

Reduced cervical sampling of hysterectomy specimens with negative margins on conization

An opportunity to improve resource utilization

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ABSTRACT

Objectives: The current recommendation for hysterectomy specimens performed for cervical cancer following conization is that the entire cervix be submitted for histologic examination. Given the high cost of medical procedures and concerns regarding difficulties with laboratory staffing, we sought to evaluate the potential for selective histologic examination in this setting.

Methods: Post-conization hysterectomy cases were reviewed for the presence of residual disease in relation to the findings of the prior conization, with consideration of margin status. Residual disease was then assessed for clinical significance. The number of submitted blocks was recorded and the associated costs were estimated.

Results: Among 32 cases with invasive carcinoma, only cases with margins positive for invasive carcinoma on the conization specimen had residual invasion in the hysterectomy (n = 7), and there were no upgrades due to subtle microscopic disease; 1 case had a change in pathologic stage from pT1b1 to pT2b due to parametrial involvement in the setting of a grossly apparent lesion. Among 20 cases performed following a diagnosis of dysplasia, none were upgraded to invasive carcinoma. Based on protocol-based submission of the entire cervix, 16 blocks of cervix were submitted on average (range, 4-41).

Conclusions: We estimate that representative sections from each cervical quadrant would save approximately 2 work hours for laboratory staff per case and up to 6 hours for larger cases, reducing costs for the laboratory accordingly. Selective cervical sampling in the setting of negative margins on conization provides an opportunity for improved resource utilization without compromising patient care; as this is a small study, confirmation of these findings in a larger number of cases may be warranted. Additional studies are necessary to determine what other contexts in surgical pathology could benefit from a similar reductive approach.

KEY POINTS

- When margins of a conization specimen are negative for invasive carcinoma, it is highly unlikely for the subsequent hysterectomy specimen to contain clinically significant findings.
- If conization margins are positive for invasive carcinoma, there is sufficient potential for actionable findings in the hysterectomy specimen to consider submitting the entire cervix for histologic examination.
- Selective sampling of the cervix following conization with negative margins is an opportunity to reduce waste in the surgical pathology laboratory.

KEYWORDS

AP gynecological; gross examination; resource utilization

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INTRODUCTION

High costs associated with operations and difficulties with maintaining appropriate laboratory staffing have shed light on the need for efficient resource utilization and elimination of waste. While this principle is not new, it has been even more salient within the backdrop of COVID-19, in which burnout manifesting from chronic job stress has become more pervasive and maintaining technical staff in clinical laboratories is increasingly challenging.¹⁻³ Demanding workloads, long hours, and staff shortages affect not only employee well-being but also patient care due to laboratory errors as a result of exhaustion.⁴ Additionally, incidental findings have the potential for inadvertent harm due to unnecessary procedures and their sequelae.^{5,6} Moreover, superfluous tasks divert time from meaningful educational opportunities for staff and residents in training.

The Choosing Wisely Campaign, led by the ABIM Foundation, has put forth more than 500 recommendations from nearly 80 specialty societies.⁶ These recommendations are intended to promote optimal clinical care by performing only necessary and evidence-based testing. Aside from the recommendation to avoid frozen sections without immediate implications for intraoperative surgical decision-making, none directly pertain to surgical pathology.⁶ Although protocols have been developed to provide optimal patient care, most are based on historical practices rather than applying evidence-based approaches, leading to largely nonstandardized methodology and substantial variation between—and even within—institutions.⁷ In an effort toward standardization, the International Society for Gynecological Pathologists (ISGyP) published grossing guidelines based on the Endocervical Adenocarcinoma Project findings, which were extended to other cervical malignancies as well.⁸ ISGyP currently recommends submission of the entire cervix for histologic examination from hysterectomy specimens that follow cervical conization for dysplasia or carcinoma, irrespective of the findings on that prior procedure.⁸ Submitting the entire cervix reduces the chance that grossly inapparent lesions will go unrecognized and likely meaningful in the setting of conization, where microscopic disease may influence the type of hysterectomy to be performed; however, there is no parallel in clinical decision-making based on the hysterectomy specimen. Here, we demonstrate that submitting the entire cervix for histologic examination can be safely omitted in the setting of negative margins on prior conization.

