Histopathological findings in hysterectomy for cervical stenosis in postmenopausal women
A retrospective case series

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Abstract

Objective: To analyze the histopathological findings in postmenopausal women who underwent hysterectomy for postsurgical cervical stenosis, evaluating the incidental findings of preinvasive or invasive uterine and cervical disease.

Methods: Retrospective case series of postmenopausal women who underwent hysterectomy for postsurgical cervical stenosis at Gynecological Oncology Unit of Istituto di Ricovero e Cura a Carattere Scientifico Centro di Riferimento Oncologico Aviano—National Cancer Institute from January 2014 to January 2021.

Results: During the study period, 36 women underwent hysterectomy for postsurgical cervical stenosis at our institution. Cervical stenosis occurred 10.2 ± 5.6 years from the onset of menopause. In particular, 26 (72.2%) patients underwent a single loop electrosurgical excision procedure or carbon dioxide (CO_2)-laser conization before the onset of stenosis. The remaining 10 (27.8%) women had multiple surgical excision before the onset of stenosis. At the final histopathological analysis, 17 (47.2%) patients had a preinvasive or invasive gynecological disease. In particular, 9 cases of cervical disease (including 1 case of endocervical squamous cell carcinoma pT1a) and 6 cases of endometrial hyperplasia emerged. Also, 2 cases of tubo-ovarian diseases were found.

Conclusions: Postsurgical cervical stenosis is a challenging clinical condition, especially in women treated for cervical intraepithelial neoplasia or microinvasive cervical cancer. As shown, cervical stenosis can prevent an adequate gynecological follow-up and a prompt diagnosis of malignancies. Therefore, postmenopausal women with cervical stenosis should be carefully counseled, and hysterectomy could be a reasonable option, especially in those cases in which a conservative approach is not feasible, failed, or is not accepted by the patient.

Abbreviations: CIN = cervical intraepithelial neoplasia, CO_2-laser conization = carbon dioxide laser conization, HRT = hormone replacement therapy, IQR = interquartile range, LEEP = loop electrosurgical excision procedure, LSIL = low-grade squamous intraepithelial lesion, SD = standard deviation.

Keywords: cervical stenosis, hysterectomy, loop electrosurgical excision procedure

1. Introduction

Cervical stenosis is a relatively uncommon condition, mostly seen after loop electrosurgical excision procedure (LEEP) or conization for cervical intraepithelial neoplasia (CIN) or microinvasive cervical cancer.[1] The surgical technique, the depth of surgical excision, and postmenopausal status at the time of cervical surgery are the most critical factors involved in the risk of cervical stenosis.[1–5]

Postsurgical cervical stenosis is a troublesome clinical problem. When it occurs in childbearing age in women with a desire for pregnancy, cervical stenosis can represent a serious impediment to embryo transfer and intrauterine insemination.[3] It can also preclude diagnostic procedures such as cervical cytology, endometrial biopsy, and hysteroscopy. In some cases, it can lead to painful hematometra, requiring surgical evacuation. Postsurgical cervical stenosis can prevent a proper gynecological evaluation in postmenopausal women, and signs of common

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gynecological cancers (e.g., bleeding in case of endometrial cancer) can be missed. Moreover, in women treated for CIN or microinvasive cervical cancer, it prevents an adequate cytological and colposcopic follow-up.[6]

There is no consensus about the treatment of postsurgical cervical stenosis, and no proper guidelines are available. Usually, regardless of the patient's age, an attempt of conservative management (recanalization) can be performed. It consists of a gentle progressive cervical dilatation with dilators of increasing diameter.[3] A cervical excision can also be considered when the stenosis involves the external cervical os.[7,8] However, a high recurrence rate after conservative treatments for cervical stenosis is reported, making recurrent stenosis a challenging condition for the gynecologist.

