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Guidelines

Diagnosis and Management of Adenocarcinoma in Situ

A Society of Gynecologic Oncology Evidence-Based Review and Recommendations

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This publication represents an extensive literature review with the goal of providing guidelines for the evaluation and management of cervical adenocarcinoma in situ (AIS). The authors drafted the guidelines on behalf of the Society of Gynecologic Oncology, and the guidelines have been reviewed and endorsed by the ASCCP. These guidelines harmonize with the ASCCP Risk-Based Management Consensus Guidelines and provide more specific guidance beyond that provided by the ASCCP guidelines. Examples of updates include recommendations to optimize the diagnostic excisional specimen, AIS management in the setting of positive compared with negative margins on the excisional specimen, surveillance and definitive management after fertility-sparing treatment, and management of AIS in pregnancy. The increasing incidence of AIS, its association with human papillomavirus–18 infection, challenges in diagnosis owing to frequent origin within the endocervical canal, and the possibility of skip lesions all make AIS a unique diagnosis whose management needs to be differentiated from the management of the more prevalent squamous cell dysplasia.

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This evidence-based review and recommendations have been endorsed by ASCCP.

Each author has confirmed compliance with the journal's requirements for authorship.

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The incidence of cervical adenocarcinoma in situ (AIS) is rising, and though an increase in the number of diagnoses of in situ squamous cell carcinoma has been associated with a concomitant decrease in the incidence of invasive squamous cell carcinoma owing to earlier diagnosis and treatment, a similar decrease in subsequent invasive adenocarcinoma has not occurred.[1] This suggests delayed diagnosis of AIS, a shorter interval of disease progression from clinically evident AIS to invasive adenocarcinoma, or both. Although other cervical cancer screening management guidelines provide specific algorithms for initial screening and management,[2–5] they do not provide detailed recommendations for management and surveillance of AIS, especially when conservative management is desired. The purpose of these guidelines is to provide clinicians with information and recommendations for diagnosis and management of cervical AIS.

BACKGROUND

Epidemiology

The incidence of cervical AIS has increased over the past few decades, especially among individuals aged 30–40 years.[1,6] The mean age at diagnosis is 35–37 years,[6,7]

and the current incidence rate is approximately 6.6 per 100,000 persons, increasing to 11.2 per 100,000 persons at the peak age of 30–39 years.[6] The average interval between a diagnosis of clinically detectable AIS and early invasive cancer is at least 5 years.[8] Additionally, approximately 55% of patients with AIS have a coexisting squamous lesion.[7]

Etiology and Risk Factors

Human papillomavirus (HPV) infection, particularly infection with HPV-16, -18, or both, is the primary risk factor for AIS and associated cervical cancer. Although HPV-18 is associated with only 8% of all high-grade dysplasia (cervical intraepithelial neoplasia [CIN] 2 or worse and AIS) diagnoses (compared with 46–58% for HPV-16), it is associated with 38–50% of AIS diagnoses and 50% of all invasive cancer diagnoses (squamous cell carcinoma plus adenocarcinoma).[6,9–11] Therefore, factors that inhibit suppression of HPV are additional risk factors for AIS, such as immunosuppression (eg, rheumatologic disease on two or more immunosuppressants, human immunodeficiency virus [HIV], solid organ transplant) and smoking. Some studies also suggest oral contraceptive pill use as a risk factor for AIS.[12] Conversely, vaccination against HPV is anticipated to be protective, with early evidence of this demonstrated by a decrease in incidence rate of AIS in the first 8 years of the HPV Vaccine Impact Monitoring Project among women aged 21–24 years, despite stable incidence rates in women aged 25–29 years and increases in women aged 30–39 years.[6]

GUIDELINE QUESTIONS

This clinical practice guideline addresses the following clinical questions: 1) What clinical evaluation and diagnostic tests should be performed for individuals with suspected cervical AIS? 2) How should diagnostic or therapeutic excisional procedures be performed? 3) What are the recommendations for patients undergoing definitive surgical management with positive compared with negative excisional biopsy margins? 4) Which patient and disease criteria should be used to identify individuals who are eligible for fertility-sparing therapy? 5) What is the recommended surveillance after treatment of AIS? 6) How should AIS be managed during pregnancy? (Fig. 1).

