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Expert Review of Cervical Cytology: Does it Affect Patient Care?

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Abstract

Objectives—To evaluate if expert review of outside cervical cytology affects patient care.

Methods—A retrospective study was conducted of 424 new patient referrals for cervical dysplasia between 2004 and 2016 at Roswell Park Cancer Institute. Records were analyzed for outside cervical cytology reports and compared with expert cervical cytology review. Differences between expert review and outside reports were documented. Charts with a difference were then assessed for additional evaluation and procedures done. We specifically analyzed the data for cytology being upgraded or downgraded after expert review.

Results—246 patient charts were eligible for this study. We identified 165 patients with congruent pathology reports. Of the 81 different reports, 41 led to significant pathologic differences. 24 reports with different pathology were LSIL lesions upgraded to HSIL lesions. Six were HSIL downgraded to LSIL, 4 LSIL downgraded to negative, 3 AGC upgraded to HSIL, 2 AGC upgraded to cancer, 1 each for HSIL downgraded to negative and AGC downgraded to negative. Of the 24 patients whose cytology changed from low grade to high grade, 17 underwent an excisional procedure and 1 had a laser ablative procedure. CIN 2 or 3 was found in 11 specimens. CIN 1 was found in 4 of excisional specimens and no dysplasia found in 2.

Conclusions—Expert review of cervical cytology significantly impacts patient management at a tertiary referral center, resulting in both upgrading and downgrading of community cytology reports.

Keywords

cervical dysplasia; cytology; CIN; LSIL; HSIL; ASCUS; abnormal pap smear

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Disclosure Statement

The authors have declared they have no conflicts of interest

Introduction

Cervical cancer is the 21st most common cancer among women in the United States with an estimated 12,820 new cases to be diagnosed in 2017¹. It accounts for 0.7% of all cancer-related deaths in the United States¹. In the developed world this cancer is increasingly rare due to improved access to medical care and effective screening programs. According to the Centers for Disease Control and Prevention roughly 19 million pap tests are performed annually⁵. The Bethesda reporting system, established in 1988, has been the standard for reporting cervical cytology. Since 1988, this reporting system has been modified several times, with the most recent update being in 2014⁴. An estimated 2.3 million women will have pap tests identified as atypical cells of uncertain significance (ASC-US), 1.3 million are identified as low grade intraepithelial lesions (LSIL) and 550,000 will be reported as high grade intraepithelial lesions (HSIL)². This in turn leads to many colposcopies, biopsies and excisional procedures.

At our National Cancer Institute (NCI)-designated Comprehensive Cancer Center in Upstate New York, over 400 new patients were referred for a second opinion for abnormal cervical cytology since 2004. These patients were initially screened by community gynecologists, family physicians, and midlevel providers. The original abnormal cytology results triggering the referral were obtained at community hospitals and clinics. As part of the routine new patient workup, all cytology slides are reviewed by an expert gynecologic cyto-pathologist and an interpretation is given.

Inter-observer differences in cervical cytology interpretations are well described, with as many as 57% ASC-US pap tests downgraded upon review³. There is also significant discordance observed with HSIL cytology, with as much as 27% reinterpreted as LSIL and 23% as ASC-US³. An additional study in *Cancer Cytopathology* showed inter-observer differences with ASC-US pap tests which were interpreted as negative, ASC-US or LSIL 86% of the time, and ASC-H pap tests being interpreted as negative, HSIL and ASC-H 69.7%⁶.

We sought to review all new patient visits for abnormal cervical cytology at our institution and compare the initial cytology report with our expert review to see if this impacts patient care with regards to newly discovered high-grade lesions and cancer diagnosis. We hypothesized that any differences between outside cytology reports and the expert review would not significantly alter patient care.

Methods

This study is a retrospective chart review consisting of all new patients seen at our institution between January 1st 2004 through December 31st 2016 for the diagnosis of cervical dysplasia. To be included in the study outside cervical cytology reports and the expert review performed by our institution needed to be available. The outside cytology review was compared to the expert review and if the reports were not congruent then additional information was collected, including any further treatments. See figure 1 for categorization

of cytology. This protocol was approved by the Roswell Park Cancer Institute Institutional Review Board.

Role of the Funding Source

This work was supported through the NIH grant T32CA108456 which provided the funding to have the medical records queried to create the study list.

Results

424 new patient visits for cervical cytology were identified and 246 met inclusion criteria. See figure 2 for patient eligibility. The majority of charts excluded were for incorrect coding. For example, the patient was not actually referred for cervical dysplasia, outside records were incomplete, or the expert review was not performed.

The majority of cytology reports (165/246, 67.1%) were congruent between the outside report and the expert review. Eighty-one (32.9%) of the reports were discordant, and of these 50.6% (41/81) led to a new diagnosis. See figure 3 for distribution of reports. 24 patients had cytology changed from low grade to high grade, 17 (71%) underwent an excisional procedure and 1 (4.2%) had a laser ablative procedure. CIN 2 or 3 was found in 11 (64.7%) of excisional procedure specimens. CIN 1 was found in 4 (23.5%) of excisional procedure specimens and no dysplasia found in 2 (11.8%).

