ASCCP Patient Management Guidelines

Pap Test Specimen Adequacy and Quality Indicators

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Abstract

Our objective was to provide management guidelines according to Papanicolaou (Pap) test specimen adequacy based on literature review and expert opinion. A task force named by the American Society for Colposcopy and Cervical Pathology (ASCCP) conducted a literature review and discussed appropriate management. The Steering Committee of the ASCCP and other experts reviewed the guidelines.

The guidelines recommend a repeated Pap test in 12 months for most women undergoing routine annual/biennial screening if the current Pap test is negative but either lacks an endocervical/transformation zone component or is partially obscured. Indications for considering an earlier repeat are also provided. The preferred management for unsatisfactory Pap tests is a repeated Pap test within a short interval of 2 to 4 months. The management guidelines will help promote optimal and uniform follow-up of women according to Pap test specimen adequacy.

The Bethesda 2001 terminology for reporting results of cervical cytology made substantial changes in specimen adequacy terminology and categorization. As a result, Bethesda conference participants were concerned that the changes might lead to confusion concerning optimal patient management according to specimen adequacy. Even before Bethesda 2001 terminology changes, there was no consensus regarding the timing of screening in women whose Papanicolaou (Pap) tests lacked a transformation zone component or exhibited partially obscuring factors. An extensive management guideline addressing all specimen adequacy concerns did not exist. The American Society for Colposcopy and Cervical Pathology (ASCCP) agreed to address these concerns by convening a task force to establish Pap specimen adequacy management guidelines.

Methods

A brief presentation and discussions regarding Pap specimen adequacy and management occurred at the ASCCP Consensus Conference for the Management of Cytological Abnormalities and Cervical Cancer Precursors, September 6-8, 2001. However, this topic was not introduced in time to reach consensus during the September meeting. A task force comprised of Bethesda 2001 forum group members and ASCCP members met by several conference calls after this September meeting. The guidelines developed were based on literature review and expert opinion of task force members. Draft guidelines were submitted to the ASCCP Steering Committee and other experts for review and additional modifications.
Results

Issue 1.0

What is the recommended follow-up for women with a negative (for intraepithelial lesion or malignancy) Pap test lacking an endocervical/transformation zone (EC/TZ) component?

Recommendation

The preferred management for most women undergoing routine annual/biennial screening is a repeated Pap in 12 months. An early repeat (within 6 months) may be beneficial for some women. Indications for considering an early repeat include: (1) a previous squamous abnormality (atypical squamous cells of undetermined significance [ASC-US] or worse) without 3 subsequent negative Paps (at least one of which contained EC/TZ component), (2) a previous Pap with unexplained glandular abnormality, (3) a positive high-risk/oncogenic human papillomavirus (HPV) test within 12 months, (4) clinician inability to clearly visualize the cervix or sample the endocervical canal, (5) immunosuppression, or (6) insufficient previous screening (not participating in at least biennial screening).

A postpartum repeat is preferred for pregnant patients.

Issue 2.0

What is the recommended follow-up for women with a negative (for intraepithelial lesion of malignancy) Pap test that has partially obscuring blood, inflammation, other partially obscuring factors, or partial air-drying?

Recommendation

The preferred management for most women undergoing routine annual/biennial screening is a repeated Pap in 12 months. An early repeat (within 6 months) may be beneficial for some women. Indications for considering an early repeat include: (1) a previous squamous abnormality (ASC-US or worse) without 3 subsequent negative Paps (at least one of which contained EC/TZ component), (2) a previous Pap with unexplained glandular abnormality, (3) a positive high-risk/oncogenic HPV test within 12 months, (4) clinician inability to clearly visualize the cervix or sample the endocervical canal, (5) immunosuppression, or (6) insufficient previous screening (not participating in at least biennial screening).

A postpartum repeat is preferred for pregnant patients.

Issue 3.0

What is the recommended follow-up for women with an unsatisfactory Pap test?

Recommendation

The preferred management for most women with an unsatisfactory Pap test result is a repeated Pap test, generally within a short interval of 2 to 4 months. If the unsatisfactory result is due to obscuring inflammation and an organism is identified, consider specific treatment prior to repeating the Pap. In cases where the Pap test is repeatedly unsatisfactory due to obscuring blood, inflammation, or necrosis, additional clinical evaluation is suggested, such as colposcopy and/or biopsies as appropriate.

Background and Discussion

The 2001 Bethesda System has 2 adequacy categories: “satisfactory for evaluation” and “unsatisfactory for evaluation”1 Table II. The “satisfactory but limited by… (SBLB)” category was eliminated. The presence or absence of EC/TZ component and any other quality indicators are provided immediately after the term “satisfactory for evaluation.” The unsatisfactory report includes reasons for the unsatisfactory designation. Any specimen with abnormal cells is by definition satisfactory for evaluation. The 2001 Bethesda System combined previous categories of “within normal limits” and “benign cellular changes” (organisms, reactive/reparative changes) into a single category, “negative for intraepithelial lesion or malignancy.”

Issues 1.0 and 2.0

The rationale for elimination of the “satisfactory but limited by…” category was that it was confusing to many clinicians and there was conflicting information regarding the necessity of an early repeat. The wording was criticized as an oxymoron: was the specimen satisfactory or limited? Thus, patient follow-up in the past was variable, leading to controversies in patient care, risk management, and third-party coverage of follow-up testing.