METHODS

Guideline Development Process

The authors reviewed the available evidence, contributed to the development of the guidelines, provided critical review of the guidelines, and finalized the guideline recommendations. The guidelines were also reviewed and approved by the Society of Gynecologic Oncology (SGO) Clinical Practice Committee, SGO Education Committee, SGO Publications Committee, and the SGO board members before submission for publication.

The recommendations were developed by a panel of gynecologic oncologists who were members of the SGO Clinical Practice and Education Committees. Panelists reviewed and considered evidence from current cervical cancer screening and dysplasia management guidelines, observational studies, and meta-analyses; phase III randomized clinical trials for management of AIS do not currently exist. A list of the MeSH terms searched are included in Appendix 1, available online at http://links.lww.com/AOG/B790.

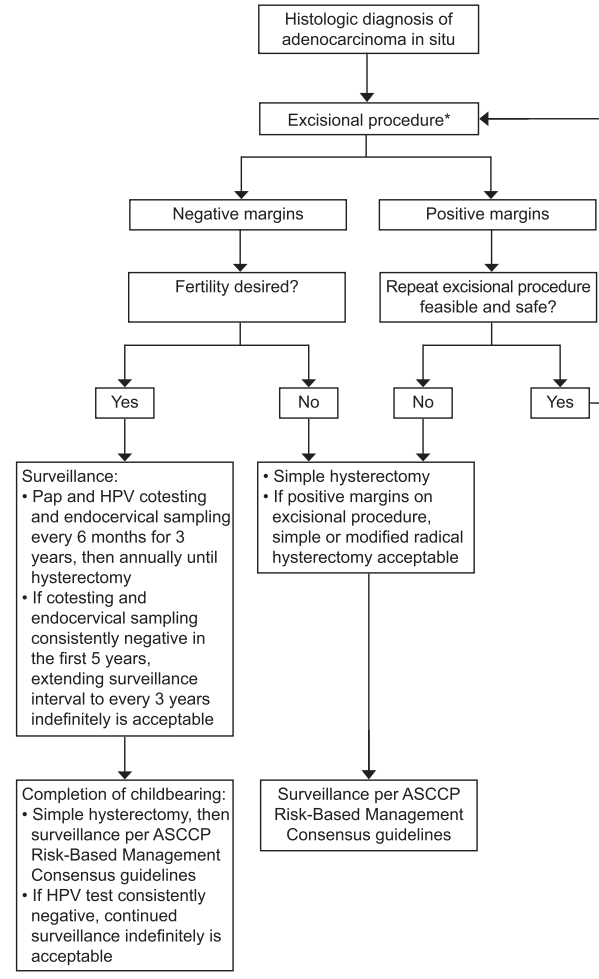

Fig. 1. Summary of adenocarcinoma in situ management recommendations. *Cold knife conization or loop electrosurgical excision procedure acceptable provided an adequate specimen can be obtained: 1) intact, nonfragmented (top-hat serial endocervical excisions unacceptable); 2) length of specimen must be at least 10 mm. HPV, human papillomavirus.

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The terminology used in these guidelines was adopted from the American Society for Colposcopy and Cervical Pathology (ASCCP) management guidelines[3] using a two-part rating system to grade the strength of recommendation and quality of evidence (Table 1). The rating for each recommendation is given in parentheses. Similar to the ASCCP guidelines, the terms "recommended," "preferred," "acceptable," "unacceptable," and "not recommended" are used to describe interventions.

CLINICAL CONSIDERATIONS AND RECOMMENDATIONS

Clinical Question 1

What clinical evaluation and diagnostic tests should be performed for patients with suspected cervical AIS?

Recommendation 1.1

Evaluation of abnormal cytology or a positive HPV test result or both is recommended per the ASCCP Risk-Based Management Consensus Guidelines (BII), and colposcopic examination should be performed using the ASCCP colposcopy standards (Table 2).[13] Atypical glandular cells (AGC) and HPV-16 and -18 are associated with AIS and should be evaluated with colposcopy, endocervical sampling, and endometrial biopsy, as recommended by the ASCCP Risk-Based Management Consensus Guidelines (http://www.asccp.org/consensus-guidelines). Given the association of HPV-18 with AIS, endocervical sampling in the setting of a positive HPV-18 test result regardless of colposcopy findings is acceptable (CIII).