Furthermore, not all cases of cervical stenosis can be safely approached conservatively (e.g., women with multiple previous cervical excisions, trachelectomy, or previous radiotherapy). Thus, hysterectomy can be considered, especially in postmenopausal women, when a conservative approach is not feasible or fails. Interestingly, hysterectomy can lead to an incidental diagnosis of dysplastic lesions or invasive cancers in these patients, both in the uterus and cervix.

This retrospective case series aims to analyze the histopathological findings in postmenopausal women who underwent hysterectomy for cervical stenosis at our institution, evaluating the incidental findings of preinvasive or invasive uterine and cervical disease.

2. Methods

This is retrospective case series of postmenopausal women who underwent hysterectomy for cervical stenosis at Gynecological Oncology Unit of Istituto di Ricovero e Cura a Carattere Scientifico Centro di Riferimento Oncologico Aviano—National Cancer Institute from January 2014 to January 2021. Patients were identified by searching our clinical databases, and the medical records of women fulfilling the study inclusion criteria were retrospectively analyzed. Only women with postsurgical stenosis (previous LEEP or carbon dioxide [CO_2]-laser conization) were considered for the present analysis. Cervical stenosis is usually defined as the narrowing of the cervical canal that prevents insertion of 2.5-mm Hegar or Pratt dilator.[9,10] However, for the present analysis, only women with "severe" stenosis (defined as the complete narrowing of the cervical canal, preventing the insertion of a cytobrush for cytological evaluation) were considered. Patients who underwent hysterectomy for reasons different from cervical stenosis and in which stenosis was incidentally found preoperatively were not included. The hysterectomy was proposed after at least 1 failed attempt of conservative management or as a first-line strategy in cases where a conservative approach was considered unsafe or unfeasible. Before surgery, a transvaginal ultrasound evaluation was routinely performed in each patient. All cases with preoperative abnormal ultrasound findings (endometrial thickness > 4 mm, ovarian cysts, abnormal uterine fibroids, and pelvic masses) were not included in the present analysis. Histopathological examinations were performed by pathologists of our institution, with expertise in the field of the lower genital tract and gynecological pathology.

2.1. Statistical analysis

Dichotomic variables were reported as numbers and percentages. The normality of each continuous variable was evaluated using the D'Agostino-Pearson test. Normally distributed variables were expressed as arithmetic mean ± standard deviation, while not-normally distributed variables are expressed as median and interquartile range.

Clinical data collected were age, age of menopausal onset, the time between menopause and the onset of stenosis, last cytology

obtained before the onset of the stenosis, number of previous conizations, number of attempts of recanalization, time between recanalization and stenosis, and final histopathological report on hysterectomy surgical specimen. Those descriptive variables were reported for those women who underwent hysterectomy for cervical stenosis in the study period.

In order to obtain information about the cervical stenosis incidence in our population and to evaluate risk factors for cervical stenosis (age at conization, menopausal status at conization, and surgical technique), we also collected data about new cases of cervical stenosis at 12 months of follow-up during the study period among women subject to conization at our center. The t test or the chi-square test were used for variable comparison as appropriate. A P value of <.05 was considered as statistically significant.

This study was carried out according to the principles of Helsinki Declaration of 1975, revised in 2013. All patients have signed informed consent at the time of surgery for data collection and for surgical procedures. Considering that this was a case series of routinely collected data, an ethical approval was not necessary.

