Published in final edited form as:

Gynecol Oncol. 2016 August ; 142(2): 283–285. doi:10.1016/j.ygyno.2016.05.030.

Role of Cervical Cytology in Surveillance after Radical Trachelectomy for Cervical Cancer

Alaina J. Brown^{1,*}, Jaimin S. Shah², Nicole D. Fleming¹, Alpa M. Nick³, Pamela T. Soliman¹, Gary B. Chisholm¹, Kathleen M. Schmeler¹, Pedro T. Ramirez¹, and Michael Frumovitz¹

¹Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

²Department of Obstetrics and Gynecology, The University of Texas Health Science Center at Houston, Houston, TX, USA

³Department of Obstetrics and Gynecology, St. Thomas Medical Partners, Nashville, TN, USA

Abstract

Objective—There are currently no standard guidelines on the use of Papanicolaou (Pap) tests for surveillance after radical trachelectomy for cervical cancer. The goal of this study was to determine the usefulness of Pap tests in routine surveillance after radical trachelectomy for cervical cancer.

Methods—Cervical cancer patients who underwent radical trachelectomy from January 2004 through October 2015 and subsequently had at least one Pap test were retrospectively identified. Demographic and clinical characteristics were described and compared between patients with and without at least one abnormal Pap test. The Kaplan-Meier method was used to estimate time to first abnormal Pap test.

Results—Forty-one patients met inclusion criteria. Of these, 30 (73%) had at least one year in which more than one Pap test per year was obtained. Twenty-four (59%) had at least one abnormal Pap test. Of 238 total Pap tests collected, 44 (18%) were abnormal. The most common abnormality was ASCUS (52%, n=23). Other findings included LSIL (20%, n=9), HSIL (2%, n=1), and AGUS (25%, n=11). Median time from radical trachelectomy to first abnormal Pap test was 17.2 months (range, 11.8–86.3). No patient had disease recurrence. Surgery type (laparoscopic, open, or robotic), trachelectomy specimen size, histology, device for stenosis prevention (pediatric Foley catheter or Smit Sleeve), and cerclage placement were not significant predictors of an abnormal Pap test.

*Corresponding author: Alaina J. Brown, MD, MPH, Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 1155 Pressler St., Unit 1362, Houston, TX 77030. Phone: (713) 563-4558. AJBrown@mdanderson.org.

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The authors declare that there are no conflicts of interest.

Conclusions—The rate of abnormal Pap tests after radical trachelectomy is high; however, the clinical significance of such abnormalities appears limited. The routine use of cervical cytology as surveillance after radical trachelectomy does not appear to substantially impact management decisions.

Introduction

Radical trachelectomy offers young patients with early-stage cervical cancer the ability to maintain fertility. Recurrence rates after radical trachelectomy are typically very low but have been reported to be as high as 10% (1). If there is a local recurrence, successful treatment with radiation therapy may be possible. Therefore, it is important to implement effective surveillance strategies to identify recurrences early among patients who have undergone radical trachelectomy.

Surveillance for patients after cervical cancer treatment often includes symptom review, physical examination, and yearly Papanicolaou (Pap) test. It was previously demonstrated that symptom review and physical examination are the components most likely to detect a recurrence and that recurrences are rarely detected solely by Pap test (2, 3). The National Comprehensive Cancer Network (NCCN) and the Society of Gynecologic Oncology (SGO) both include annual Pap tests within their surveillance guidelines for all patients after cervical cancer treatment, but both organizations acknowledge that the use of Pap tests in cervical cancer surveillance is not well supported by published data (4, 5).

Currently, there are no standard recommendations regarding the use of Pap tests for surveillance after radical trachelectomy for cervical cancer. The goal of this study was to determine the rate of abnormal Pap tests and their impact on clinical decision making during surveillance after radical trachelectomy.

Methods

All women who underwent radical trachelectomy for early-stage cervical cancer and who had at least one postoperative Pap test (cervical cytologic examination) with or without a human papillomavirus test performed between January 2004 and October 2015 were enrolled in this study, which was approved by the Institutional Review Board of The University of Texas MD Anderson Cancer Center. Patients were eligible for inclusion if they had both their surgery and their postoperative Pap tests performed at MD Anderson. Patients were excluded if they had incomplete medical records, had their trachelectomy aborted intraoperatively, required a completion hysterectomy for close or positive surgical margins, or did not have at least one postoperative Pap test at MD Anderson.