Recommendation 1.2

A diagnostic excisional procedure is recommended for all patients with AIS diagnosed on cervical biopsy, as well as all patients whose cervical biopsy and endocervical curettage results are negative in the setting of cytology results showing AIS or AGC-favor neoplasia. For persistent AGC-not otherwise specified, refer to ASCCP Risk-Based Management Consensus Guidelines. A diagnostic excisional

Table 1. Rating the 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 supports 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 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 one randomized, controlled trial.
II	Evidence from at least one clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one 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 one 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.

* Modified with permission from: Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Disease 1994;18(3):421 *and* Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001;32(6);851–4. These tables are available in free-to-view only with the permission of Oxford University Press on behalf of the Infectious Diseases Society of America.

† The assignment of these terms represents an opinion ratified by vote during the 2012 consensus conference.

Table 2. ASCCP Risk-Based Colposcopy Standards and Atypical Glandular Cells Evaluation

Precolposcopy Test Results	Colposcopic Finding*	Recommendation(s)
Low risk: cytology less than HSIL and HPV-16 and -18–negative	Normal	No biopsies
	Acetowhitening, metaplasia, other abnormality	2–4 targeted biopsies of acetowhite, metaplastic, or abnormal lesions
Intermediate risk: cytology HSIL, ASC-H, or HPV-16– or -18–positive	Normal	Nontarget biopsies can be considered[†] For HPV-18–positive: endocervical sampling[‡] acceptable regardless of colposcopic findings (SGO-specific recommendation)
	Acetowhitening, metaplasia, other abnormality	2–4 targeted biopsies of acetowhite, metaplastic, or abnormal lesions
High risk: combination of 2 of the following: HSIL HPV-16– or -18–positive High-grade colposcopic impression Refer to The ASCCP Risk-Based Management Consensus Guidelines for other history–test result combinations that have a 50% or greater risk of high-grade dysplasia		Excisional treatment without colposcopic examination (preferred if risk of high-grade dysplasia is 60% or higher per ASCCP Risk-Based Management Consensus Guidelines[†]) OR Colposcopy with biopsies
AGC, AIS	Normal	Endocervical sampling[‡] Endometrial sampling if 35 y of age or older, risk factors, or atypical endometrial cells specified on cytology Nontarget biopsies can be considered[§]
	Acetowhitening, metaplasia, other abnormality	2–4 targeted biopsies of acetowhite, metaplastic, or abnormal lesions Endocervical sampling[‡] Endometrial sampling if 35 y of age or older, risk factors, or atypical endometrial cells specified on cytology
AIS, AGC-favor neoplasia	Biopsy and endocervical sampling histology negative	Diagnostic excisional procedure recommended
Any of the above	Squamocolumnar junction not fully visualized (regardless of other findings)	Endocervical sampling[‡]

HSIL, high-grade squamous intraepithelial lesions; HPV, human papillomavirus; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions; SGO, Society of Gynecologic Oncology; AGC, atypical glandular cells; AIS, adenocarcinoma in situ.

Data from Wentzensen N, Schiffman M, Silver MI, Khan MJ, Perkins RB, Smith KM, et al. ASCCP colposcopy standards: risk-based colposcopy practice. J Low Genit Tract Dis 2017;21:230–4.

* ASCCP minimal colposcopic reporting standards: squamocolumnar junction visibility (fully visualized or not fully visualized); acetowhitening (yes or no); lesion(s) present (yes or no; acetowhite or other); colposcopic impression (normal or benign; low-grade; high-grade; cancer).

† Insufficient evidence for or against nontarget biopsies in this population.

‡ Endocervical sampling can be done with a curette or a brush.

§ ASCCP Risk-Based Management Guidelines: http://www.asccp.org/consensus-guidelines.

procedure is recommended to rule-out an invasive adenocarcinoma, even when definitive hysterectomy is planned (AII).

