Gynecologic Oncology 137 (2015) 270–273

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Usefulness of vaginal cytology tests in women with previous hysterectomy for benign diseases: assessment of 53,891 tests

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HIGHLIGHTS

- The value of vaginal cytology after hysterectomy for benign disease was analyzed.
- This study evaluated 53,891 women who had undergone hysterectomy.
- The prevalence rates of abnormal cytology were much lower after hysterectomy.
- The prevalence of abnormal cytology did not show significant variation with age.

ARTICLE INFO

Article history:
Received 24 October 2014
Accepted 9 February 2015
Available online 19 February 2015

Keywords:
Uterine cervical neoplasms
Mass screening
Hysterectomy
Vaginal neoplasms
Guideline adherence

ABSTRACT

Objective. To assess the value of vaginal screening cytology after hysterectomy for benign disease.

Methods. This cross-sectional study used cytology audit data from 2,512,039 screening tests in the metropolitan region of Campinas from 2000 to 2012; the object was to compare the prevalence of abnormal tests in women who had undergone a hysterectomy for benign diseases (n = 53,891) to that of women who had had no hysterectomy. Prevalence ratios (95% confidence intervals, 95% CI) were determined, and chi-square analysis, modified by the Cochrane–Armitage test for trend, was used to investigate the effects of age.

Results. The prevalence of atypical squamous cells (ASC), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion or squamous-cell carcinoma (HSIL/SCC) was 0.13%, 0.04% and 0.03%, respectively, in women who had undergone hysterectomy, and 0.93%, 0.51% and 0.26% in women who had not undergone hysterectomy. The prevalence ratios for ASC, LSIL and HSIL/SCC were 0.14 (0.11–0.17), 0.08 (0.06–0.13) and 0.13 (0.08–0.20), respectively, in women with a hysterectomy versus those without. For HSIL/SCC, the prevalence ratios were 0.09 and 0.29, respectively, for women <50 or ≥50 years. The prevalence rates in women with a previous hysterectomy showed no significant variation with age.

Conclusion. The prevalence rates of ASC, LSIL and HSIL/SCC were significantly lower in women with a previous hysterectomy for benign disease compared with those observed in women with an intact uterine cervix. This study reinforces the view that there is no evidence that cytological screening is beneficial for women who have had a hysterectomy for benign disease.

Introduction

Vaginal cytology has not been routinely recommended for women who have undergone a hysterectomy and removal of the cervix for benign reasons. However, it is well known that the human papillomavirus (HPV) has the ability to infect the squamous and glandular epithelium of the lower genital tract, and some argue that persistent HPV infection in the vaginal epithelium could cause precursor or invasive vaginal lesions.

Invasive vaginal cancer is a rare female malignancy, with a reported incidence of <1 per 100,000 women (median age: 68 years) [1]. The prevalence of HPV infection in vaginal cancer ranges from 43.8% in Asia to 76.8% in Europe, and the most common HPV type found is HPV16 [2].

Although there is no consistent recommendation for maintaining cancer screening in women who have undergone a hysterectomy [3–5], testing is still performed, particularly in regions with opportunistic screening. A systematic review of the literature found only 19 studies with the minimal requirements necessary for analysis, and concluded that the value of cytology tests has still not been established because of

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http://dx.doi.org/10.1016/j.ygyno.2015.02.011
0090-8258/

inconsistent study design and limited methodological quality [6]. Therefore, the purpose of this study was to assess the value of vaginal screening after hysterectomy for benign diseases, using data from 2.5 million cytology tests for cervical cancer screening in the Campinas region of Brazil.

Methods

This was a cross-sectional study of data from a cytology Pap smear audit of 2,512,039 tests obtained for cervical cancer screening purposes in the Campinas metropolitan area, Brazil, from 2000 to 2012. The cytopathology laboratory database classified the test purpose as screening, follow-up of a previous abnormal test, or follow-up after treatment for cervical neoplasia. This study included only those tests performed for screening purposes, with 53,891 tests in women who had undergone a hysterectomy for benign diseases and 2,458,148 tests in women who had not undergone a hysterectomy. We considered that women who had a hysterectomy for benign diseases had undergone the cytology test for screening purposes.

Campinas is a densely populated urban area in South-Eastern Brazil (Sao Paulo State). The data from the tests were obtained from the cytopathology laboratory database of Dr José Aristodemo Pinotti Women's Hospital at Unicamp (State University of Campinas). The laboratory receives samples of tests performed in patients from nearly 70 municipalities in the Campinas region, and has a wide experience in cytology training and research. Screening is opportunistic in Brazil: i.e., women have a cervical cancer screening test performed when they attend primary healthcare clinics for any reason. There is no call and recall system or similar alternatives for cervical cancer screening in Brazil. The provision of local cervical cancer cytology services was consistent during the study period.

We excluded incorrectly labeled tests, tests classified as unsatisfactory, or those performed for a purpose other than screening, such as pre-treatment and post-treatment testing. We also excluded tests from women who had had a previous hysterectomy with laboratory results showing the presence of glandular or metaplastic cells, because such tests might correspond to incorrect information of hysterectomy.