3. Results

From January 2014 to January 2021, a total of 36 postmenopausal women with postsurgical cervical stenosis who underwent hysterectomy at our institution and fulfilled the study inclusion criteria were identified. All included women had cervical stenosis after cervical excisions (LEEP or CO_2-laser conization) previously performed for CIN or microinvasive cervical cancer. In particular, 26 patients underwent a single LEEP or CO_2-laser conization (72.2%) before the onset of stenosis. The remaining 10 women (27.8%) had multiple surgical excision before the onset of stenosis. More in detail, 6 patients underwent 2 excisions (13.9%), 4 patients had 3 excisions (11.1%), and 1 woman (2.8 %) had 5 excisions before the onset of stenosis. The mean ± standard deviation age of patients was 59.4 ± 8.1 years, and cervical stenosis occurred 10.2 ± 5.6 years from the onset of menopause. Among women included, 14.8% were smokers, and none of them was taking hormone replacement therapy at the time of stenosis. Preoperative pap smear (only ectocervical evaluation) was negative or low-grade (atypical squamous cells of undetermined significance or low grade squamous intraepithelial lesion) in 83.5% of cases (30/36); atypical glandular cells in 5.5 % (2/36), and unsatisfactory in 11.1 % (4/36). Sixteen patients (44%) were eligible for conservative management and underwent a recanalization. Among them, 2 (12.5%) patients underwent 2 recanalizations. All these patients had a recurrence of stenosis (median time from recanalization to stenosis 24 months – interquartile range 10–48 months). These 16 patients underwent hysterectomy after the failure of recanalization and recurrence of stenosis. The remaining 20 women were not eligible for an attempt of recanalization or refused it, so they underwent hysterectomy as a first-line approach.

The final histopathological reports are shown in Table 1. Seventeen patients (47.2%) had a preinvasive or invasive gynecological disease. In particular, 9 cases of cervical disease (including 1 case of endocervical squamous cell carcinoma pT1a) and 6 cases of endometrial hyperplasia emerged. Also, 2 cases of tubo-ovarian disease were found. No case of intraoperative or postoperative complications occurred.

During the study period, a total of 998 conizations (LEEP or CO_2-laser) were performed. Data regarding surgical stenosis were not available for 166 (16.6%) women: 52 (5.2%) underwent hysterectomy for invasive histopathological diagnosis at the cone specimen and 114 (11.4%) were lost at follow-up. Among the remaining 832 women, 31 (3.7%) developed a cervical stenosis at 12 months of follow-up. Those 31 women presented a higher age at conization and were more frequently in

Table 1

Histopathological results

	Cases (n = 36)	%
Cervical disease		
CIN1	6	16.7
CIN2	1	2.8
CIN3	1	2.8
Endocervical squamous cells carcinoma (stage pT1a)	1	2.8
Endometrial disease		
Simple endometrial hyperplasia	3	8.3
Atypical endometrial hyperplasia	3	8.3
Tubal disease		
STIC	1	2.8
Ovarian disease		
Low-grade serous carcinoma of the ovary (stagepT1a)	1	2.8

CIN = cervical intraepithelial neoplasia, STIC = serous tubal intraepithelial carcinoma.

Table 2

Risk factors for cervical stenosis.

Factor	Cervical stenosis (n = 31)	No cervical stenosis (n = 801)	P*
Age at conization	45.5 ± 11.5	37.5 ± 8.5	<.001
Menopause at conization	11 (35.4)	33 (4.1)	<.001
LEEP	14 (45.2)	374 (46.7)	.87
CO_2 laser	17 (54.8)	427 (53.3)	.87

Data are reported as mean ± SD or n (%) as appropriate.

LEEP = loop electrosurgical excision procedure, SD = standard deviation.

*t test or chi-square test as appropriate

menopause at the time of conization with respect to the 801 women who did not develop a cervical stenosis at 12 months of follow-up (Table 2). The surgical technique (LEEP or CO_2-laser) was not associated with the risk of cervical stenosis (Table 2). Six (19.4%) of these women with cervical stenosis were managed with hysterectomy, while the remaining 25 (80.6%) underwent recanalization.

4. Discussion

Cervical stenosis is a relatively uncommon condition; it can occur at all levels within the cervical canal but is most frequent at the internal os.[3] However, in some cases, especially after cervical surgery, it can occur at the external cervical os. Previous cervical excision for CIN or microinvasive cervical cancer is the most important risk factor for developing stenosis (postsurgical stenosis). The incidence of postsurgical cervical stenosis reported in the literature is highly heterogeneous: some authors reported an incidence ranging from 4% to 16% for LEEP and CO_2-laser conization, respectively.[4,5,11,12] Our data of cervical stenosis incidence of 3.7% are substantially in line with those previous reports. However, an impressive postsurgical risk of stenosis up to 60% has been reported by some authors for postmenopausal women treated with LEEP.[2]