Literature Review

Nearly all AIS lesions are asymptomatic and thus are diagnosed during cervical cancer screening examinations. A cytologic diagnosis of AGC results in a diagnosis of AIS in 3–4% of cases and invasive cervical adenocarcinoma in 2%.[14] However, any degree of cytologic atypia can be indicative of AIS, and one study showed AIS diagnosis is most often preceded by a low-grade cytologic abnormality (atypical squamous cells of undetermined significance, low-grade

squamous intraepithelial lesion).[6] Moreover, because these lesions originate from inside the endocervix, the abnormal cells are often missed on cytology.[3] The ASCCP Risk-Based Management Consensus Guidelines provide individualized recommendations for evaluation of abnormal cytologic or positive HPV test results or both (http://www.asccp.org/consensus-guidelines). Although not specified by the ASCCP management guidelines, given the high rate of HPV-18–positive AIS, endocervical sampling for any patient who tests positive for HPV-18 is acceptable. An endocervical sample can be obtained using an endocervical curette, which may provide cervical stroma to aid in grading of dysplasia, or an endocervical brush, which is less prone to insufficient sampling and may have higher sensitivity.[3,15,16]

Adenocarcinoma in situ frequently coexists with squamous dysplasia. When concomitant AIS and CIN are diagnosed, management should proceed per the recommendations for AIS. When AIS is diagnosed on cervical biopsy, approximately 15% will be associated with an invasive adenocarcinoma.[17] Therefore, the next step in evaluation is a diagnostic excisional procedure to confirm the diagnosis, assess the extent of disease, evaluate for coexisting squamous lesions, and exclude invasive adenocarcinoma before definitive management. A diagnostic excisional procedure is also recommended when cervical biopsies and endocervical curettage are negative in the setting of cytology results of AIS, AGC-favor neoplasia, or persistent AGC-not otherwise specified. A diagnostic excisional procedure before definitive management with hysterectomy is recommended to evaluate for invasive adenocarcinoma, which may require radical hysterectomy; if negative margins are not achieved on the first excision specimen, a second excisional procedure is recommended before hysterectomy to exclude an invasive cancer unless this cannot be performed safely.

Clinical Question 2

How should diagnostic or therapeutic excisional procedures be performed?

Recommendation 2.1

Excisional procedures optimally result in removal of an intact specimen to facilitate accurate interpretation of margin status. Thus, excision by cold knife conization is preferred unless the surgeon is able to consistently remove an intact ("top hat" endocervical excision is unacceptable) specimen of adequate length and width (AII).

Recommendation 2.2

Length of the excisional specimen of at least 10 mm is preferred and can be increased to 18–20 mm in patients who have completed childbearing (BII). Endocervical sampling above the excisional bed to evaluate for residual disease is preferred (CIII).

Literature Review

Traditionally, cold knife conization has been recommended over loop electrosurgical excision procedures (LEEP) owing to concern that cautery artifact could obscure the diagnosis. However, a meta-analysis of retrospective studies showed no difference in residual disease (LEEP 9.1% vs cold knife conization 11%) or recurrence risk (LEEP 7.0% vs cold knife conization 5.6%) by excisional method despite a higher risk of positive margins with LEEP (44%) compared with cold knife conization (29%; relative risk 1.55, 95% CI 1.34–1.80).[18] Thus, the ASCCP management guidelines allow diagnostic excision using any modality, but it is imperative that, "care must be taken to keep the specimen intact and margins interpretable, avoiding fragmentation of the specimen, including 'top-hat' serial endocervical excisions."[3] Therefore, except in the hands of a highly skilled LEEP surgeon who is able to obtain an adequate specimen without fragmentation (ie, one intact specimen removed with one pass of the loop; "top hat" excision is unacceptable), excision by cold knife conization is preferred because there is a higher likelihood of the specimen being removed in one piece with adequate depth and width. Length of the conization specimen should be at least 10 mm and can increase to 18–20 mm for patients who have completed childbearing.[19,20] For surgeons who are not able to consistently obtain intact excisional specimens with adequate length, referral for the initial excisional procedure to a gynecologic oncologist or other surgeon who specializes in the management of cervical dysplasia is preferred. Data on utility of sampling above the excisional bed are conflicting, but endocervical sampling with endocervical curettage or endocervical brushing above the excisional bed to evaluate for residual disease is preferred owing to the frequent location of AIS within the endocervical canal, which makes determining the extent of the lesion more difficult, and the potential for multifocal disease.[7,21,22]

Clinical Question 3

What are the recommendations for patients undergoing definitive surgical management with positive compared with negative excisional biopsy margins?