MATERIALS AND METHODS

Using natural language search processing within our laboratory information system for quality improvement purposes, hysterectomies performed following in-house conization procedures for cervical dysplasia or carcinoma were identified. Clinicopathologic data were extracted from the medical record, including diagnosis prior to conization, type of conization, disease at time of conization and hysterectomy, and margin status (including which margin was involved and if it was involved by dysplasia and/or invasive carcinoma). Pathologic stage at conization and hysterectomy was compared to

determine if there was an increased T stage. The number of blocks submitted to examine the cervix was also recorded. Technical staff was informally interviewed to assess time use.

RESULTS

Our cohort of 52 patients included 32 patients diagnosed with invasive carcinoma (19 squamous cell carcinoma and 13 adenocarcinoma) and 20 patients with human papillomavirus (HPV)-related disease but without invasive carcinoma (8 high-grade squamous intraepithelial lesion [HSIL] alone, 9 adenocarcinoma in situ [AIS] alone, 3 with both AIS and HSIL). Of the 27 cases with invasive carcinoma on the prior conization, 7 had residual invasion in the hysterectomy specimen; all 7 cases with residual invasive carcinoma had margins that had been positive for invasive carcinoma at the time of conization. There were no clinically significant findings based on subtle microscopic disease; a single case resulted in a change in pathologic stage from pT1b1 to pT2b due to parametrial involvement, but this case notably had a grossly apparent lesion suggestive of residual disease. Five additional cases had margins positive for invasive carcinoma without residual invasive carcinoma in the hysterectomy specimen; conization margins had been positive for dysplasia on an additional 5 cases, which also demonstrated no residual invasion in the hysterectomy specimen. Among the 19 cases performed following a diagnosis of HSIL and/or AIS, none were upgraded to invasive carcinoma; similarly, 4 cases with benign findings in a prior conization that had been performed for invasive carcinoma revealed no additional disease. Details regarding worst disease prior to hysterectomy, pre-hysterectomy margin status, and residual disease at the time of hysterectomy are presented in **TABLE 1**.

The number of blocks submitted ranged from 4 to 41, averaging 16, with no apparent difference according to the prior diagnosis. Accordingly, representative sampling by quadrant **FIGURE 1** would result in 12 fewer blocks per case, on average—and up to 37—with an associated reduction in costs to the laboratory. Based on informal interviewing of laboratory staff regarding the various tasks involved in processing a single cassette, we estimate that the combined time of grossing, embedding, microtomy, staining, cover-slipping, slide distribution, and slide filing, an average block occupies at least 10 minutes of technical work. Submitting 12 fewer blocks would therefore save laboratory staff 2 hours of work per case, and more than 6 hours could be saved in more extreme cases. Time spent viewing slides by pathologists is highly variable, but representative sampling of quadrants in the setting of negative margins would also save time for both attending pathologists and trainees.

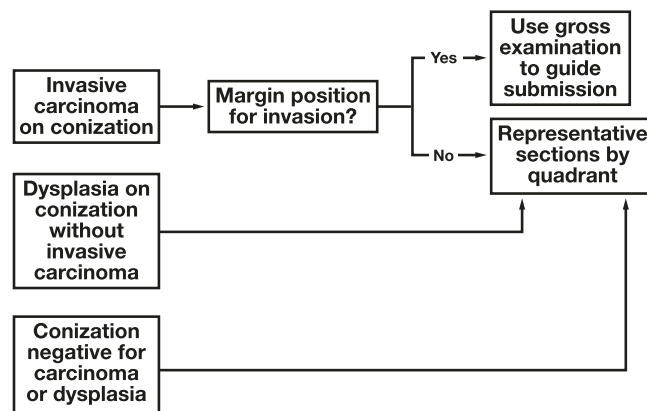
DISCUSSION

Although cervical cancer remains the fourth most common cancer in women worldwide, the success of screening and surgical removal of premalignant lesions has transformed the landscape of cervical cancer in developed nations to one in which most patients are treated at an early stage and can be managed with more conservative treatment. Indeed, per National Comprehensive Cancer