The following data were collected from the medical records of enrolled patients: demographic data, pathologic data (findings on surgical pathology and postoperative Pap test cytology), and surgical data (date of surgery, surgical approach).

Demographic and clinical characteristics were described using simple descriptive statistics. Summarization was performed overall, for patients who had no abnormal Pap tests, and for patients who had at least one abnormal Pap test. The rate of abnormal cervical cytology was

estimated using the mean, median, and associated measures of dispersion. The time to first abnormal Pap test was estimated using the Kaplan-Meier method. Selected patient characteristics were tested as predictors of an abnormal Pap test. Statistical analysis was performed using SAS 9.4 for Windows (SAS Institute Inc., Cary, NC).

Results

During the study period, 61 patients were taken to the operating room for a planned radical trachelectomy for cervical cancer. Eight of these patients were excluded from this study because the radical trachelectomy was aborted intraoperatively, 1 was excluded because a simple trachelectomy was performed, and 11 were excluded because they did not have at least one follow-up Pap test at MD Anderson, leaving 41 patients for this analysis. The median follow-up time was 39 months (range, 25–67). Patient demographics and tumor characteristics are summarized in Table 1.

Median time from radical trachelectomy to first abnormal Pap test was 17.2 months (range, 11.8–86.3). The median number of Pap tests to first abnormal Pap test was 4 (range, 2–13). None of the patients have had a recurrence at the time of this report. Surgery type (laparoscopic, open, or robotic), trachelectomy specimen size, histology, device for stenosis prevention (pediatric Foley catheter or Smit sleeve), and cerclage placement were not significant predictors of an abnormal Pap test.

Over half of the patients (24 of 41; 59%) had at least one abnormal Pap test in the follow-up period. Of the total 238 Pap tests collected, 44 (18%) had abnormal cervical cytology. The most common abnormal finding was abnormal squamous cells of undetermined significance (ASCUS), which was present in 23 of the 44 abnormal Pap tests (52%). Other abnormal findings were low-grade squamous intraepithelial lesion (LSIL) in 9 Pap tests (20%), high-grade squamous intraepithelial lesion (HSIL) in 1 (2%), and atypical glandular cells of undetermined significance (AGUS) in 11 (25%) (Table 2).

Seven patients (17%) underwent at least one colposcopic evaluation in the follow-up period. Two of these patients received two colposcopies each, for a total of nine colposcopies performed. Six patients (15%) underwent a biopsy. One of the patients underwent two biopsies, for a total of seven biopsies (Table 3). One of the biopsies demonstrated CIN 3 and that patient ultimately underwent a completion hysterectomy which demonstrated CIN3 and adenocarcinoma in situ on the final pathology. Thirty patients (73%) had at least one year in which more than one Pap test was collected. Twenty of the patients (49%) had a normal pap test following an abnormal pap test. Sixteen of the patients (39%) were tested for HPV at the time of their pap test. Only 1 of these patients was HPV positive.

Discussion

Our study shows that the rate of abnormal Pap tests after radical trachelectomy for cervical cancer is high; however, the clinical significance of these findings appears to be limited. Our data suggest that routine Pap tests for patient surveillance after radical trachelectomy may lead to increased office visits for follow-up pap tests and colposcopic examinations with little improvement in actionable information gained during surveillance.

Our findings are in agreement with those of previous studies showing that for women with a history of cervical cancer who are currently in surveillance, Pap tests do not appear to substantially impact management decisions (3, 6, 7). Previous studies have also shown that among patients with dysplasia, Pap tests may be a source of additional office visits, procedures, and anxiety (6–9). No studies have specifically evaluated the anxiety associated with surveillance Pap tests among patients with a history of cervical cancer, but it is likely that these patients also experience a significant amount of anxiety associated with routine Pap tests for surveillance.

In our study, 73% of patients experienced at least one year in which they underwent a Pap test more frequently than the NCCN and SGO recommendations of once per year for surveillance. Seventeen percent of our patients also underwent colposcopic evaluation. A potential reason for the high frequency of Pap tests in our cohort is that the NCCN and SGO guidelines are general recommendations for surveillance after treatment of an invasive cervical cancer. No comprehensive guidelines exist for surveillance after trachelectomy, which leaves decisions regarding the appropriate Pap test frequency up to the individual provider, resulting in wide variability. Current SGO recommendations with the Choosing Wisely campaign have recommended that providers not perform colposcopy in patients treated for cervical cancer with pap tests of LSIL or lower. In our population 5 of the 9 patients (55%) undergoing colposcopy, did so unnecessarily per these guidelines. As a result of the findings from this study and the Choosing Wisely campaign, we have moved to standardize our surveillance practice such that patients undergo Pap tests only once per year after radical trachelectomy and we do not perform colposcopy following LSIL or lower pap tests.

