MP 2.04.03  Cervicography

Medical Policy

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Description

Cervicography refers to the use of a specialized camera to take standardized images of the cervix after application of acetic acid. Proposed uses of cervicography include as a primary technique to screen for cervical cancer, as an adjunct to Pap smear screening, and as a triaging strategy for patients who have low-grade lesions with Pap smear testing.

Cervicography involves the use of a specialized camera which is described as easy to use and not requiring experience in colposcopy. The photographs, referred to as cervigramsTM, are static photographic images of the cervix similar to those seen during low-level magnification colposcopy. The images are sent to a central laboratory (National Testing Laboratories, the worldwide exclusive licensee of the product) for interpretation by colposcopists who have received specialized training in interpretation of cervigrams. Cervigrams are interpreted as negative, atypical, positive, or defective.

Cervicography has been investigated in 3 general settings:

- As an alternative to Pap smear screening as a primary screening technique for cervical cancer.
  This application has been investigated primarily in 'resource poor' areas that do not have cytology expertise to interpret Pap smears.

- As an adjunct to routine Pap smear screening to improve the sensitivity of Pap smear screening for cervical cancer. For example, it is estimated that negative cytology reports are issued on 20% or more of all invasive cervical cancers.

- As a triage technique for colposcopy in patients found to have low-grade lesions on Pap smear specimens.

The management of low-grade lesions, i.e., atypical squamous cells of uncertain significance (ASCUS), has been a subject of investigation. For example, colposcopy is an option for further workup of ASCUS lesions, and yet at colposcopy only 20% of these patients actually have a high-grade lesion. Furthermore, many low-grade lesions that may prompt colposcopy will spontaneously regress. If cervicography can be used to identify which ASCUS cytology results are most likely to harbor higher grade lesions and thus need colposcopy and biopsy,
unnecessary colposcopies in patients with innocuous cytologic abnormalities would decrease. Other triaging strategies include repeat Pap smears or evaluation for human papilloma virus (HPV) infection.

**FDA Approval or Marketing Clearance of Devices**

In June 1982, the Cerviscope Optical System (Fotomedics) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing devices for viewing tissues of the vagina and cervix.

**Policy**

Cervicography is considered investigational.

**Policy Guidelines**

The CPT category III code specific to this procedure – 0003T – was discontinued after 2006 so there is no longer a specific CPT code for this procedure. The procedure would now be coded with an unlisted code such as 58999 -unlisted procedure, female genital system (nonobstetrical).

**Rationale**

Cervicography has been the subject of several randomized studies that have studied its use in various settings, i.e., as a primary screening technique, an adjunct to Pap smear screening as a primary screening technique, and a triaging strategy for patients found to have low-grade lesions on Pap smear.

Cervicography as an Alternative to Pap Smear as a Primary Screening Technique

Schneider and colleagues reported on a study comparing cervicography with conventional Pap smear, a conventional Pap smear interpreted with the aid of PapNet (neural network semiautomatic screening device), and a Pap smear prepared from a ThinPrep solution and interpreted conventionally. (1) The study included 8,460 women from Costa Rica, considered a high-risk population for cervical cancer. Patients were referred for colposcopy and potential biopsy if there was an abnormal cytologic result by any 1 of these 3 methods. The sensitivities and specificities of the cytologic testing and cervicography for the most clinically important high-grade lesions compared to a referent diagnosis* are summarized in the following table.

<table>
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<th>Sensitivity of Cytology, %</th>
<th>Sensitivity of Cervicography, %</th>
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<tr>
<td>High-grade lesions; women over 50 years old</td>
<td>84.6</td>
<td>26.9</td>
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<tr>
<td>High-grade lesions; women under 50</td>
<td>75.5</td>
<td>54.6</td>
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As noted in Table 1, the sensitivity of cervicography sharply drops among older, predominantly postmenopausal women. This observation is explained by the cephalad movement of the transformation zone in postmenopausal women. The transformation zone is the site of origin of most cervical cancers, and as it moves cephalad into the cervical canal, it is no longer well visualized with cervicography. The authors concluded that cytologic testing performed better than cervicography for the detection of high-grade intraepithelial lesions, while cervicography was only marginally better in the detection of invasive cervical cancer.

