinary incontinence, which was confirmed using multichannel urodynamics. All specimens underwent microscopic histopathological examination.

Statistical analyses were performed using Stata 11.0 software (Stata Corp., College Station, TX, USA). Descriptive statistics of data are expressed as means \pm standard deviation (SD) and 95 % confidence intervals (CIs).

Results

A total of 393 patients who underwent a VH for UVP met the inclusion criteria. We excluded 7 patients with a history of a recent cervical pathological condition (5 patients with low-grade squamous intraepithelial lesion [LGSIL] and 2 patients with high-grade squamous intraepithelial lesion [HGSIL]), 9 patients with a history of an adnexal or uterine pathological condition, and 12 patients with undiagnosed AUB. Three patients who were on tamoxifen and 1 who had had HRT were excluded. Seven of the asymptomatic postmenopausal and 10 of the premenopausal women were excluded as they were found to have an ET ≥ 8 mm or an abnormal endometrial appearance on ultrasound respectively. Last, 11 cases with ultrasound reports stating a non-normal ovarian morphology were excluded.

A total of 333 out of 393 patients (84.7 %) were included for assessment. Mean age was 63.6 ± 10.0 years (range 38–91, 95 % CI=62.3–64.4), with a mean body mass index (BMI) of 26.9 ± 4.1 (range 18.4–40.1, 95 % CI=26.4–27.2). Most patients were postmenopausal (275 out of 333; 82.5 %). A

detailed description of the procedures performed is presented in Table 1.

In total there were 14 patients with abnormal findings (4.2 %) on histopathological examination (Table 2). Among them, there were 9 cases of endometrial hyperplasia (of any degree; 2.7 %) and 5 patients with cervical premalignant or malignant pathological conditions (1.5 %). One case of a 49-year-old premenopausal woman with normal menses and an ET of 7 mm on the 22nd day of her cycle was found to have complex endometrial hyperplasia with atypia (0.3 %). Three out of four cases of complex endometrial hyperplasia without atypia were found in postmenopausal women with an endometrial thickness ranging from 3.5 to 6 mm and three out of four cases of simple endometrial hyperplasia were found in premenopausal women with endometrial thickness ranging from 6 to 7 mm. There were no cases of endometrial cancer (0 %). One case of cervical cancer (0.3 %) was found in a 71-year-old patient. This was a grade 2, squamous carcinoma of the cervix, measuring 1.5×1.3×0.6 cm, located in the endocervix with free surgical limits. There was also 1 case of cervical intraepithelial neoplasia (CIN) III (0.3 %) in a 66-year-old woman and 3 cases of CIN I (0.9 %). Finally, among women who underwent BSO ($n=86$) 3 simple serous cysts (with diameters ranging from 6 to 9 mm) were found, all in postmenopausal women (3 out of 80; 3.8 %).

Discussion

In the present study we estimated the incidence of unexpected malignant and premalignant gynecological pathological conditions in patients undergoing vaginal hysterectomy for UVP. All patients were asymptomatic with a negative diagnostic workup, including a preoperative TVS showing no gynecological abnormalities. The incidence of endometrial and ovarian cancer was 0 % and the incidence of cervical cancer was 0.3 %. However, the inclusion of all precancerous conditions increased the incidence to 4.2 % (Table 2).

In the literature the incidence of unanticipated endometrial malignant and premalignant endometrial pathological

Table 1 Type of surgical procedures performed for uterovaginal prolapse

($n=333$)	USL	Mesh	VALS	SSF
Vaginal hysterectomy	237 (71.1 %)	8 (2.4 %)	85 (25.5 %)	3 (0.9 %)
+ PFR	295 (88.5 %)			
+ BSO	86 (25.8 %)			
+ MUS	116 (34.8 %)			

PFR anterior and/or posterior colporrhaphy, *BSO* bilateral salpingo-oophorectomy, *MUS* midurethral slings, *SSF* sacrospinous fixation, *USL* uterosacral ligament fixation, *VALS* vaginally assisted laparoscopic sacrocolpopexy

Table 2 Patients with abnormal histopathological findings

	Total, $n=333$ (%)	Premenopausal, $n=58$ (17.4 %)	Postmenopausal $n=275$ (82.5 %)
Uterus			
Leiomyomas	50 (15.0)	11 (19.0)	39 (14.1)
Adenomyosis	101 (30.3)	24 (41.4)	77 (28.0)
Endometrium			
Endometrial hyperplasia			
Simple	4 (1.2)	3 (5.2)	1 (0.4)
Complex	4 (1.2)	1 (1.7)	3 (1.1)
Complex with atypia	1 (0.3)	1 (1.7)	0
Endometrial cancer	0	0	0
Cervix			
CIN I	3 (0.9)	0	3 (1.1)
CIN II–III	1 (0.3)	0	1 (0.4)
Cervical carcinoma	1 (0.3)	0	1 (0.4)
Cervical inflammation	24 (7.2)	5 (8.6)	19 (6.9)
Ovaries, $n=86$ (25.8 %)			
Simple serous cyst	3 (3.5)	0/6 (0)	3/80 (3.8)
Ovarian cancer	0	0	0

