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Colposcopy Standards: Guidelines for Endocervical Curettage at Colposcopy

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Objective: The most recent guidelines for colposcopy practice in the United States, the 2017 Colposcopy Standards Consensus Guidelines, did not include recommendations for endocervical curettage (ECC). This document provides updated guidelines for use of ECC among patients referred for colposcopy.

Methods: Consensus guidelines for the use of ECC were developed in 2012. To update these guidelines in concordance with the 2017 Colposcopy Standards process, an expert workgroup was convened in 2021. Literature had been previously reviewed through 2011, before the 2012 guideline. Literature from the years 2012–2021 and data from the NCI Biopsy study were reviewed, focusing on the additional yield of ECC.

Results: Endocervical curettage is recommended for patients with high-grade cytology, human papillomavirus 16/18 infection, positive results on dual staining for p16/Ki67, for those previously treated for known or suspected cervical precancer or considering observation of cervical intraepithelial neoplasia grade 2, and when the squamocolumnar junction is not fully visualized at colposcopy. Endocervical curettage is preferred for all patients aged older than 40 years. Endocervical curettage is acceptable for all nonpregnant patients undergoing colposcopy but may be omitted when a subsequent excisional procedure is planned, the endocervical canal does not admit a sampling device, or in nulliparous patients aged younger than 30 years, with cytology reported as atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesion regardless of whether the squamocolumnar junction is fully visualized. Endocervical curettage is unacceptable in pregnancy.

Conclusions: These guidelines for ECC add to the 2017 consensus recommendations for colposcopy practice in the United States.

Key Words: endocervical curettage, colposcopy, screening

(*J Low Genit Tract Dis* 2023;27: 97–101)

Colposcopy is the primary triage modality for the evaluation of patients with abnormal cervical cancer screening tests. However, colposcopy is limited by inability to evaluate at-risk cervical epithelium within the endocervical canal. Endocervical specula can allow inspection of the distal portion of the endocervix, but inspection may be limited and directed biopsy difficult. Endocervical curettage (ECC) traditionally has been used to sample the endocervix, but the procedure is painful and may increase colposcopy and pathology charges.

In 2006, the American Society for Colposcopy and Cervical Pathology (ASCCP) first developed US consensus guidelines for performing ECC.[1] These guidelines stated that ECC is contraindicated in pregnancy because of the risk of injury to membranes or the placenta. For nonpregnant patients, the 2006 guidelines state that ECC is preferred for individuals with abnormal cervical cancer screening results when colposcopy shows no lesion and when the squamocolumnar junction (SCJ) is not entirely visible, but ECC is acceptable in all cases. This guideline was linked to recommendations for managing patients with low-grade squamous intraepithelial lesions (SILs), and no guidance was given for patients with other grades of cytologic abnormality; subsequent iterations of guidelines did not refine these recommendations, although they were reviewed and reapproved after literature review at a 2012 guidelines conference.[2] In 2017, ASCCP promulgated standards for colposcopy for the United States; standards for ECC were deferred.[3] This article presents updated evidence-based guidelines for ECC.

TECHNIQUE

In 2013, an ASCCP literature review through 2011 established that endocervical sampling with a curette is more specific and sampling with a brush is more sensitive, leading a national consensus conference to determine that both are acceptable techniques.[2] One study suggested that sampling with a Pipelle device yields similar tissue volume with a similar proportion of adequate results with less pain compared with an endocervical curette.[4] Other devices have been developed for endocervical sampling but peer-reviewed evidence is sparse and seems insufficient for the development of firm guidelines for or against use. Most studies have focused on ECC, and for the purposes of this report, the term "ECC" is used to encompass all methods of endocervical sampling.