TABLE 1 Worst Disease Prior to Hysterectomy, Prehysterectomy Margin Status, and Residual Disease at the Time of Hysterectomy

Characteristic	Worst diagnosis prior to hysterectomy, No.	Invasive disease at prior conization margin, No.	Residual invasive carcinoma at hysterectomy, No.	Increase in T stage between cone and hysterectomy, No.	Clinical implications?
SCC	19	7	4	1	Yes
Adenocarcinoma	13	5	3	0	No
AIS	9	0	0	0	No
AIS/HSIL	3	0	0	0	No
HSIL	8	0	0	0	No
None	0	0	0	0	No

AIS, adenocarcinoma in situ; HSIL, high-grade squamous intraepithelial lesion; SCC, squamous cell carcinoma.


FIGURE 1 Algorithm for representative sampling by quadrant.

Network guidelines, conization without hysterectomy is sufficient for patients with minimal invasion who wish to retain fertility, and further treatment is reserved for patients who do not desire fertility and/or have more advanced disease. The data presented here demonstrate that apart from cases in which margins have been positive at the time of conization, hysterectomy specimens following conization are unlikely to contain clinically significant disease, and comprehensive histologic examination can safely be avoided if margins were negative at the time of conization.

Guidelines from the ISGyP recommend to entirely submit tumors that are 2 cm or less and representatively sample tumors larger than 2 cm; if a tumor is not grossly visible or the most severe disease on record is dysplasia, then the entire cervix is to be submitted.⁸ In our series of 52 patients undergoing hysterectomy following conization, only 1 case had significant remaining disease in the hysterectomy specimen, and this risk could be anticipated by the presence of a positive margin on the prior conization specimen and a discrete gross lesion. Of note, the shift in T stage from pT1b to pT2b is associated with radiation therapy, reinforcing the need for thorough examination of the parametrium. The absence of significant findings in all other cases without the risk factor of a positive margin on the prior cone suggests that more conservative sampling in the setting of negative cone margins will not harm patient care.

Adjusting protocols where excess tissue submission reveals no added clinical benefit has the potential to reduce technical time spent during grossing, embedding, and performing microtomy for each block and also has implications for pathologists and trainees. We estimate

that representative sections by cervical quadrant could save ~2 hours of work for laboratory staff on average and more than 6 hours in some cases. Given the relatively low volume of cases being processed for this indication, changing practice for these specimens alone will yield only a modest benefit, but there is existing literature to support extending the scope of this principle more broadly. As an example, in the setting of gender-affirming surgeries, which are typically performed in young, healthy patients, Hernandez et al⁹ reported that an average 2.8× slides were submitted in these cases in comparison to reduction mammoplasty, but they had a 2.5× lower rate of significant findings and therefore recommended submitting only 4 blocks in gender-affirming mastectomies. Similarly, Hamza et al.¹⁰ have demonstrated that additional sections are often low yield despite a high cost associated with their use. Cumulatively, incorporating a reductionist approach across various areas propagates time efficiency for all staff and physicians involved, reduces cost and resource utilization, and lessens the chance of errors in the laboratory.

In a world of increasingly complex pathologic evaluation and burnout, which inevitably impacts patient care and also affects institutions financially, we must focus our efforts strategically for both pathologists and laboratory staff.¹¹⁻¹³ It stands to reason that when data-driven evidence supports a decrease in sample processing, protocol changes should be followed for more effective resource utilization. Ultimately, these changes will increase the efficiency of time management for the health care team and ensures optimal patient care, but it is essential that an adequate number of cases be studied prior to implementation, and establishing what constitutes sufficient evidence for a change in practice has not been established in this context. Further research is also necessary to better understand what other protocols may benefit from more conservative tissue submissions in surgical pathology.

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