Recommendations to Minimize Unnecessary Surgical Procedures for Women with Abnormal PAP Smears

Daniel M. Avery, MD and Amanda Elise Dailey

Abstract

Millions of women undergo cervical cytology screening for cervical cancer yearly in this country. About seven percent of these are abnormal and require further evaluation. Abnormal cervical biopsies have been treated with cervical conization, laser ablation, cryotherapy and loop electrosurgical excision procedures. Multiple surgical procedures performed on the cervix may destroy vital tissue and increase the number of women with incompetent or stenotic cervices. Since many low-grade lesions will regress spontaneously if given sufficient time, especially in young women, minimizing unnecessary surgical procedures is appropriate. The "2001 Consensus Guidelines for the Management of Women with Cervical Cytological Abnormalities" discusses strategies to safely avoid unnecessary procedures.[1] We recommend the use of a modified version of these guidelines developed at the University of Alabama in Birmingham and discussed in this article to ensure the best possible patient outcomes.

Introduction

Each year about 50,000,000 women undergo screening for cervical cancer with Pap smears in this country.[1] About seven percent of these or 3,500,000 are abnormal and require further evaluation.[1] It is estimated that 10,520 new cases of cervical cancer and 3,900 cervical cancer deaths occur annually.[2] A major public health challenge is trying to determine which women are at risk for progression to cervical cancer, what diagnostic procedures they need and what treatment, if any, is indicated.[1]

Before colposcopy, gynecologists performed hysterectomies for abnormal Pap smears. A Class III (moderate or severe dysplasia) or Class IV (invasive cervical cancer) Pap smear meant major surgery. With the advent of colposcopy and directed biopsies, many gynecologists treated anything with cytologically abnormal results with some form of therapy, including hysterectomy. Subsequently, physicians have treated abnormal cervical biopsies with cervical conization, laser ablation, cryotherapy and loop electrosurgical excision (LEEP). Table 1 lists current treatments for abnormal Pap smears.

New Language of Pap Smear Results

An expert panel of more than 400 pathologists, cytotechnologists, clinicians and patient advocates from more than 44 professional societies and from more than 20 countries convened in 2001 to develop the "2001 Bethesda System for reporting cervical cancer screening results."[3] This established the terminology for reporting Pap smear results is now used universally and is presented in Table 2.

Treatment Guidelines for Pap Smear Results

The Bethesda System gives guidelines for the management of abnormal Pap smears.[3] A simplified version of the "Bethesda Guidelines" developed by the Department of Obstetrics and Gynecology at the University of Alabama in Birmingham[4] is presented in Table 3. An algorithm for management of abnormal Pap smears based on the University of Alabama in Birmingham modified guidelines is presented in Diagram 1 and is discussed on the next page.

Pap smears should utilize liquid-based cytology because this technique has the advantage of fewer artifacts and provides an easier to read, more uniform slide. It also can be utilized by computer programs to assist in the reading of Pap smears, improving speed of testing, accuracy, quality assurance and reproducibility.[5]

This technique also allows for qualitative detection of High Risk or carcinogenic HPV Types 16/18/31/33/35/39/45/51/

Table 1: Treatments for Abnormal Pap Smears

HPV Typing for High Risk Types
Colposcopy with Directed Biopsies & Endocervical Curettage
Conservative Management with Repeat Screening
Cryotherapy
Laser Vaporization
Cold Knife Conization
LEEP Conization
Endometrial Biopsy
D&C/Hysteroscopy

52/56/58/59/68 DNA in cervical specimens. It also helps determine the need for colposcopy in ASCUS Pap smear results, according to Laboratory Corporation of America.[6]

Patients with NILM (No Evidence of Intraepithelial Lesion or Malignancy) only need to have their Pap smear repeated in one year.

Patients who have ASCUS (Atypical Squamous Cells of Undetermined Significance) need HPV typing for High Risk or carcinogenic types as described above. Those that are negative for High Risk HPV should be treated like patients with NILM and return for annual screening in one year. Patients positive for High Risk HPV should undergo colposcopy and biopsy.

Patients with Pap smears showing ASC-H (Atypical Squamous Cells, cannot rule-out High Grade Dysplasia), LGSIL (Low Grade Dysplasia) or HGSIL (High Grade Dysplasia) should undergo colposcopy with biopsy. If the biopsy shows mild dysplasia or less, that patient only needs repeat HPV typing in one year or repeat Pap smear in six months.