Most clinicians use a curette for ECC. The technique of ECC has not been standardized or evaluated in targeted observational studies or comparative trials; the following is based on expert consensus. Curettage is performed with a Kevorkian-Younge curette, ideally under colposcopic guidance, either using an in-and-out motion to use the distal blade or a rotating motion to use the lateral blades, applying a corkscrew motion to ensure comprehensive sampling of the full circumference of the canal.[5] A 2019 systematic review and meta-analysis of 11 trials failed to show an impact of local anesthesia on pain from ECC,[6] so use of an anesthetic is not recommended. Regardless of technique, the sample should consist of both tissue removed on the curette along with tissue, mucus, and blood collected after curettage with forceps or brush to minimize risk of insufficient sampling.[7] If brushings are substituted for curetting, the brush should be compressed to release all material in the bristles and then swished in fixative numerous times. The sample should be inspected, and more tissue may need to be obtained if visibly inadequate. Samples may be processed for histology or cytology. Sequencing ECC before or after cervical biopsy also has not been standardized; the former avoids bleeding from the biopsy site that

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L.S.M. has testified in malpractice cases alleging delay in cervical cancer diagnosis. No authors received compensation from ASCCP for guidelines development. The other authors have declared they have no conflicts of interest.

DOI: 10.1097/LGT.0000000000000710

may obscure visualization, whereas the latter allows directed biopsy without disruption of obscuring blood from the ECC.[5] Opportunities for future research include impact on yield of various curettage/brushing instruments, use of colposcopic guidance, number of circuits or strokes used, and postprocedure processing.

LITERATURE REVIEW

The ECC literature was comprehensively reviewed through 2011 before development of the 2012 guideline.[2] Under these guidelines, performance of endocervical sampling was the preferred management for patients with indications for colposcopy in whom no lesions were identified and for those with an "inadequate" colposcopy, defined in the terminology of the time as cases for which the SCJ was not fully visible at colposcopy. Endocervical curettage was deemed acceptable management for patients with an entirely visualized SCJ and a lesion identified in the transformation zone.

We undertook a review of subsequent literature. The PubMed database was searched for the years 2012–2021 using the terms "endocervical curettage," "endocervical curettings," "endocervical sampling," and "ECC". Articles were reviewed to determine the yield of cervical intraepithelial neoplasia (CIN)2 or a more severe lesion (CIN2+) identified by ECC greater than that obtained from colposcopically directed biopsies ("additional yield"). We included only articles in English, and because we wanted to derive guidance for US practitioners, we only included studies conducted in populations with widely available cervical cancer screening. We excluded articles that did not include ECC for all patients with cytologic abnormalities, those that included ECC only for specific cytologic results, those that focused on postprocedure ECC, and others that did not allow calculation of the additional yield of ECC in all patients undergoing colposcopy.

We identified 5 reports that allowed calculation of additional yield in patients undergoing colposcopy.[8–12] Additional yield of CIN2+ from ECC greater than that obtained by ectocervical biopsy was 0.5% to 12%, although the study with the lowest yield[10] incorporated random biopsies that are not part of routine US clinical practice. Two important studies were analyzed in detail.

Van der Marel et al.[8] studied 126 patients at colposcopy, all of whom had ECC. The additional yield of CIN2+ was 15/126 (12%). All of the 15 patients had high-grade squamous intraepithelial lesions (HSIL) on the cytology preceding colposcopy; the additional yield of ECC among 50 patients with preceding cytology read as atypical cells of undetermined significance (ASCUS) or low-grade SIL (LSIL) was 0. Of the 15 patients contributing to the additional yield of CIN2+, 10 (67%) had negative colposcopic impressions. Of 21 patients with SCJ fully visualized, 4 (19%) had additional yield from ECC, whereas 11/105 (10%) of patients who did not have fully visualized SCJ had additional yield of CIN2+ from ECC.

In a subanalysis of 280 women participating in the Biopsy Study, sponsored by the National Cancer Institute, Liu and associates[9] reported that the likelihood of a positive ECC increased with age, with yield rising from 10% among patients aged 20 to 29 years (10 of 99) to 25% among patients aged 60 to 69 years (2 of 8), although these findings did not reach statistical significance ($p = .55$). Endocervical curettage showing CIN2+ was associated with higher cytology grade, detection of human papillomavirus (HPV)16, and high-grade colposcopic impression. The additional yield of ECC greater than that identified in colposcopically directed ectocervical biopsies fell with the number of ectocervical biopsies taken; ECC had an additional yield of 14.4% when no ectocervical biopsies were taken, but only 3.9% when 4 additional ectocervical biopsies were performed. Recent reanalysis of this dataset showed that only 5/181 (3%) patients aged at least 30 years had additional yield of CIN2+ from ECC (not shown). When stratified by cytology grade and visualization of the SCJ, only 1/53 (2%) patients with ASCUS/LSIL and fully visualized SCJ had additional yield of CIN2+ from ECC; alternatively, 50 ECCs would have to be done for similar patients to identify 1 CIN2+. Only 1/23 (4%) of women with ASCUS/LSIL and no colposcopic lesion had additional yield of CIN2+ from ECC. Further subanalysis was not feasible because of small numbers, which also limited the precision of estimates.