CIN cervical intraepithelial neoplasia

conditions among asymptomatic women who undergo a hysterectomy for POP varies between 0.7 and 2.6 % [3–5]. Renganathan et al. [3] in a retrospective study found that among 517 asymptomatic women (with no AUB) who underwent hysterectomy for POP, 4 (0.8 %) had unexpected endometrial carcinoma, with no information regarding the incidence of endometrial hyperplasia. However, when considering only postmenopausal women, as all of these cases were found in menopausal women, the incidence rises to 1.14 %. It should be noted that in the institution where the hysterectomies were performed no routine TVS was performed in asymptomatic women. In view of this, the authors concluded that a preoperative ultrasound should be performed in all cases, followed by endometrial sampling in women with thickened endometrium, without, however, suggesting a cut-off value. In another retrospective study by Frick et al. [4], 1 out of 421 asymptomatic postmenopausal (0.2 %) and none of the 115 premenopausal women (0 %) were found to have endometrial carcinoma. In total, 11 out of 421 asymptomatic postmenopausal women were found to have endometrial cancer or hyperplasia (2.6 %). The authors suggest that although the risk of missing a malignancy is low, this may be further reduced by a routine preoperative endometrial biopsy or ultrasound. In a recent retrospective study Wan et al. [5] found 3 out of 456 cases of endometrial premalignant and malignant pathology among asymptomatic patients (0.7 %), an incidence that was within the lower range of what was previously reported in the literature. The authors hypothesized that this

may be due to the lower prevalence of endometrial cancer observed in Asian populations.

The above-mentioned suggestion of performing routine TVS before POP surgery [3, 4] is reinforced by the results of the present study as no cases of unexpected endometrial cancer were found among patients undergoing VH for UVP. One could argue that if the cutoff for endometrial biopsy was lower than 8 mm it would have been possible to diagnose more cases of unexpected endometrial hyperplasia preoperatively, at least in postmenopausal women. It is generally not known how best to manage asymptomatic patients in whom a thick endometrium is observed incidentally [7]. Based on a decision analysis in a theoretical cohort, Smith-Bindman et al. [8] concluded that in asymptomatic postmenopausal women with an endometrial thickness of ≥ 11 mm an endometrial biopsy should be performed. Other studies used cut-off values of ET in asymptomatic postmenopausal women between 3 and 10 mm [7]. In any case, all women included in our study had their uterus removed, which would be an appropriate treatment for all cases of endometrial hyperplasia. However, this is particularly important when counseling patients regarding uterus-sparing procedures, as endometrial hyperplasia, especially with nuclear atypia, is known as a precursor lesion of endometrial carcinoma [9]. In a classic retrospective study of 170 women the likelihood of progression from endometrial hyperplasia to carcinoma was found to be between 1 % in cases of simple hyperplasia without atypia and 29 % in cases of complex atypical hyperplasia [10].

The value of performing a routine TVS was also reflected in the fact that among the 86 women who underwent a BSO there were no cases of ovarian cancer, and only 3 cases of small serous cysts were detected, without any clinical consequences. The results confirm the excellent specificity and negative predictive value of TVS [11] as all patients had a normal ovarian morphology on ultrasound. The practice of other units that do not routinely perform preoperative TVS is to remove the ovaries upon patient request or if an ovarian pathological condition is detected during the hysterectomy. However, it may sometimes be technically difficult to remove the ovaries safely transvaginally. This is particularly important in cases of macroscopically abnormal ovarian cysts when care should be taken to minimize the risk of rupturing the cyst intraoperatively. Should this involve an ovarian malignancy, this would raise the stage of the ovarian cancer from IA to IC1, with significant implications for the postoperative management [12].

There was 1 case (0.3 %) of cervical cancer in a 71-year-old patient who had negative smear tests up till 14 months before surgery and one case (0.3 %) of CIN3 in a 66-year-old patient with normal smear test results, the last one being 3 years before surgery. The remaining 3 patients with CIN1 also had normal smear tests 6 months to 3 years before surgery, with the exception of an 82-year-old patient who had had her last

smear test 15 years before surgery, but had always had normal smear tests up to the age of 67. These missed cases may reflect the moderate sensitivity of the conventional Pap smear test, ranging between 50 and 70 % [13].

There are several limitations of the current study that must be considered when interpreting the data presented. The retrospective nature of the study could create selection as well as information bias regarding gynecological history. Pap smear tests were performed in various settings, public and private, frequently without the availability to review the results preoperatively. Cytopathological assessment of smear tests may be performed in laboratories with no systematic monitoring of quality control results and quality practice parameters. In addition, there is no consensus about the definition of abnormal endometrial thickness in asymptomatic postmenopausal women and the subsequent need for endometrial biopsy. As this study does not include a large number of patients, future investigations including a larger number of patients could evaluate the risk of gynecologically malignant pathological conditions based on age, BMI, and other risk factors. Last, the number of oophorectomies performed is too low to make any safe assumptions, and future studies with a larger number of patients undergoing concomitant oophorectomies are needed to provide more robust evidence.

In this study, we assessed the risk of missing a gynecologically malignant or premalignant pathological condition among women with a defined preoperative diagnostic workup. This included a negative history of gynecological pathological conditions, an unremarkable clinical examination, and a normal preoperative TVS. Among women fulfilling these clinical characteristics we did not find any cases of endometrial or ovarian cancer (0 %), with the exception of 1 case of cervical cancer (0.3 %). However, the inclusion of endometrial and cervical lesions with a high carcinogenic potential increased the incidence to 2.1 % (7 out of 333). We believe that these results provide valuable information for similar populations and evidence for the preoperative counseling of this selected group of asymptomatic patients. This is particularly important when a conservative procedure is contemplated for the treatment of UVP, such as a uterus-sparing procedure or a procedure involving the conservation of the cervix.

Conflicts of interest None.

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