Status/Post Hysterectomy for Cervical Intraepithelial Neoplasia: When to Discontinue Pap Smear Surveillance

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Abstract

Women with a prior hysterectomy for cervical intraepithelial neoplasia may continue to be screened by Papanicolaou smears for vaginal cancer. The evidence for continuing to screen for vaginal cancer is sparse. Different organizations have recommended guidelines to screen for vaginal cancer after a hysterectomy for cervical intraepithelial neoplasia, however the guidelines are inconsistent leaving many in disagreement. The objective of the article is to identify the evidence of vaginal cancer after a hysterectomy for cervical intraepithelial neoplasia. The systematic search found eight research studies, which met the criteria. A total of 2676 women were followed after a hysterectomy with five documented vaginal cancers over a time period ranging from 1 to 20 years. Given the lack of recent evidence available as to how often patients be screened after a hysterectomy for cervical intraepithelial neoplasia, no new recommendations can be made.

INTRODUCTION

Research has shown too many vaginal vault smears have been done in the United States (US) unnecessarily (1). The US Services Preventative Task Force (USPSTF), the American College of Obstetrics and Gynecology (ACOG), and the American Cancer Society (ACS) recommend stopping the Papanicolaou (Pap) smear after a hysterectomy if the surgery was done for benign causes (2-4). However, guidelines are inconsistent for women who had a hysterectomy for precancerous reasons leaving many clinicians in disagreement. The paper will discuss the need to screen women for vaginal intraepithelial lesion and vaginal cancer, who had a hysterectomy for cervical intraepithelial neoplasia or precancer. Research studies will be reviewed which have focused on the subjects of vaginal intraepithelial lesions and vaginal cancer status-post a hysterectomy for cervical intraepithelial lesions. Recommendations of future research will be discussed concerning the length of time screening should occur, how often, and the necessity of screening.

SOURCES

A systematic literature review was conducted in PubMed for all peer-reviewed studies published until September 2009, with no specified start date. Studies were included if the authors reported cervical intraepithelial neoplasia as a cause for hysterectomy. Studies not reporting the use of a hysterectomy or articles written in languages other than English were excluded.

CLINICAL MANAGEMENT ISSUE

The US had 11,070 cervical cancer cases and 3,870 deaths for the year 2008 (5). Cervical cancer is the second most common cancer in women worldwide with an estimated 493,000 new cases per year (6). Due to the introduction of the Pap test, cervical cancer has decreased by 70% in the US (7). Cervical cancer results from the progression of preinvasive precursor lesions called cervical intraepithelial neoplasia (CIN), or dysplasia. CIN is graded into mild dysplasia (CIN 1), moderate dysplasia (CIN 2), or severe dysplasia (CIN 3) (8). The American Society for Colposcopy and Cervical Pathology guidelines for the management of women with persistent or recurrent cervical intraepithelial lesion 2 (CIN 2) and CIN 3 include hysterectomy as treatment only when other treatments are not feasible (8). Women with CIN 3 have a 31% risk factor of developing carcinoma of the cervix if left untreated over a 30-year time span. Women who are treated for CIN pose a risk of 0.7% for developing carcinoma of the cervix over a 30-year time-span (8, 9).

Vaginal cancer is a rare occurrence, comprising approximately 0.3% of all invasive cancers in women and 1-2% of all gynecological malignancies. Approximately 3460 women in the US were diagnosed with vaginal cancer,

and 870 women died in the year 2008 from vaginal cancer (5). Women with a history of CIN grade 3 are at an increased risk for cancer of the vagina (10). Other risk factors for vaginal cancer include a previous abnormal Pap smear, early hysterectomy, cigarette smoking, less education and a low family income, a history of genital warts, radiation therapy, diethylstilbestrol (DES) exposure, and a compromised immune system (11-13).

The natural history of vaginal cancer remains unclear (14). Prevalence of persistent human papillomavirus (HPV) infections is similar in both cervical and vaginal specimens. The HPV infection has rarely shown to cause a cytology abnormality in patients with a hysterectomy, especially when compared to cervical cytology in non-hysterectomized patients. The transformation zone of the cervix maybe more predisposed to a carcinogenic insult by HPV rather than the vaginal canal resulting in less common occurrences of HPV-related vaginal cancers (6, 15). Seventy to eighty-percent of all vaginal cancers are from squamous cell carcinoma, which has been associated with HPV infection (11, 14). Vaginal intraepithelial neoplasia (VAIN) is known to be a precursor to malignancy (13).

EVIDENCE

Approximately 20% of women in the US have undergone a hysterectomy. About 6-10% of the hysterectomies were done for precancerous reasons or CIN (1). Continuing to screen for vaginal cancer is not necessary if the hysterectomy was done for benign reasons (2-4). The USPSTF (3) recommends discontinuing screening with Pap smears after a hysterectomy which was done for benign causes, excluding the women who had a hysterectomy for cervical neoplasia or cancer. The USPSTF recommends continuing cytologic screening, but gives no recommended time frame.