Aside from the psychological burden for patients, Pap tests for cervical cancer surveillance are associated with significant healthcare costs. As we are moving to a new phase of health care in which the need for interventions must increasingly be proven, we must examine the value of Pap tests for cervical cancer surveillance following surgical management. Our data are in agreement with data from prior studies that indicate that surveillance Pap tests following radical trachelectomy are of limited clinical value (10).

The strengths of our study include the relatively large single-institution cohort of patients who underwent radical trachelectomy. We believe that we are the first to report results of postoperative Pap tests in a cohort this large. Our center is a primary referral center for radical trachelectomy procedures, and we are able to follow our patients for an extended period of time. One of the limitations of our study is that it was retrospective and accordingly was limited to information that could be collected from the medical record alone. Some patients in our cohort did not have adequate follow-up and were excluded from our study.

The use of Pap tests in routine surveillance following radical trachelectomy must be further evaluated. Our data suggest that Pap tests are of limited clinical utility in the surveillance of patients who have undergone a radical trachelectomy. At this time, we recommend that Pap tests in such patients be performed as recommended by the NCCN and SGO guidelines: only once a year instead of at each surveillance visit. Additional research should be

undertaken to evaluate if this patient population can be followed per current guidelines for dysplasia that use a combination of HPV and cytology results to determine the frequency of surveillance pap tests.

Acknowledgments

Supported by the NIH/NCI under award number P30CA016672

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Highlights

- 59% of patients had at least one abnormal Pap smear after radical trachelectomy for cervical cancer
- None of the patients had a recurrence during the study period
- The routine use of cervical cytology as surveillance after radical trachelectomy does not appear to substantially impact management decisions

Table 1

Patient demographics and tumor characteristics (N=41)

Variable		N	%
Race/ethnicity			
	Asian	3	(7)
	Black	1	(2)
	Hispanic	8	(20)
	White	29	(71)
Histology (pre-op)			
	Adenocarcinoma	21	(51)
	Adenosquamous	2	(5)
	Mixed	2	(5)
	Squamous cell carcinoma	16	(39)
Grade (pre-op)			
	1	7	(17)
	2	16	(39)
	3	15	(37)
	Not reported	3	(7)
LVI (pre-op)			
	Negative	24	(59)
	Not Reported	3	(7)
	Positive	14	(34)
Stage			
	IA1 + LVI	6	(15)
	IA2	12	(29)
	IB1	23	(56)
Surgery type			
	Radical laparoscopic trachelectomy	1	(2)
	Radical abdominal trachelectomy	20	(49)
	Radical robotic trachelectomy	20	(49)

LVI, lymphovascular space invasion; pre-op, preoperative.

Table 2

Findings in abnormal Pap smears (N=44)

Characteristic	N	%
ASCUS	23	52
LSIL	9	20
HSIL	1	2
AGUS	11	25

ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGUS, atypical glandular cells of undetermined significance.

Table 3

Colposcopies and biopsies following abnormal pap tests (N=9)

Colposcopy	Pap result	Biopsy performed	Biopsy finding
1	ASCUS-H	Yes	No Abnormality
2	HSIL	Yes	CIN2
3	LSIL	No	N/A
4	Normal	No	N/A
5	AGUS	Yes	CIN3
6	AGUS	Yes	Benign endometrium
7	Normal	Yes	Benign endometrium
8	ASCUS	Yes	No Abnormality
9	ASCUS	Yes	No Abnormality

ASCUS-H, atypical squamous cells of undetermined significance, cannot exclude high grade; HSIL, high-grade squamous intraepithelial lesion; CIN2, cervical intraepithelial neoplasia grade 2; LSIL, low-grade squamous intraepithelial lesion; ; AGUS, atypical glandular cells of undetermined significance; CIN3, cervical intraepithelial neoplasia grade 3; ASCUS, atypical squamous cells of undetermined significance;