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Utility of conization with frozen section for intraoperative triage prior to definitive hysterectomy☆

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HIGHLIGHTS

► Conization with frozen section accurately triages patients to simple or radical hysterectomy.
► Conization with frozen section performs equivalently in both an academic cancer center and community hospitals.
► Inexperienced pathologists should undertake intraoperative assessment of glandular lesions with caution.

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ABSTRACT

Objective. To review our experience with conization with intraoperative frozen section analysis and to compare results from our tertiary cancer center with those from 2 community hospitals.

Methods. The records of all women who underwent conization with intraoperative frozen section analysis from January 1, 1997, through April 30, 2011, at The University of Texas MD Anderson Cancer Center and 2 community hospitals—The Woman's Hospital of Texas and St. Luke's Episcopal Hospital—were reviewed. Findings on pathologic analysis of frozen sections, permanent loop electrosurgical excisional procedure/conization specimens, and hysterectomy specimens were compared for each patient, and the results from the cancer center were compared to those from the community hospitals.

Results. One hundred fifty-three patients met the inclusion criteria. Rates of accuracy of conization with frozen section analysis in predicting definitive pathologic findings were as follows: cervix with no residual disease after prior extirpative procedure, 96.5% (95% CI 86.9–100%); cervical squamous carcinoma in situ, 95.4% (95% CI 84.5–100%); cervical adenocarcinoma in situ, 98.7% (95% CI 92.7–100%); microinvasive carcinoma, 97.4% (95% CI 90.1–100%); and invasive carcinoma ≥ 3 mm, 100%. Most importantly, conization with frozen section analysis was 100% accurate for triaging patients to simple or radical hysterectomy. Finally, this approach performed equally well in the cancer center with subspecialized pathologists and the 2 community hospitals with general pathologists.

Conclusion. Conization with frozen section analysis is an effective technique for intraoperative triage of patients to immediate simple or radical hysterectomy and can be accurately performed in both academic and community hospitals.

Introduction

Cervical cancer is the second most common cancer and the third leading cause of cancer-related death among women worldwide [1]. The surgical treatment of cervical cancer varies greatly by stage at diagnosis and typically is based on clinical stage at diagnosis. Patients with stage IA1 disease (microinvasive disease, nonvisible lesion < 3 mm deep and < 7 mm wide) can usually be treated with conization or simple hysterectomy without removal of regional lymph nodes. Patients with stage IA2 disease (nonvisible lesion 3–5 mm deep and < 7 mm wide or stage IB1 disease (nonvisible lesion > 5 mm deep or ≥ 7 mm wide or visible lesion < 4 cm in size limited to the cervix) are often dispositioned to radical hysterectomy or radical trachelectomy with pelvic lymphadenectomy [2]. As the morbidity of radical surgery and lymphadenectomy is much greater than that of simple hysterectomy

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or conization [3], accurate determination of depth of invasion (< or ≥3 mm) is critically important for triaging patients with nonvisible lesions to the proper surgical treatment.

As an office biopsy at time of colposcopic examination is often insufficient to accurately determine depth of invasion, in most patients with nonvisible lesions, a loop electrosurgical excisional procedure (LEEP) or cone biopsy must be performed to procure enough tissue to establish this critical prognostic factor. LEEP requires an office environment with adequate space, equipment, and support staff; cone biopsy requires an operating room with the associated costs and anesthesia risks. In addition, both approaches cause significant edema of the cervix starting 24 to 48 h later, which makes surgical dissection difficult. Therefore, before performing definitive procedures after LEEP or cone biopsy, surgeons generally must wait at least 6 weeks to allow for swelling to recede, a delay in treatment that can cause substantial anxiety for patients. For those reasons, some centers offer conization with intraoperative frozen section analysis to determine depth of invasion followed by simple hysterectomy or radical hysterectomy/lymphadenectomy performed at the same surgery according to the intraoperative pathologic findings.

Other investigators have reviewed their experience with conization and intraoperative frozen section analysis and have reported that findings on intraoperative analysis and findings on examination of permanent pathologic specimens correlate 75% to 100% of the time [4–9]. However, these studies were limited to patients at single academic centers. The applicability of those findings to general practice remains unknown. The objective of this study was to review our experience with conization with intraoperative frozen section analysis and to compare the results from our tertiary cancer center with those from 2 community hospitals.

Methods

After approval was obtained from the MD Anderson Institutional Review Board, the records of all women who underwent conization with intraoperative frozen section analysis from January 1, 1997, to April 30, 2011, at The University of Texas MD Anderson Cancer Center, The Woman's Hospital of Texas, and St. Luke's Episcopal Hospital were reviewed. The start date of January 1, 1997 was chosen as this was when conization with intraoperative frozen section analysis was first performed at MD Anderson. This procedure was performed at the community hospitals starting in 2007. Only patients with a preoperative diagnosis of squamous carcinoma or adenocarcinoma in situ [AIS] or microinvasive cervical cancer (<3 mm) were included. Patients with a visible lesion (by definition a stage IB1 cervical cancer) or a final diagnosis of a non-cervical primary lesion (e.g., stage II endometrial cancer with cervical involvement) were excluded. All frozen specimens were obtained in an operating room by either LEEP or cold knife conization under general anesthesia.