The 2006 and 2012 ASCCP guidelines recommended ECC when the SCJ was not fully visible based on the rationale that lesions, including some cancer, may be hidden in the endocervical canal if part or all of the SCJ is not seen. This assumption would be reasonable if colposcopic assessment of the SCJ is reproducible; if reproducibility is poor, incorrectly assessing the SCJ as fully visible would allow colposcopists to omit ECC when actually indicated, potentially missing high-grade lesions or cancer. Sideri and associates[13] found acceptable agreement in the visualization of the SCJ in an Italian study (group $\kappa = 0.48$). Vallikad et al.[14] found moderate agreement in an Indian study ($\kappa = 0.53–0.66$). Luyten et al.[15] found that identification of the SCJ was reproducible across centers in Germany. However, the Van der Marel[8] study done in multiple centers in Europe noted no difference in ECC yield among patients with or without a fully visible SCJ. Furthermore, we were unable to identify US research to determine the reproducibility of colposcopists' identification of the location of the SCJ, and most studies have used digital images to assess reproducibility of this finding, although in practice, cervical manipulation may enhance visualization.

The cost-effectiveness of ECC has been explored. Shepherd et al.[16] assessed various age thresholds for ECC. In their modeling study, ECC was both less expensive and more effective in reducing cancer incidence and death for women aged older than 50 years.[16] Cost-effectiveness fell in younger cohorts but seemed to remain within accepted ranges.

GUIDELINES FROM OTHER SOCIETIES

Other national and international organizations have not developed standards for ECC. The British Society for Colposcopy and Cervical Pathology does not recommend ECC at colposcopy, including for glandular lesions.[17] The Society of Canadian Colposcopists recommends ECC for patients with atypical glandular cells on cytology, for patients with a high-grade cytology result when aged older than 40 years, or when no colposcopic lesion is seen.[18] The Irish National Screening Programme guidelines for evaluation of abnormal screening tests do not comment on the utility of ECC.[19] The Cancer Council of Australia offers equivocal guidance: "It is possible, despite a lack of evidence, that ECC could be used in Australian practice".[20] The International Federation of Cervical Pathology and Colposcopy does not have a position on the role of ECC at colposcopy. The International Federation of Cervical Pathology and Colposcopy endorses World Health Organization screening and treatment guidelines, but these do not comment on ECC.[21]

METHODS

The ASCCP convened a working group that reviewed the literature on ECC and developed a manuscript. The manuscript was reviewed by the ASCCP Board of Directors as a panel of experts for peer review. The revised document was then presented to the National Cancer Institute/ASCCP Consensus Stakeholders Group established at the 2019 Consensus Conference to develop and modify guidelines without requiring an in-person meeting.

RECOMMENDATIONS

Endocervical curettage is a low-yield, low-morbidity procedure that can identify CIN2+ when other modalities do not. The risk of cancer among younger patients is declining as those vaccinated against HPV mature, and the benefit of ECC in identifying

occult cancer can be expected to be lower now than in historical studies of mostly unvaccinated patients, especially those currently aged 30 years and younger.[22] The following recommendations apply to the performance of ECC among patients referred to colposcopy for abnormal cervical cancer screening tests. These guidelines do not apply to performance of ECC at the time of excisional procedure, or to ECC performed for the purpose of surveillance, such as after loop electrocautery excision procedure with positive margins or after conization for adenocarcinoma in situ. Assessment of the level of evidence (I–III) and strength of recommendation (A–E) was established according to criteria established for previous consensus guidelines[23] (Table 1).

- ECC is unacceptable in pregnancy (EIII).

Rationale: The cervix is softened during pregnancy in anticipation of labor, and perforation risk is increased. A curette also may perforate fetal membranes or injure the placenta, resulting in pregnancy loss. These risks of ECC are considered to outweigh possible benefits during pregnancy.