Recommendation 3.1
Simple hysterectomy is preferred for patients with confirmed diagnosis of AIS with negative margins on the conization specimen (BIII).

Recommendation 3.2
Either modified radical hysterectomy or simple hysterectomy is acceptable for patients with confirmed diagnosis of AIS with positive margins on the conization specimen (CIII).

Recommendation 3.3
Surgical assessment of lymph nodes is acceptable at the time of hysterectomy (CIII).

Literature Review
Margin status is a predictor for residual and recurrent disease and progression; thus, it is essential that the margin status can be assessed and that margins are negative. Recurrence risk of AIS is only 2.6% with negative margins but increases to 19% when margins are positive.[7] Adenocarcinoma in situ is also associated with "skip lesions"–foci of adenocarcinoma cells that are not contiguous. Therefore, even with negative margins, the risk of residual AIS on a second excisional specimen is 20% (compared with 53% if margins are positive), and 2% of patients will be diagnosed with an invasive cancer (compared with 6% if margins are positive). Therefore, simple hysterectomy is recommended for all patients with a confirmed diagnosis of AIS with negative margins on conization. For patients with a persistent positive margin despite repeat excisional procedures, a modified radical hysterectomy or radical trachelectomy for those who desire future pregnancy is acceptable owing to an increased risk of diagnosing an occult invasive carcinoma.[23,24] Although, historically, radical hysterectomy has been the treatment of choice for microinvasive adenocarcinoma of the cervix owing to concerns about skip lesions and difficulty determining depth of invasion, retrospective observational studies have not shown that radical surgery for microinvasive adenocarcinoma is associated with a survival benefit compared with simple hysterectomy[25–28]; therefore, simple hysterectomy even for patients in whom a negative margin cannot be achieved with excisional procedures is acceptable. The ongoing prospective Gynecologic Oncology Group protocol 278 (NCT01649089), in which patients with stage IA1–IB1 cervical carcinomas, including adenocarcinomas, will be surgically treated with simple hysterectomy and pelvic lymphadenectomy, may help clarify whether simple hysterectomy is sufficient for all microinvasive cervical cancers.

For patients who are ultimately diagnosed with microinvasive adenocarcinoma after hysterectomy, the risk of lymph node metastases ranges from less than 1% to 3%, with observational study data limited by the fact that lymphadenectomy was not performed in all patients.[27,28] Therefore, lymph node assessment at the time of surgery for AIS is acceptable but not required and should be guided by the surgeon's risk assessment, which may include factors such as margin status of the preceding excisional specimen or postexcisional endocervical sampling results, pathologist concern for malignancy, HPV results (HPV-16– or -18–positive vs other high-risk HPV type), and patient risk factors (eg, immunosuppression).

The risk of ovarian metastases in patients with invasive adenocarcinoma is 2–5%[29–34] (compared with a less than 1% risk in the setting of squamous cell carcinoma). Risk of ovarian metastases increases with increasing clinical stage of disease and deeper stromal invasion and thus is rare in the setting of microinvasive disease.[29–32] Furthermore, retrospective observational studies have not shown a difference in recurrence rates or survival when ovaries are left in situ. Therefore, decisions regarding ovarian management at the time of hysterectomy should be individualized based on patient age, hormonal status, and other risk factors. Opportunistic salpingectomy at the time of hysterectomy should be discussed with patients for potential ovarian or fallopian tube cancer risk reduction per the American College of Obstetricians and Gynecologists' Committee Opinion[35] but is not required for management of AIS or adenocarcinoma of the cervix.

Clinical Question 4

Which patient and disease criteria should be used to identify patients who are eligible for fertility-sparing surgery?

Recommendation 4.1
For patients of reproductive age who desire future pregnancy, for whom negative margin status on conization has been achieved, and who are willing and able to adhere to surveillance recommendations, fertility-sparing management with a conization procedure is acceptable (AII).