In the high grade downgraded to low grade group one excisional procedure was performed with CIN 3 found on the specimen. The one patient that had an ASC-H read outside pap smear and was read as cancer on expert review was diagnosed with a Stage 1A1 adenocarcinoma of the cervix after excisional procedure and went on to have a laparoscopic hysterectomy.

In the AGC to cancer group the first patient was diagnosed with a stage 1A1 squamous cell carcinoma of the cervix after excisional procedure and then underwent minimally invasive hysterectomy. The second AGC to cancer patient underwent an excisional procedure and was diagnosed with a stage 1B2 serous adenocarcinoma of the cervix and was treated with chemo-radiation.

Discussion

This study highlights the known inter-observer differences when evaluating cervical cytology. Although previous studies^{3,6} have demonstrated inter-observer differences in interpreting cytology results, there is a paucity of reports comparing community practice results with academic review since the widespread introduction of HPV co-testing in clinical practice. The purpose of this paper was to evaluate if the routine practice of expert review of community cytology reports impacted patient care. The six patients identified as having negative cytology on expert review avoided colposcopy and biopsies altogether. The one patient which had high grade cytology downgraded to low grade cytology and the excisional procedure pathology showed CIN 3 highlighted that expert review was not useful in this situation. Also included in this study is one patient who self-referred for a second opinion,

who had a history of cervical dysplasia but most recent pap test was normal so the reason for expert review in her case is not clear. The total cost of second cytologic review amounted to an estimated \$84,000 for the entire study group. One could imagine that if the practice of expert review was eliminated this could potentially lead to more unnecessary colposcopies, biopsies and potentially excisional procedures, especially in the low grade cytology category of patients as we identified negative cytology in this group but our numbers were small. A specific limitation of this study is that 179 patient records were excluded which may have impacted our findings as well as the high risk HPV report not being in many outside records therefore this information was not included in our findings.

In the majority of cases, when a patient has an ASC-US HPV positive, LSIL, or HSIL pap test the ASCCP guidelines are followed and this is immediately followed up with colposcopy and cervical biopsies. The patients with a low grade pap test that is upgraded to high grade would have had a colposcopy and biopsy regardless so the change in pathology was not clinically significant in this situation.

One way to eliminate the inter-observer difference seen with cytology would be to use primary HPV testing. In 2015, The Society of Gynecologic Oncology endorsed primary HPV testing for cervical cancer screening in women 25 years of age and greater as an alternative to traditional cytology with HPV testing⁷. One clear advantage of primary high risk HPV testing is that a negative high risk HPV test provides greater reassurance that CIN 3 or greater is absent compared to a negative cytology alone⁷. Patients testing positive for HPV 16 and 18 are recommended to have a colposcopy with possible biopsies. Although accepted as an alternative screening method by the American College of Obstetricians and Gynecologist and the Society of Gynecologic Oncology, this screening method has not been universally adopted. Reasons for the lack of universal acceptance of primary high risk HPV screening over cytology and co-testing is the lack of evidence on comparative effectiveness studies looking at projected lifetime number of screening tests, colposcopies, follow up visits, direct cost comparisons and the confusing screening and management algorithms available⁷.

Conclusion

Expert review of cervical cytology led to diagnosing higher grade lesions from lower grade lesions and also downgrading some high and low grade reports to negative cytology thereby avoiding invasive procedures with the added cost and patient risk. Universal expert review may not be practical in all settings. In a low resource setting expert review could be considered in younger women desiring children to potentially avoid a primary or repeat excisional procedure which may negatively impact future pregnancies. Consideration could be given to more widespread use of primary HPV testing to eliminate the inter-observer differences on pap test review.

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Review Board Status: STUDY00000158 / BDR 083117 has IRB approval

List of all Abbreviations and Acronyms

RPCI	Roswell Park Cancer Institute
LSIL	low grade squamous intraepithelial lesion
HSIL	high grade squamous intraepithelial lesion
ASCUS	atypical squamous cells of uncertain significance
AGC	Atypical glandular cells
AGC-NOS	Atypical glandular cells not otherwise specified
ASC-H	Atypical squamous cells cannot exclude a high grade squamous intraepithelial lesion
CIN	Cervical intraepithelial neoplasia

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Study classification of cytology	Cytology Report
Low grade	ASC-US, LSIL, ASC Cannot rule out LSIL
High grade	HSIL, ASC-H, LSIL Cannot rule out HSIL
Negative	Negative
Cancer	Squamous cell carcinoma, Adenocarcinoma
Atypical glandular cells	AGC, AGUS

Figure 1.

Figure 2.

		Outside Pathology				
		Negative	Atypical Glandular Cells	Low Grade	High Grade	Cancer
Roswell Pathology	Negative	1	1	4	1	0
	Atypical Glandular Cells	0	3	0	0	0
	Low Grade	0	0	110	6	0
	High Grade	0	3	24	88	0
	Cancer	0	2	0	0	3

Figure 3.