For frozen section analysis, the cone specimen was entirely submitted as radial sections following differential inking of the endocervical and ectocervical margins. One to two sections per slide were then placed on a brass chuck, and sections were covered in OCT (optimal cutting temperature). The chuck was placed in a freeze box packed with dry ice (−40 °C) until the OCT material was opaque (30–45 s). Following transfer and cutting of thin sections (4–5 μm) in a cryostat (−20 °C), the tissue was immediately fixed in methanol for 5 s. Once dry, slides were stained with hematoxylin and eosin in an automatic stainer and then read. At The Woman's Hospital of Texas and St. Luke's Episcopal Hospital, all specimens were reviewed by general pathologists. At MD Anderson Cancer Center, all specimens were reviewed by pathologists subspecialized in the area of gynecologic pathology.

For both squamous and glandular lesions, when analysis of frozen sections revealed no residual dysplasia, low- or high-grade dysplasia, or microinvasive carcinoma, a simple hysterectomy with or without a bilateral salpingo-oophorectomy was performed. When analysis of frozen sections revealed invasive carcinoma (≥3 mm), a radical hysterectomy and pelvic lymphadenectomy with or without bilateral salpingo-oophorectomy was performed.

Results on pathologic analysis of frozen sections, LEEP/conization specimens, and hysterectomy specimens were compared for each patient. Sensitivity and accuracy were also calculated. Finally, results from MD Anderson Cancer Center were compared to those from the 2 community hospitals. For cancer patients, recurrence rates were also assessed.

Fisher's exact test, the Mann–Whitney test, and the chi-squared test were used to evaluate differences between groups. Missing data were coded as "unknown," and those data points were excluded from the analysis. Unless otherwise noted, *P* values were not adjusted for multiple comparisons. *P* values of <.05 were considered statistically significant. All data were analyzed using SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL).

Results

One hundred fifty-three patients met the inclusion criteria. For the entire group, the median age was 42.9 years (range 19.5–82.6), and the median body mass index was 26.9 kg/m^2 (range 17.5–49.7 kg/m^2). For frozen section analysis prior to hysterectomy, 146 (95%) had a cold knife cone while the remaining 7 (5%) had a LEEP. Ninety-two patients (60%) were in the cancer center group, while 61 (40%) were in the community hospital group. Demographic data for both groups are shown in Table 1. There were no differences between the 2 groups in age, body mass index, prior pregnancies, menopausal status, ethnicity, or presenting symptoms.

Forty-four (48%) of 92 patients in the cancer center group had a previous extirpative procedure (LEEP or cone biopsy), compared to only 12 (20%) of 61 patients in the community hospital group (*P*<.001). In addition, 47 patients (51%) in the cancer center group had a preoperative diagnosis of at least a microinvasive carcinoma, compared to only 5 patients (8%) in the community hospital group (*P*<.001).

Table 1
Patient demographics and preoperative pathologic findings.

	Cancer center (n=92)	Community hospital (n=61)	*P*
Median age (range), years	42.9 (19.5–82.6)	42.9 (26.1–77.9)	NS
Median BMI (range), kg/m^2	26.5 (18.4–49.7)	28.3 (17.5–48.8)	NS
Median gravidity (range)	3 (0–12)	2 (0–11)	NS
Median parity (range)	2 (0–10)	2 (0–11)	NS
Menopausal, no. of patients (%)	25 (27)	14 (23)	NS
Ethnicity, no. of patients (%)			
Caucasian	62 (67.4)	42 (68.8)	NS
Hispanic	19 (20.6)	8 (13.2)	
African American	6 (6.5)	11 (18)	
Asian	5 (5.5)	0 (0)	
Presenting symptom, no. of patients (%)			
Abnormal Pap test	69 (75)	47 (77)	NS
Abnormal bleeding	21 (23)	12 (20)	
Unknown	2 (2)	2 (3)	
Preoperative diagnosis			
Abnormal Pap test	4 (5)	17 (28)	<.001
CIN II/III	27 (29)	33 (54)	
AIS	14 (15)	6 (10)	
Microinvasive cancer (<3 mm)	47 (51)	5 (8)	
Method of diagnosis			
Pap only	0 (0)	12 (20)	<.001
Office biopsy	48 (52)	37 (60)	
LEEP/cone biopsy	44 (48)	12 (20)	

AIS, adenocarcinoma in situ; BMI, body mass index; CIN, cervical intraepithelial neoplasia; LEEP, loop electrosurgical excisional procedure; NS, not significant.