Recommendation 4.2
For patients in whom negative margins cannot be achieved after multiple excisional procedures, fertility-sparing management is not recommended (DIII).

Recommendation 4.3

For patients who initially underwent fertility-sparing management of AIS and have subsequently completed childbearing, either hysterectomy or continued surveillance is acceptable for those who have had consistently negative HPV test results during surveillance (CIII). For patients who have had positive HPV test results during surveillance, hysterectomy after completion of childbearing is preferred (CIII).

Literature Review

Unfortunately, AIS is often diagnosed in patients of reproductive age who desire future pregnancy. For these individuals, conservative management with an excisional procedure achieving negative margins is acceptable. Data on long-term outcomes after conservative management of AIS are limited, with small study populations ranging from 28 to 136 patients and average follow-up period of 3–5 years. The recurrence risk for AIS among patients undergoing an excisional procedure is approximately 3%[36–41] but has been reported to be as high as 12%.[42] One study showed positive HPV test results during surveillance to be the only significant predictor for recurrence (odds ratio [OR] 2.72, 95% CI 1.08–6.87) and positive HPV test results (OR 3.74, 95% CI 1.85–7.62) and positive margins (OR 5.0, 95% CI 1.09–20.0) to be the only predictors for progressive disease.[42] Therefore, for patients with consistently negative HPV test results during surveillance, either hysterectomy or continued observation without hysterectomy after completion of childbearing is acceptable. However, for patients who have positive HPV test results during surveillance, hysterectomy after completion of childbearing is preferred.

For patients in whom negative margins cannot be achieved after multiple excisional procedures, hysterectomy is recommended, and fertility-sparing management should be pursued only in select cases and after a frank discussion about the significantly increased risk of persistent or recurrent AIS and cancer. Data are lacking on outcomes after radical trachelectomy for treatment of persistent AIS, but it could be considered as an alternative for patients who strongly desire future fertility.

Clinical Question 5

What is the recommended surveillance after treatment of AIS?

Recommendation 5.1

For patients who undergo definitive management with hysterectomy, surveillance per the ASCCP Risk-Based Management Consensus guidelines (http://www.asccp.org/consensus-guidelines) is recommended for at least 25 years after diagnosis, even if that extends the testing period beyond the age of 65 years (CIII).

Recommendation 5.2

i) For patients who undergo fertility-sparing management, surveillance with Pap plus HPV co-testing and endocervical sampling is recommended every 6 months for the first 3 years, then annually for at least 2 years or until hysterectomy is performed (BII).
ii) For patients who have consistently negative co-testing results in the first 5 years of surveillance, extending surveillance to every 3 years indefinitely is acceptable (CIII).

Literature Review

Owing to an increased risk of developing vaginal dysplasia after a history of cervical dysplasia, it is recommended that definitive surgical management should be followed by at least 25 years of surveillance per the ASCCP Risk-Based Management Consensus Guidelines, with vaginal colposcopy performed to evaluate high-grade cytology results, persistent low-grade cytology results, or persistent positive HPV test results (two or more); although the HPV test is not currently U.S. Food and Drug Administration–approved for vaginal screening or surveillance, the high negative predictive value of the test can identify those individuals who are at low risk for developing vaginal cancer.[43] Management of abnormal vaginal cytology and positive HPV test results in this setting is beyond the scope of these management guidelines and is well-defined in the review article by Khan et al.[43]

After fertility-sparing management, "long-term follow-up with a combination of co-testing and colposcopy with endocervical sampling" is recommended per the ASCCP guidelines.[3] However, the ASCCP guidelines do not specify the frequency of follow-up. A prospective study of 119 conservatively treated patients with AIS showed a persistent, recurrent, or progressive disease rate of 13%, with 4% of recurrences occurring as late as 3 years after the initial excisional procedure.[42] Notably, there were no recurrences among patients whose posttreatment surveillance HPV test results were negative, and multivariate analysis showed that HPV status was the strongest predictor for recurrent disease. Sensitivity of HPV testing for persistent, recurrent, or progressive disease is 90%, compared with 60% for cytology.[44] Preliminary data