The ACS (2) recommends after a hysterectomy women discontinue cervical cancer screening, unless the surgery was performed for pre-cancer. CIN 2 and 3 are not considered benign, and follow-up cytology is recommended every four to six months until three negative documented and consecutive cytology tests have been achieved. The recommended time frame to continue screening is within an 18-24 month period following the hysterectomy. Although the ACS has guidelines in place for women with hysterectomies for CIN, the guidelines state the data is limited to support the recommended guideline (7).

The ACOG (4) recommends continuing cytologic screening after a hysterectomy for women with a history of abnormal cell growth (classified as CIN 2 or 3) annually until three consecutive negative vaginal cytology tests are confirmed. Once three negative cytology tests are confirmed, the women may discontinue routine screening. The recommended guidelines are listed in detail in Table 1.

Figure 1

TABLE 1 Recommendations for Screening after a Hysterectomy for CIN

Agency	*Frequency*	*Time Frame*	*Discontinue*
USPSTF*	Inconclusive	Inconclusive	Inconclusive
ACS**	Every 4-6 months	18-24 months after hysterectomy	3 negative and consecutive tests
ACOG[1]	Inconclusive	Annually	3 consecutive negative tests

* United States Preventative Services Task Force
** American Cancer Society

Due to the lack of agreement in recommendations, many clinicians are left without clear guidelines as to when it is appropriate and safe to stop screening for VAIN after a hysterectomy for CIN (1, 14). The USPSTF recommendations assume an indefinite amount of time for vaginal vault smears after a hysterectomy, while ACS and ACOG do not. The recommendations are based on the rationale both pre-invasive and invasive carcinoma of the vagina have been found years after a hysterectomy (16). The recommended guidelines do not mention the impact of HPV types on the incidence of VAIN.

Pap smears can cause considerable stress and anxiety to the patient (17). Given the low detection rates of vaginal cancer, a review of the literature will be used to weigh the risks of cancer in order to justify the cost of frequent vaginal smears and the potential stress and anxiety to the patient of frequent vaginal vault screening. The opinions of the research authors as to the recommendations for screening will be discussed. The question raised is how often and for how long should women be screening for vaginal cancer after a total hysterectomy for CIN 2 or CIN 3.

RESEARCH STUDIES

Table 2 summarizes the data from the abstracted papers. Schockaert et al. (18) performed a retrospective study and analyzed women who had a hysterectomy for CIN. Eighty-nine women had a hysterectomy for CIN 3 and 11 had a hysterectomy for CIN 2. Seven patients had VAIN between five and 103 months after the hysterectomy. Two of the women developed invasive vaginal cancer. One developed

cancer at 103 months after the hysterectomy and the other patient at 67 months. The mean interval between hysterectomy and the first confirmed VAIN 2+ diagnosis was 45 months, with a median of 35 months. The study had no reported deaths from cancer. The study results found VAIN occurred in seven percent of women who received a hysterectomy and invasive vaginal cancer occurred in two percent. The author concluded careful follow–up with vaginal vault smears was necessary during the first 4-years post-hysterectomy (18).

Babarinsa et al. (19) studied outcomes for abnormal vaginal cytology in nine women with a history of a hysterectomy for CIN. The time frame ranged between 12 and 60 months, post-hysterectomy. None of the women developed cancer, however four (44%) of the women developed VAIN and all Paps returned to normal by 44 months. The researchers did not discuss any treatment done for VAIN in all of the four women. The authors suggested a routine vaginal cytology for at least 12 months following a hysterectomy for CIN and colposcopic assessment of the vagina before the hysterectomy. The authors noted the very small sample size and the need for larger studies.

Kalogirou, et al. (20) studied 993 women who underwent a hysterectomy for CIN between 1981-1991. The women were asked to undergo vaginal vault cytology every six months for the first year, then annually over a 10-year period. At the end, 793 women completed the study in order to record abnormal cytology. The results found five percent (41 subjects) of the women had an incidence of VAIN following the hysterectomy. The authors did not state the time frame for acquiring VAIN, however gave recommendations on screening. The authors recommended Pap smears and colposcopy exams be performed every six months for the first two years and then annually for the next five years (20).