Several studies show that squamous intraepithelial lesion (SIL) cells are more prevalent in specimens in which EC/TZ cells are present.2-13 Other studies have found no difference in SIL detection related to EC/TZ status.13-17 One study found more SIL in the subset of cases with EC/TZ...
component, but there was no increase in SIL detection over time when devices promoting increased EC/TZ collection were used. Several retrospective longitudinal cohort studies have shown that women with smears lacking EC/TZ cells are not more likely to have squamous lesions on follow-up than are women with EC/TZ cells. Finally, retrospective case-control studies have failed to show an association between false-negative interpretations of Paps and lack of EC/TZ cells. Birdsong recently reviewed this subject extensively.

Endocervical cells are less frequently identified in women who use oral contraceptives, are pregnant, or are postmenopausal. Clinician feedback, improved technique, modern sampling devices, and experience tend to increase the collection of EC/TZ cells. However, despite good collection technique and use of appropriate endocervical sampling devices, some women will have repeated Pap tests that lack EC/TZ cells. Identification of EC/TZ components by the laboratory is also subject to interobserver variability.

There is very limited data on the significance of partially obscuring blood and inflammation. One study found that atypia was more likely to be present in limited smears than satisfactory smears. Two retrospective case-control studies examining Paps from women with biopsy-proven cervical intraepithelial neoplasia (CIN) 3 showed no significant relationship between partial obscuring factors and a false-negative report. Prospective studies have not been done.

While there are conflicting data on the value of an early repeat in an individual patient, the inclusion of adequacy information in Pap reports has value in improving overall specimen adequacy. Regular feedback on specimen quality promotes heightened awareness of adequacy, use of better sampling devices, and development and use of more sensitive Pap technologies. The implications of transformation zone sampling and other quality indicators could change with the increasing incidence of cervical adenocarcinoma and the adoption of new technologies. Inclusion of adequacy information is the only means for tracking possible trends.

A repeated Pap in 12 months is the preferred management for women with a satisfactory Pap either (1) lacking EC/TZ component or (2) exhibiting partially obscuring factors, air drying, etc. This approach is a reasonable compromise in light of the conflicting data regarding the significance of an EC/TZ component and the paucity of data on other obscuring indicators. While longitudinal studies fail to show that women lacking such components are at increased risk for squamous lesions, cross-sectional studies show differing results and adenocarcinoma cases are also increasing. Many clinicians recommend annual screening for all their patients, but published screening guidelines and coverage rules vary. A repeat in 2 years instead of 1 may be considered if the woman has been screened regularly for several years without abnormalities noted. In the pregnant patient, a postpartum repeat is preferred as a pragmatic approach.

Selected patients lacking EC/TZ component or with partially obscuring factors may benefit from an early repeat, generally within 6 months. Examples are women with insufficient prior screenings and women with a history of abnormalities or a recent positive high-risk HPV test. In contrast, a recent negative high-risk HPV test suggests a low risk for cervical pathology and would support a regular screening interval. Careful attention should be given to the laboratory reporting of quality indicators on prior Paps, including presence of EC/TZ component, especially in women with a history of a glandular abnormality or CIN 3.

**Issue 3.0**

Unsatisfactory Paps include those that are rejected (not processed) generally because of insufficient labeling, slide breakage, or leakage of liquid specimens. Most unsatisfactory Paps are processed and fully evaluated by the laboratory but meet morphologic criteria for an unsatisfactory specimen. The 2001 Bethesda System provided more specific criteria for minimum squamous cellularity in both conventional smears and liquid-based Paps and clarified criteria for unsatisfactory Paps obscured by blood, inflammation, etc.

An unsatisfactory Pap test is considered unreliable for evaluation of epithelial abnormalities; however, those that are processed and evaluated by the laboratory may provide some information such as background elements (blood, inflammation), presence of organisms, etc. A longitudinal study found that unsatisfactory Paps were more often from high-risk patients, and significantly more had SIL/cancer on follow-up when compared to a cohort of patients with satisfactory index Paps. Retrospective rescreening of prior false-negative Paps in patients with current CIN 3 and cancer have shown many to be unsatisfactory upon review.

**Additional Clinical Evaluation**

Inflammation and bleeding associated with CIN 3/carcinoma and some benign pathologies may cause partially obscured or unsatisfactory Pap tests. This guideline primarily addresses the issue of repeated Pap testing. However, additional clinical evaluation is suggested in women with symptoms, abnormal physical findings, or repeated bloody/inflamed unsatisfactory Pap tests. Examples are women with visible lesions, friable cervix, polyps, postcoital or other abnormal bleeding, pelvic pain, or abnormal discharge.
Technical Issues

Improved patient preparation or clinician technique may correct the cause of the unsatisfactory or partially obscured Pap. With feedback on quality indicators, the rate of unsatisfactory Pap tests decreased substantially in 1 study.33 When there are obscuring factors, liquid-based technologies may be considered with subsequent Pap tests, as liquid-based sampling generally decreases obscuring problems.42,43 Air-drying problems can be addressed by either liquid-based sampling or careful attention to proper fixation.

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