Cervicography as an Adjunct to Primary Pap Smear Screening

The combined use of Pap smear screening, cervicography, and human papilloma virus (HPV) testing has been investigated as a technique to reduce the false negative rate of Pap smear screening alone.

Autier and colleagues performed a randomized study comparing cytology alone vs. cytology and cervicography. (2) A total of 5,550 women considered at low risk of cervical neoplasia were randomized to one of the screening strategies and rescreened 1 year later with combined cytology and cervicography. Women positive for either of the 2 initial screening tests were referred for colposcopy-biopsy. The principal study endpoint was the rate of histopathologically confirmed cervical intraepithelial neoplasia (CIN) lesions. In the cytology only group, 13 of the 2,772 (0.47%) Pap smears were read as abnormal. In contrast, in the combined group, 12 Pap smears were read as abnormal in addition to 101 cervigrams that were read as abnormal. No woman was positive for both Pap smear and cervigram. A total of 13 patients in the cytology alone group were referred to colposcopy, compared to 113 in the combined group. CIN 2-3 (cervical intraepithelial neoplasia grade 2-3) was identified in 4 of the patients in the cytology alone group compared to 6 in the combined group. Therefore, the majority of the patients with abnormal cervigrams were either found to have no lesion or CIN 1 on subsequent colposcopy. CIN 1 lesions are generally thought to be transient in nature and require no specific treatment, but may be followed up with repeat Pap smears. While the addition of cervicography to cytology improved the detection of CIN 1 lesions, it did so at a cost of a decreased specificity. In addition, detection of CIN 2 and 3 lesions represents the most clinically significant target of screening.

Costa and colleagues reported on the results of 992 patients undergoing routine Pap smears who underwent simultaneous cervicography and HPV testing. (3) All patients also underwent colposcopy as the reference tool. The combination of Pap testing with cervicography resulted in an increase in sensitivity but a decrease in specificity. The positive predictive value of combined Pap and cervicography (43%) was similar to that of Pap smear alone (45%).

Cervicography as a Triaging Strategy in Women with ASCUS or LSIL on Pap Smears

The ASCUS/LSIL Triage Study (ALTS) was a multicenter, randomized trial that compared 3 different management strategies for 3,488 women with either ASCUS or LSIL (low-grade squamous intraepithelial lesion) on an initial Pap smear. (4) The strategies included: 1) immediate colposcopy (considered the reference standard), 2) triage to colposcopy based on the results of HPV testing, or 3) triage based on cytology results alone. The main study endpoint
was detection of CIN 3, since there is a general consensus that this lesion is at high risk of progressing to invasive cancer and requires definitive treatment. All patients also underwent cervicography, as a 'fail safe' mechanism in the noncolposcopy groups to prevent a missed cancer diagnosis. The cervicography results were then interpreted separately as a triaging technique for mildly abnormal cervical cytology results by comparing the results of the cervicography with the histologic results of those patients who underwent colposcopy. (5) Cervigrams were categorized as defective, negative, atypical, or positive. Positive cervigrams were further subdivided into additional categories: positive, LSIL, HSIL (high-grade intraepithelial lesion), or cancer. If one considered an atypical cervigram as an indication for referral to colposcopy, the sensitivity of cervicography to detect CIN 3 lesion (i.e., high-grade lesion requiring treatment) was 79.3% and would have required the referral of 41.8% of women for colposcopic examination. When increasing the threshold for colposcopic referral to cervigrams interpreted as positive for LSIL, the sensitivity of detected CIN 3 dipped to 65.8%, requiring referral of 26.5% of women for colposcopic exam. In the ALTS trial, cytology and HPV testing were explored as triaging options. Table 2 shows the comparative results:

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<th>Cervicography, %</th>
<th>Cytology, %</th>
<th>HPV Testing, %</th>
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<tr>
<td>Sensitivity for detecting CIN 3 lesions</td>
<td>79.3</td>
<td>86.3</td>
<td>96.3</td>
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<tr>
<td>Percentage referred for colposcopy</td>
<td>37</td>
<td>58</td>
<td>56</td>
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<tr>
<td>Positive predictive value for detecting CIN 3 lesions</td>
<td>8</td>
<td>9</td>
<td>10</td>
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<tr>
<td>Negative predictive value for detecting CIN 3 lesions</td>
<td>99</td>
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The authors conclude by stating that cost utility analyses will determine whether and when cervicography, compared with other clinical options, is useful in the management of mildly abnormal cervical cytology results.