suggest the median time to HPV clearance is longer for patients with AIS compared with those with CIN, and thus prolonged surveillance is recommended.[44] Given the increased risk of recurrent or progressive disease in the first 36 months after excisional procedure, we recommend co-testing (Pap plus HPV tests) with endocervical sampling (endocervical curettage or endocervical brushing) every 6 months for 3 years, then annual co-testing with or without endocervical sampling for at least 2 years or until hysterectomy at the completion of childbearing.[45] For patients with a history of AIS who have at least two consecutive negative co-test results after treatment, the 5-year risk of CIN 2 or worse is 1.5%.[45] Although this risk is still substantial compared with the 5-year risk of CIN 2 or worse after negative screening test results without a history of high-grade dysplasia, lengthening the surveillance interval to every 3 years is acceptable for individuals who have consistently negative co-testing results in the first 5 years of surveillance.

Clinical Question 6

How should AIS be managed during pregnancy?

Recommendation 6.1

In the absence of a clinical or histologic suspicion of invasive cancer, excisional procedures are not recommended during pregnancy. Colposcopy omitting endocervical sampling is recommended each trimester, with an excisional procedure performed postpartum. Delaying excision to approximately 6–8 weeks postpartum is preferred, but an excisional procedure as early as 4 weeks postpartum is acceptable (BII).

Recommendation 6.2

If an excisional procedure is performed during pregnancy owing to suspicion for an invasive cancer, placement of a prophylactic cerclage is acceptable (CIII).

Literature Review

Excisional procedures during pregnancy are associated with an increased risk of hemorrhage, spontaneous abortion, and preterm delivery. Additionally, there is a higher rate of residual disease after excisional procedures performed during pregnancy compared with those performed in a nongravid state.[46] Therefore, although conization is generally recommended for evaluation of AIS diagnosed on biopsy, it is not recommended during pregnancy unless there is suspicion for an invasive cancer, which would affect the timing of delivery, owing to risk of hemorrhage, infection, premature rupture of membranes, and preterm delivery. If conization is necessary during pregnancy, ideal timing of the procedure is during the second trimester. Excisional procedures should not be performed within 4 weeks of expected delivery owing to increased risk of hemorrhage or extension of the wound. If an excisional procedure is performed during pregnancy, immediate postprocedure placement of a prophylactic cerclage should be considered to decrease risk of hemorrhage and preterm delivery.[47,48] If conization is delayed until after delivery, colposcopy each trimester with conization after delivery is recommended owing to a high rate of persistent high-grade dysplasia.[49,50] Delaying an excisional procedure until 6–8 weeks postpartum is preferred, but, owing to concern for loss to follow-up resulting from expiration of health insurance postpartum or other factors, performing an excisional procedure as early as 4 weeks postpartum is acceptable.

SUMMARY OF RECOMMENDATIONS

- Incorporating age-appropriate HPV testing into cervical cancer screening is recommended, because HPV testing increases the sensitivity of screening for adenocarcinoma lesions, which often originate inside the endocervical canal and may not be detected on cytology.
- An excisional procedure to rule out an invasive adenocarcinoma before definitive surgical therapy with hysterectomy is recommended. Obtaining an intact specimen ("top hat" excision is unacceptable) with a length of at least 10 mm is preferred, with a goal of achieving negative margins. For surgeons who are unable to consistently obtain intact excisional specimens with adequate length, referral to a gynecologic oncologist or other cervical dysplasia specialist for excisional biopsy is preferred. Endocervical sampling above the excisional site is preferred to evaluate for residual disease.
- Hysterectomy is preferred for all patients who have completed childbearing. If negative margins on the excisional specimen(s) cannot be achieved, either a modified radical hysterectomy or simple hysterectomy is acceptable, recognizing the increased (6%) risk of an occult invasive adenocarcinoma. Surgical assessment of lymph nodes is acceptable at the time of hysterectomy.
- For patients who desire future pregnancy, conservative management with close follow-up provided negative margins can be achieved is acceptable. Co-testing with endocervical sampling every 6 months for 3 years followed by annual co-testing with or

without endocervical sampling for at least 2 years or until hysterectomy at the completion of childbearing is recommended. Lengthening the surveillance interval to every 3 years is acceptable for patients who have consistently negative co-testing results in the first 5 years of surveillance.

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