- ECC is recommended in patients with cytology reported as HSIL; atypical squamous cells cannot exclude HSIL, atypical glandular cells, or carcinoma (BII).

Rationale: Yield of CIN2+ at ECC is higher for patients with high-grade cytology results, and colposcopy may miss endocervical disease. Van der Marel[8] found that 30% of patients referred for HSIL cytology were diagnosed based on ECC alone, 20% of whom had negative colposcopic impressions. Liu et al.[9] similarly noted higher additional yield of ECC in patients with high-grade cytology.

TABLE 1. Definitions for Grading and Recommendations

Strength of recommendation

A. Good evidence for efficacy and substantial clinical benefit support recommendation for use.

B. Moderate evidence for efficacy or only limited clinical benefit support recommendation for use.

C. Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.

D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Quality of evidence

I. Evidence from at least 1 randomized, controlled trial.

II. Evidence from at least 1 clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than 1 center), or from multiple time-series studies, or dramatic results from uncontrolled experiments.

III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

Terminology used for recommendations

Recommended. Good data to support use when only 1 option is available

Preferred. Option is the best (or one of the best) when there are multiple options

Acceptable. One of multiple options when there is either data indicating that another approach is superior or when there are no data to favor any single option

Not recommended. Weak evidence against use and marginal risk for adverse consequences

Unacceptable. Good evidence against use

Furthermore, Liu et al.[9] noted that the benefit of ECC increased as the number of ectocervical biopsies decreased. Of note, the Liu et al.[9] study included random biopsies when fewer than 4 ectocervical biopsies were taken, a more aggressive regimen than recommended by current ASCCP Colposcopy Standards guidelines.[3] Therefore, recommending ECC in patients with suspicion for precancer or cancer on cytology may protect against missing disease, especially among patients with low-grade or normal colposcopic impressions.[8,9]

- ECC is recommended for all patients undergoing colposcopy for a known positive test for HPV types 16 or 18 (BIII).

Rationale: HPV 16 alone accounts for more than half of cancers; therefore, patients with HPV 16 require special consideration because of the aggressive nature of their infections.[24] The HPV 16 infections are also more likely to progress to precancers than infections with other types.[25] The HPV 18 accounts for an additional 20% of cancers, with a predilection for adenocarcinomas.[24] Adenocarcinomas are more difficult to detect in a preinvasive stage and therefore represent a rising proportion of cancer cases in well-screened populations.[26] Recommendations for performing ECC in patients with HPV18 infections align with the 2020 Society of Gynecologic Oncology guidelines for management of adenocarcinoma.[27]

- Endocervical curettage is recommended at colposcopy after positive results on dual staining for p16/Ki67 (CIII).

Rationale: Dual staining for p16/Ki67 has been Food and Drug Administration-approved as an alternative to cytology triage to determine the need for colposcopy referral for patients who screen HPV-positive or have a negative cytology result but any positive HPV test using the cobas 4800 assay (Roche Diagnostics, Rotkreuz, Switzerland).[28] Studies comparing dual stain to cytology found that patients with positive dual stain results have a higher risk of precancer than those with minor abnormalities.[29] In addition, currently available dual stain technology does not indicate if high-grade morphology is present, such as HSIL, ASC-H or AGC. Therefore, to avoid missing CIN2+, ECC is recommended.

- Endocervical curettage is recommended for all patients previously treated for known or suspected cervical precancer, regardless of the indication for colposcopy (BIII).

Rationale: Patients who have undergone treatment for cervical precancer remain at elevated risk for cervical cancer for at least 25 years.[23] Studies indicate that patients recently treated for precancer have twice the risk of underlying CIN3+ when diagnosed with a minimally abnormal cytology result compared with patients without a history of precancer.[30] Furthermore, scarring from previous treatment may hinder complete visualization of the SCJ, increasing the risk of missing occult disease within the endocervical canal. Because patients with a history of precancer treatment remain at elevated cancer risk and may have difficult colposcopic examinations, ECC is recommended.

- Endocervical curettage is recommended for patients considering observation of CIN2 (CIII).