Other Information

In 2001, the American Society for Colposcopy and Cervical Pathology (ASCCP) published guidelines for the management of women with cervical abnormalities, in part based on the results of the ALTS study. These guidelines do not recommend cervicography as a triaging strategy. (6, 7)

The U.S. Preventive Services Task Force specifically does not recommend cervicography as part of a cervical cancer screening program. (8) The Task Force states that the sensitivity of cervicography is similar to that of Pap smears, but that both the specificity and positive predictive value are considerably lower than Pap smears. The positive predictive value is only about 1%–26% and up to 10%–15% of cervigrams are unsatisfactory in quality. The Task Force concludes, “There is insufficient evidence to recommend for or against routine screening with cervicography.” This recommendation was issued in 1996.
Summary

Cervicography alone has an inferior sensitivity compared to cytology, and therefore is not recommended in settings where adequate cytology services are available. As an adjunct to Pap smear screening, cervicography may increase the sensitivity for detecting cervical abnormalities, but will decrease the specificity, potentially resulting in increased referrals for colposcopy. As a triaging strategy for patients with mildly abnormal cytology results, cervicography is a promising technique that appears to be similar in terms of positive and negative predictive values compared to other options, including repeat cytology or HPV testing. However, if the original Pap smear was collected in a liquid medium, subsequent HPV testing in patients whose cytologic result was mildly abnormal could be done on the same sample. Therefore, these patients do not need to return for a repeat office visit. Both repeat Pap smear and cervicography would require an additional office visit. At present, no clinical guidelines are available from the American College of Obstetricians and Gynecologists, U.S. Preventive Services Task Force, or related organizations that recommend the use of cervicography in any of the above clinical situations.

2003-4 Update

A review of the peer-reviewed literature on MEDLINE for the period of 2002 through November of 2004 found 2 clinical trials that evaluated screening methods for cervical abnormalities. Ferris and colleagues compared cervicography to on-site colposcopy and telecolposcopy in 264 women. (9) The authors found no statistically significant difference in rates of agreement or sensitivity and specificity for each of the screening methods when CIN 1 cases were considered. However, when evaluating CIN 2 and 3 cases, on-site colposcopy out-performed cervicography in rate of agreement and sensitivity (Table 3). Therefore, the authors indicated telecolposcopy detected more cervical neoplasia than cervicography.

2003-5 Update

A review of the peer-reviewed literature on MEDLINE for the period of 2002 through October 2005 found 3 clinical trials that evaluated screening methods for cervical abnormalities. Ferris and colleagues compared cervicography to on-site colposcopy and telecolposcopy in 264 women. (9) The authors found no statistically significant difference in rates of agreement or sensitivity and specificity for each of the screening methods when CIN 1 cases were considered. However, when evaluating CIN 2 and 3 cases, on-site colposcopy out-performed cervicography in rate of agreement and sensitivity (Table 3). Therefore, the authors indicated telecolposcopy detected more cervical neoplasia than cervicography.

Table 3

<table>
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<th>On-site Colposcopy</th>
<th>Cervicography</th>
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<td>Rates of Agreement – CIN 2/3</td>
<td>50.0</td>
<td>19.1</td>
<td>.04</td>
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<tr>
<td>Sensitivity – CIN 2</td>
<td>47.7</td>
<td>18.2</td>
<td>.049</td>
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In Cronje, 1,286 women were each screened with cytologic examination, cervicography, direct acetic acid test, and speculoscopy. (10) Results were compared to histologic examination to
identify a suitable method for screening in a developing country. The authors concluded that none of the methods were individually sufficient for screening in a developing country. Cervicography results were 48.9 for sensitivity and 87.5 for specificity and were noted to be inadequate for the study purpose due to the low specificity. Finally, Howard and colleagues compared the diagnostic yield of cervicography and HPV testing among 304 women with ASCUS lesions detected on Pap smears. (11) The adjunctive tests were compared to the gold standard of colposcopy. The authors concluded that while both adjunctive tests increased the sensitivity of cytology, there was insufficient power to determine whether observed sensitivities were statistically significantly higher than the expected, given that the adjunctive tests could improve the sensitivity by chance alone.