Primary healthcare physicians or nurse practitioners performed the vaginal cytology tests in primary healthcare units; they also recorded patient identification, purpose of the test, woman's age, interval since the last cervical screening test, and clinical information including a previous hysterectomy. In the laboratory, these forms had test results added and the data were incorporated using optical character recognition into the database used in this analysis.

At the cytopathology laboratory, cytotechnologists performed routine screening of the smear. All suspicious tests were reviewed by cytopathologists. Negative tests were randomly selected for quality control that was carried out by senior cytotechnologists and cytopathologists. Cytological findings were classified according to the Bethesda System. To include data from the last 13 years, subcategories such as atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells in which high-grade squamous intraepithelial lesions (ASC-H) could not be excluded were classified as atypical squamous cells (ASCs).

Guidelines for tests with abnormal findings in the public health system have recommended that women with ASC-US and low-grade squamous intraepithelial lesions (LSILs) should have a repeat cervical cytology test after 6 months. Women with other abnormal results should be referred for colposcopy.

Although almost all cytological tests from the region are assessed in the cytopathology laboratory, other centers for colposcopy, diagnosis and treatment of invasive cervical cancer also exist. Data on histological diagnoses established at these centers were not available to this study.

The prevalence ratio (PR) with 95% confidence interval (95% CI) was calculated for abnormal tests in women who underwent a hysterectomy for benign diseases compared with abnormal tests in women who had not undergone a hysterectomy. Values of <1 were considered as indicating a protective effect. The chi-square test modified by the Cochrane–Armitage test for trend was used to investigate prevalence according to age.

The Institutional Review Board of the Dr José Aristodemo Pinotti Women's Hospital at Unicamp approved this study. The database was constructed for screening management and quality assessment purposes. The data in this analysis were anonymized and retrospective; therefore, the Institutional Review Board waived the requirement to obtain signed informed consent.

Results

The prevalence of ASC, LSIL, and high-grade squamous intraepithelial lesions or squamous-cell carcinoma (HSIL/SCC) is shown in Table 1. The prevalence of ASC, LSIL, and HSIL/SCC was 0.13%, 0.04%, and 0.03%, respectively, in women who had undergone a hysterectomy, and 0.93%, 0.51%, and 0.26%, respectively, in women with no prior hysterectomy. The PR (95% CI) was 0.14 (0.11–0.17) for ASC, 0.08 (0.06–0.13) for LSIL, and 0.13 (0.08–0.20) for HSIL/SCC in women who had undergone a hysterectomy versus women with no prior hysterectomy. No types of atypical glandular cells were observed in tests obtained from women who had undergone a hysterectomy (data not shown).

Table 2 shows the effect of age on PRs. For ASC, the PRs were 0.14, 0.13, 0.15, and 0.36 for women aged <40, 40–49, 50–59, and ≥ 60 years, respectively. For LSIL, PRs were 0.08, 0.19, 0.26, and 0.93, respectively. Women ≥ 60 years of age comprised the only group with a 95% CI that was not statistically significant (ranging from 0.43 to 2.00). For HSIL/SCC, the PRs were 0.09, 0.09, 0.29, and 0.29 for women aged <40, 40–49, 50–59, and ≥ 60 years, respectively.

The prevalence of ASC, LSIL, and HSIL/SCC in women who had undergone a hysterectomy did not show any statistically significant variation as a function of age. In women with no previous hysterectomy, there was a statistically significant trend for a decrease in prevalence of any abnormal test results with age (Table 2).

Discussion

According to this study, the prevalence of ASC, LSIL, and HSIL/SCC in cytology test results was significantly lower in women who had had a previous hysterectomy for benign diseases compared with those from women with an intact cervix. These data reinforce the idea that cancer screening has a reduced role in the detection of precursor lesions in women who have had a previous total hysterectomy.

The overall prevalence of ASC, LSIL, and HSIL/SCC in women who had undergone a hysterectomy for benign diseases was shown to be 0.2%. The prevalence of HSIL/SCC in these women was 0.03%, compared with a prevalence of 0.26% in women with an intact cervix. This protective effect was more evident in women younger than 50 years, which could be explained by the decreasing trend in prevalence with age in

Table 1
Prevalence of abnormal squamous cytology results in 53,891 tests from women who had undergone a hysterectomy for benign diseases and in 2,458,148 tests from women who had not undergone a hysterectomy.

Result	Hysterectomy		No hysterectomy		
	n	Prevalence %	n	Prevalence %	Prevalence ratio (95% CI)
ASC	69	0.13	22,913	0.93	0.14 (0.11–0.17)
LSIL	23	0.04	12,473	0.51	0.08 (0.06–0.13)
HSIL/SCC	18	0.03	6409	0.26	0.13 (0.08–0.20)
Total	110	0.20	41,795	1.70	0.12 (0.10–0.15)

Prevalence ratio, positive tests from women who had undergone a hysterectomy/positive tests from women who had not undergone a hysterectomy; ASC, atypical squamous cells; LSIL, low-grade intraepithelial lesion; HSIL, high-grade intraepithelial lesion; SCC, squamous-cell carcinoma; CI: confidence interval.