Rationale: The 2019 ASCCP Risk-Based Management guidelines allow observation with serial HPV, cytology, and colposcopy at 6-month intervals for patients with CIN2 on biopsy whose concerns for future pregnancy complications outweigh their concerns for cancer.[23] However, treatment is always recommended for CIN3 unless the patient is pregnant. To ensure that no CIN3 or higher lesion is present that would preclude observation, ECC is recommended at

all colposcopic examinations for patients undergoing observation for CIN2.

- ECC is recommended when the SCJ is not fully visualized at colposcopy (BII).

Rationale: Colposcopy cannot evaluate disease hidden within the endocervix. Although a multicenter European study noted similar CIN2+ yield in patients with and without adequate SCJ visualization,[8] a US-based study noted a CIN2+ yield of 20.3% among 74 women with unsatisfactory examination compared with 10.5% among 105 women with satisfactory examination ($p = .07$).[9] Therefore, if the SCJ is not fully visualized, ECC is recommended to exclude the presence of a nonvisible lesion within the endocervical canal.

- ECC is preferred for patients aged 40 years and older undergoing colposcopy (BIII).

Rationale: Patients aged 40 years and older are unlikely to have been impacted by changes in HPV epidemiology resulting from HPV vaccination, and therefore have a higher risk for cervical precancer and cancer than younger patients. Among those in perimenopause and menopause, the SCJ recedes with age into the endocervical canal, which increases the importance of ECC in detecting disease, leading to associations of older age with additional yield of ECC.[3,31] Among patients with ASCUS or LSIL cytology, higher yield of ECC was noted among patients aged 40 and older.[32] Therefore, ECC is preferred for patients undergoing colposcopy at ages 40 and older.

- ECC is acceptable for all nonpregnant patients undergoing colposcopy (CIII).

Rationale: These recommendations do not cover all clinical situations, and risk profiles including factors not considered here may justify ECC in some additional situations. The 2019 ASCCP Risk-Based Management Consensus Guidelines recommend deferral of colposcopy for patients with a current result of HPV-positive and minimally abnormal cytology (ASCUS or LSIL) preceded by a colposcopy at which CIN2+ was not found. Because colposcopy findings are used to determine future management, ensuring adequate histology at each examination is paramount.

- These recommendations notwithstanding, omitting ECC at the time of colposcopy is acceptable under the following circumstances:
  - o when a subsequent excisional procedure is planned (CIII)

Rationale: ECC may increase pain and cost and is unlikely to alter management when a cervical excisional procedure is planned because the latter will assess the endocervix.

  - o when the endocervical canal does not admit a sampling device (CIII)

Rationale: If the os is stenotic, efforts may be made to access the endocervix, including dilation. Misoprostol and other cervical ripening agents have shown potential for improving access to the endometrial cavity at hysteroscopy[33] but have not been assessed as agents to improve the yield of ECC in patients with endocervical stenosis; until such research has been conducted, ripening agents should not be used outside clinical trials. Given the low yield of ECC, if the endocervical canal does not admit a sampling device, ECC may be omitted rather than subjecting the patient to a surgical procedure to access the endocervix.

  - o In nulliparous patients aged younger than 30 years with cytology reported as ASCUS or low-grade SIL, regardless of whether the SCJ is fully visualized (BII).

Rationale: The additional yield of ECC among young women with ASCUS/LSIL cytology and/or HPV types other than 16/18 is low, even when the SCJ is obscured. Liu et al.[9] noted only 10 CIN2+ among 99 women aged 21 to 29 years undergoing ECC. Separately, they noted only a 7% yield among women with low-grade cytologic abnormalities. Similarly, Van der Marel et al.[8] found 0 cases of CIN2+ on ECC among women presenting with ASCUS/LSIL results. Because individuals currently aged younger than 30 years have lower rates of oncogenic HPV infections because of HPV vaccination,[34] the yield of ECC in patients aged younger than 30 years with minor cytologic abnormalities is likely to further decrease in the future.

ACKNOWLEDGMENT

This work was prepared by a military or civilian employee of the US Government (Elizabeth Kostas-Polston) as part of the individual's official duties, and therefore, is in the public domain and does not possess copyright protection (public domain information may be freely distributed and copied; however, as a courtesy, it is requested that the Uniformed Services University and the author be given an appropriate acknowledgement).

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