None of the findings from these 3 studies would alter the conclusions reached above. Therefore, the policy statement is unchanged.

2005-2007 Update

A literature search was conducted for the period of November 2004 through December 2006. No studies were identified that would alter the policy statement above. Studies continue to evaluate the potential role of cervicography in settings where adequate cytology services are not available. In addition, studies are evaluating the potential impact of combining cervicography with other tests as a risk-stratification or triage technique. For example, Wang and colleagues reported that combining results of liquid-based cytology, HPV testing, and cervicography could help to determine the risk of subsequent development of cervical precancers. (12) Before this could be used in practice, replication/validation of these findings would be needed.

2008 update

A MEDLINE search was conducted for the period January 2007 to April 2008. None of the studies led to a change in the policy statement. Two studies of interrater reliability using cervigrams were published; both used convenience samples of cervigrams obtained for other studies. In the first, 72 experienced (4 expert) colposcopists from 5 countries reviewed a sample of 50 cervigrams, representing a spectrum from normal to cancerous, for the presence of lesions and the site of suggested biopsy. (13) Their results were compared to those of the consensus (not histology). Agreement was 70% (65% - 75%), which was sufficient, the authors concluded, for all centers to participate in a trial assessing the best management strategy for biopsy proven CIN1. The second study involved 919 cervigrams from the ASCUS-LSIL Triage Study (all subjects referred to the study had either ASCUS or LSIL). (14) Each cervigram was evaluated by 2 expert colposcopists for lesion severity and the number of lesions. The evaluators had complete agreement in 56.8% of cases, disagreement between high- and low-grade lesions in 37.8%, and absolute disagreement in 5.3%. HPV status and age were predictive of agreement. The authors concluded that caution is needed when using static images, even of high quality, for teaching and testing of colposcopists. Although neither study was intended to assess the screening capacity of cervicography, they illustrate challenges for the technology.

A multispectral digital colposcope, a modified colposcope with a video camera adapter, with automated digital image analysis is in development, and a report of the performance of this technology in a pilot study of 29 patients was identified. (16) Sensitivity was reported at 79% and specificity was 88%. Much larger study populations will be necessary to evaluate the test characteristics of this emerging technology.

2009-2010 update
A MEDLINE search was conducted for the period April 2008 to November 2009. One study was identified, and, as noted below, this did not lead to a change the policy statement. Chen and colleagues conducted a study in Taiwan evaluating cervicography as an adjuvant screening tool for women with precancerous lesions identified by Pap smear. (17) A total of 125 women were enrolled, and 119 underwent cervicography. The investigators created a digital cervicography instrument using a digital camera with a macro lens and a circular-shaped continuous light source. They evaluated images in-house using the Reid colposcopic index (RCI) scoring system. Scores were dichotomized to a total RCI score of 0-2 (predictive of mild dysplasia) and a total RCI score of 3-8 (predictive of moderate or severe dysplasia). There were 112 cases of ASCUS or LSIL (by the Pap smear); 92 of these received an RCI score of 0-2 and 20 received an RCI score of 3-8. Of the 7 cases of HSIL (by the Pap smear), 1 received an RCI score of 0-2 and 6 received an RCI score of 3-8. A McNemar test to evaluate changes in classification after performing digital cervicography was statistically significant (p <0.01). The investigators used findings from digital cervicography primarily to show patients visual images with the goal of reducing their anxiety over having an abnormal Pap smear. No conclusions were made regarding the impact of digital cervicography on patient management e.g., referral to colposcopy. It is important to note that the Chen study did not use standard cervicographic equipment or analysis methods so it is not clear whether their technique would be considered cervicography.

There remains insufficient evidence on the reliability and diagnostic accuracy of cervicography, and insufficient evidence that cervicography has a benefit on net health outcome. Moreover, cervicography may no longer be commercially available. The continued existence of Fotomedics, the manufacturer of the FDA-cleared Cerviscope Optical System and the National Testing Laboratories, previously mentioned as the worldwide exclusive licensee for analyzing cervigrams, could not be verified (e.g., no websites or current contact information were identified).

References:


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<td>(nonobstetrical)</td>
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<td>67.19</td>
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