Patients with biopsies worse than low-grade dysplasia need treatment with cryotherapy, laser vaporization, LEEP or cold-knife conization. Cryotherapy and laser ablate the surface cells and allow new, hopefully normal cells to regrow. Both are less damaging to cervical tissue than the other methods discussed below and can be performed in an office setting. Cryotherapy is relatively inexpensive. Many gynecologists believe that laser therapy may destroy the HPV virus in adjacent tissue. LEEP and cold-knife conization remove considerably more tissue and hence increase the risk for cervical incompetence or cervical stenosis. LEEP may be performed either in an office or outpatient surgery setting. Cold-knife conization is usually performed in an outpatient surgery setting.

Carcinoma-in-situ is usually treated with LEEP or cold-knife conization, not only to provide a tissue diagnosis but also to exclude invasive cancer. When there are significant differences in Pap smear and cervical biopsy results then there is a need for further evaluation with LEEP or cold-knife conization.

Patients with AGUS (Atypical Glandular Cells of Undetermined Significance) need colposcopy, biopsy and endocervical curettage if under the age of 35. Patients with AGUS who are 35 or older need colposcopy, biopsy and endocervical curettage plus an endometrial biopsy.[4] An abnormal endometrial biopsy needs to be further evaluated with dilatation and curettage under hysteroscopic guidance.

Table 2: New Language of Pap Smear Results[3]

NEW CLASSIFICATION	OLD CLASSIFICATION
No Evidence of Intraepithelial Lesion or Malignancy (NILM)	Normal; Class I
Atypical Squamous Cells of Undetermined Significance	Class II
Atypical Squamous Cells, Cannot Rule out High Grade Dysplasia	Class II
Low Grade Squamous Intraepithelial Lesion (LGSIL)	Class III; CIN I
High Grade Squamous Intraepithelial Lesion (HGSIL)	Class III; CIN II & III; Moderate and Severe Dysplasia; Carcinoma-in-situ
Squamous Cell Carcinoma	Class IV; Invasive cervical cancer
Atypical Glandular Cells of Undetermined Significance (AGUS)	Class II

Discussion

Multiple surgical procedures on the cervix may destroy vital tissue and increase the number of women with incompetent or stenotic cervices. Adequate colposcopy is difficult when there is excision of large portions of the cervix. Sometimes only remnants of what used to be cervix are present. Occasionally the cervical os is only barely visible; sometimes the cervix is not even apparent.

LEEP is a commonly performed procedure on the cervix. It is quick, has minimal blood loss and yields a tissue diagnosis. It can be performed either in the office or outpatient surgery setting. However, according to Samson et al, LEEP is associated with an increased risk of preterm delivery, preterm delivery after preterm rupture of membranes and low birth-weight infants.[6] That study found no difference in other neonatal complications or characteristics of the LEEP procedure itself such as depth of excision.[6] In contrast, more ablative rather than excisional surgery, such as cryotherapy or laser therapy, has not been shown to have a negative effect on pregnancy outcome.[6]

Initially, the 1988 Bethesda System implied that all grades of squamous intraepithelial lesions were closely linked precursors of cervical cancer and required colposcopy and treatment.[3] There has been a shift in the management of low grade squamous intraepithelial lesions in this country based on the realization that most low grade lesions are self-limited, especially in young women.[3]

The 2001 Bethesda System was developed as a system of terminology that would provide clear guidelines for the management of abnormal Pap smears. The system terminology reflected the virological, molecular and clinical evidence that low-grade lesions are probably a transient infection with HPV.

Table 3: University of Alabama in Birmingham Modified Cervical Cancer Screening Guidelines[4]

1. All Pap smears for annual cervical cancer screening should use liquid-based cytology.
2. Patients with NILM should have a repeat Pap smear in one year.
3. Patients with ASCUS should have HPV testing for High Risk HPV Types 16/18/31/33/35/39/45/51/52/56/58/59/68 (carcinogenic types).
4. Patients with ASCUS who are negative for High Risk HPV Types should have a repeat Pap smear in one year.
5. Patients with ASCUS who are positive for High Risk HPV Types should undergo colposcopy.
6. Patients with ASC-H, LGSIL or HGSIL should undergo colposcopy.
7. Patients with ASCUS who are positive for High Risk HPV types and those with ASC-H or LGSIL who are then found to have Mild Dysplasia or less on biopsy (as recommended above) are managed with repeating HPV testing in one year or repeating Pap smear in 6 months.
8. Patients with AGUS need colposcopy with endocervical curettage plus endometrial biopsy if age 35 or greater.[4]

Diagram 1: Management of Abnormal Pap Smears From the Modified University of Alabama in Birmingham Guidelines[4]