According to the current literature, the surgical technique seems to influence the risk of stenosis, with a higher risk for CO_2-laser conization than LEEP.[4,5,9–12] However, other factors such as the length of excised specimens, the size and location of the lesion, and previous cervical treatments seem to affect the risk of postsurgical stenosis as well.[1,3,4,13] Moreover, the patient's age at the time of intervention is described as an independent risk factor for postsurgical stenosis.[4,12] This is probably due to the lack of estrogen structural support on the cervical epithelium in postmenopausal women, potentially affecting the postsurgical healing process on the cervix and facilitating the development of stenosis.

Postsurgical cervical stenosis is a troublesome clinical problem, especially in women treated for CIN or microinvasive cervical cancer, since the stenosis prevents a proper cytological and colposcopic follow-up.[6] Therefore, cervical stenosis should be treated, but there is no consensus about treatment modalities. Usually, regardless of the patient's age, an attempt of recanalization can be performed. It consists of a gentle progressive dilatation with dilators of increasing diameter.[3] A cervical excision can also be considered in case of severe, impassable stenosis involving the external cervical os.[7,8] Other conservative approaches such as cervical stent placement or intrauterine device insertion had been described,[14–16] but they are burdened by a high risk of recurrence and are not always applicable (e.g., in case of impassable stenosis).

Moreover, not all cases of cervical stenosis can be safely approached conservatively (e.g., women with multiple previous cervical excisions, trachelectomy, and previous radiotherapy). Thus, hysterectomy can be considered when a conservative approach is not feasible or failed (or not accepted by the patient), especially in postmenopausal women. In our opinion, analyzing the histopathological findings in women who underwent hysterectomy for postsurgical cervical stenosis is extremely interesting. Only a few data from small and heterogeneous case series are available in the literature. For example, Newman and Finan,[17] in a small cohort of 25 women who underwent hysterectomy, found 12% cervical dysplasia and 4% uterine cancer. We found histopathological abnormalities in 17 patients (47.2%). In particular, 1 case of invasive cervical cancer, 2 cases of high-grade cervical dysplasia, and 3 cases of atypical endometrial hyperplasia emerged.

All the patients were asymptomatic at the time of hysterectomy, but the presence of cervical stenosis prevented a proper gynecological evaluation with endometrial/endocervical cytology and adequate colposcopy. However, a routine pap smear (only ectocervical evaluation) and transvaginal ultrasound were performed before surgery. No case of high-grade cytological abnormality or suspicious ultrasound findings was found before surgery. It can be argued that in the absence of cervical stenosis and with a proper gynecological follow-up, all these conditions should have been properly diagnosed. However, with untreated stenosis, all the cases of preinvasive or invasive lesions should have been missed without surgery.

The limitation of our study is that we were not able to evaluate the incidence and risk factors for cervical stenosis in the 36 patients who underwent hysterectomy. Therefore, we evaluated this risk in all patients subjected to conization at our institution in the study period.

In conclusion, cervical stenosis is a challenging clinical condition that can occult malignancies, leading to a delayed or missed diagnosis of preinvasive and invasive cervical and endometrial lesions. Moreover, it usually occurs in women treated for CIN or microinvasive cervical cancer, in whom an adequate follow-up is mandatory due to the potential relapse of dysplasia or progression to cancer. Therefore, all cases of cervical stenosis need to be diagnosed and treated. In particular, postmenopausal women with stenosis in which a conservative approach is impossible, failed, or is not accepted, should be carefully counseled, and hysterectomy could be a reasonable option.

Author contributions

FS and NC: conceptualization, formal analysis, investigation, and writing - original draft preparation; MP, ADF, MS, and GG: methodology, formal analysis, and investigation; MB: data curation and investigation; MF: formal analysis, investigation, and

writing - review & editing; GDC: formal analysis, investigation, and writing - original draft preparation; AC: conceptualization, supervision, and writing - review & editing.

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