Normal (NILM)		Repeat in 1 year
ASCUS	HPV Negative HPV Positive	Repeat in 1 year Colposcopy/Biopsy
ASC-H, LGSIL, HGSIL		Colposcopy/Biopsy
Mild dysplasia or less on biopsy		Repeat HPV typing in 1 year or repeat Pap smear in 6 mos.
Moderate dysplasia or worse on biopsy		Cryotherapy or Laser of cervix or LEEP or Cold-knife cone
Significant discrepancy between Pap smear and cervical biopsy		LEEP or cold-knife cone
AGUS under age 35		Colposcopy/Biopsy Endocervical curettage
AGUS over age 35		Colposcopy/Biopsy Endocervical curettage Endometrial biopsy
Abnormal endometrial biopsy		D&C/Hysteroscopy

Moscicki's work attests to the high rate of regression of LGSIL in young women.[8] In other words, most low-grade lesions will resolve if given sufficient time, as suggested by HPV testing in one year. The risk of invasive cervical cancer in a woman with a low-grade lesion is low. High-grade lesions are most often associated with viral persistence and greater risk of cancer. As a result, the current emphasis is on detection and management of biopsy-confirmed high-grade lesions.[3]

To minimize unnecessary procedures and hence preserve cervical tissue as much as possible, the management of women with cervical cytological abnormalities on Pap smears is best managed by the guidelines outlined in the landmark paper "2001 Consensus Guidelines for the Management of Women With Cervical Cytological Abnormalities."[1] We follow a simplified version of these guidelines developed by the University of Alabama in Birmingham in 2002, summarized in Diagram 1.[4]

So why is it that many physicians still treat low grade lesions in light of evidence-based research and guidelines to the contrary? Many physicians still treat ASCUS and LGSIL surgically because they always have. A common misconception is that low-grade lesions need some type of treatment but less than high-grade lesions, making a case for cryotherapy. Sometimes physicians screen low risk patients more often because of the patient's anxiety and request for more frequent screening despite guidelines to the contrary to minimize overtesting.[2] Patients themselves often request treatment of any cervical abnormality especially when they are not educated about the problem.

Practicing physicians may not follow current practice guidelines for management of abnormal Pap smears.[9] Sometimes they are unaware of guidelines; sometimes they are uncomfortable with the recommendations and choose to screen patients more often despite a low likelihood of finding a malignancy.[10] Gynecologists may be too aggressive in following patients with abnormal Pap smears and insist on colposcopy with directed biopsies every three months or fol-

lowing some type of procedure, when time or the previous procedure may have been sufficient treatment.

Conclusions

The end result of overzealous treatment of abnormal Pap smears may be the inadvertent excision or ablation of cervical tissue to the point of cervical incompetence or stenosis. The effect of LEEP on the cervix and subsequent preterm delivery is documented in the literature.[2] Many patients with abnormal Pap smears are young and nulliparous, with childbearing still ahead of them.

A vast amount of effort went into the development of the "2001 Bethesda System"[3] and the "Consensus Guidelines for the Management of Women With Cervical Cytological Abnormalities."[1] It behooves all physicians that screen women with cervical cytology to use the Guidelines as described. Adherence to the guidelines discussed in this paper will minimize unnecessary procedures and will improve consistency and uniformity for treatment of patients with abnormal cytology on Pap smears.

References:

1) Wright TC, Cox JT, Massad LS, et al: 2001 Consensus Guidelines for Management of Women with Cervical Cytological Abnormalities. JAMA 2002; 287:2120-29.

2) Saint M, Gildengorin G, Sawaya GF: Current cervical neoplasia screening practices of obstetrician/gynecologists in the US. AJOG 2005; 192: 414-21.

3) Solomon D, Dave D, Kerman R, et al: The 2001 Bethesda System. JAMA 2002; 287: 2114-19.

4) University of Alabama IN Birmingham, Department of Obstetrics & Gynecology: New Cervical Cancer Screening Guidelines. Birmingham, AL: June 3, 2002.

5) Beckmann CR, Ling FW, Lube DW, et al: Healthcare for Women, Obstetrics and Gynecology, Philadelphia, Lippincott, Williams and Wilkins, 2002; 22.

6) Sampson SA, Bentley JR, Fahey TJ, et al: The Effect of Loop Electrosurgical Excision Procedure on Future Pregnancy Outcome. Obstetric Gynecology 2005: 105: 325-32.

7) Laboratory Corporation of America: Report Explanation. 2003

8) Mesick AB, Chibouk S, Hills NK, et al: Regression of low-grade squalors intraepithelial lesions in young women. Lancet 2004; 364: 1678-83.

9) Sharpness KE, Schmitz PF, Mandeville S, et al: Lack of Adherence to Practice Guidelines for Women With Atypical Glandular Cells on Cervical Cytology. Obstetric Gynecology 2005; 105: 501-6.

10) Suh-Burgmann E, Drag T, Smith-McCune K: Atypical squalors cells of undetermined significance: Management patterns at an academic medical center. AJOG 1998; 178: 991-5.