Wiener et al. (16) studied women with a history of pre-invasive carcinoma of the cervix who received a hysterectomy. One hundred and ninety-five women were screened annually for abnormal Pap smears for 10-20 years after the hysterectomy. All 195 women had a hysterectomy for either CIN or adenocarcinoma in situ between the years 1955-1977. One hundred and twenty-seven had a prior cone biopsy and 35 had a colposcopy before the hysterectomy. Of the 195 subjects, five developed abnormal smears with one being invasive carcinoma. The authors noted not all women had colposcopies because colposcopy did not become routine until the late 1970's. A total of five abnormal vaginal smears were found in the study. The results found 98.4% of the women had a negative cytology at ten years, 97.7% were negative at 15 years, and 96.5% were negative at 20 years. Thus, 1.6% developed abnormal cytology within 10 years and 3.5% within 20 years. Two cases of vaginal epithelial lesions were reported after 12 years and one with a cancer diagnosis 16 years after the hysterectomy. The authors concluded the cause of vaginal epithelial lesions was due to the original CIN lesion, which was not completely removed with the hysterectomy. Recommendations by the authors were to perform vaginal cytology of women with a hysterectomy for CIN for two years. Once all three smears are confirmed negative, the follow up schedule can conform to the population guidelines.

Gemmell et al. (21) performed a retrospective longitudinal review of 219 women who had hysterectomy for CIN 3. The study followed the patients for 15 years. Of the 219 women who had follow-up after 10 years, eight (4%) had abnormal smears. Of the eight abnormal findings, six reverted back to normal with no treatment. Two women had an abnormal cytology the first year after the hysterectomy. One had VAIN at 10 months, was treated and found to be normal at five years. One subject had VAIN at seven months, had a total vaginectomy and was found to be normal at five years. Another subject had VAIN at 16 years after the hysterectomy and was lost to follow up. None of the subjects in the study developed vaginal carcinoma. The authors conduced a second retrospective study with 60 subjects identified from the gynecological cancer registry from 1957-1987. All 60 subjects were diagnosed with vaginal carcinoma in the Tayside Region. Of the 60 subjects, one vaginal carcinoma occurred in association with a diagnosis of previous CIN at hysterectomy. The author concluded the incidence of VAIN after a hysterectomy for CIN 3 was 0.91%. The author recommended women who had a hysterectomy for CIN 3 be screened every six months for the first year, then at year two for a total of three screenings. Once all smears are normal, screening with the normal population guidelines is recommended. The author noted screening at 5-year intervals would have a cost savings of 113 visits/smears over 10 years, thus decreasing a clinician's workload by 0.3%.

Hellberg and Nilsson (22) followed 154 women who had hysterectomies for CIN 2 and continued to have vault smears annually. Out of the 154 women who had a hysterectomy, four had a recurrence of the disease in 10 years. None of the

subjects progressed to cancer. The authors concluded the 10-year cure rate is 96.4% for women after a hysterectomy for CIN (22).

A study by van Nagell et al. (23) followed 144 patients with confirmed CIN who underwent hysterectomies within four weeks of colposcopy without a cervical conization. All subjects had a colposcopic examination of the vagina to rule out vaginal extension of cervical neoplasia. The participants were followed for 12-120 months receiving a vaginal cytology every three months for two years and every six months thereafter. No cases of VAIN or vaginal cancer were reported. The author noted some complications related to hysterectomies such as blood transfusions and urinary tract infections. As a result, consideration of patient morbidity and postoperative complications should be considered as to the necessity of hysterectomies. The authors concluded adequate colposcopy and hysterectomy is an effective therapeutic procedure in women with CIN. The authors gave no recommendations for screening for follow-up.

Fawdry (24) studied 1062 women, all who had hysterectomies. Twenty-seven had a hysterectomy for severe dysplasia and 1035 had carcinoma-in-situ. Out of the subjects, nine women had an early recurrence of VAIN in the first year and one was diagnosed with cancer eight months after the hysterectomy. None of the women died from cervical, vaginal, or vulvar neoplasia. The author noted on 100 occasions in 45 women, false positives results were reported. The author concluded that performing at least two smears in the two years after a hysterectomy was essential. No recommendations for screening after the two years were discussed; however, the author pointed out the very low detection rate does not justify an annual visit for screening.

Figure 2

TABLE 2 Literature Review on Vaginal Neoplasia and Cancer after Hysterectomy for CIN

Study	*No. Subjects*	*Follow up*	*Vaginal Neoplasia*	*Vaginal Cancer*
Schockaert et al. (18)	100	5-103 months	7	2
Barbarinsa et al. (19)	9	12-60 months	4	0
Kalogirous et al. (20)	993	10 years	41	0
Wiener et al. (16)	195	10- 20 years	4	1
Gemmell et al. (21)	219	15 years	3	1
Hellberg & Nilsson (22)	154	10 years	4	0
Van Nagell et al. (23)	144	12-120 months	0	0
Fawdry (24)	1062	Ave. follow up 4.9 years	9	1

DISCUSSION

A review of the literature found a total of 2676 subjects who had a hysterectomy for CIN. All subjects were followed for vaginal cancers over a time period ranging from 1 to 20 years. Five cases of vaginal cancers were documented in the research. Further research is needed to assess the effectiveness of Pap smears in detecting vaginal cancer following hysterectomy. Research related to HPV testing and vaginal cancers need to be evaluated. Most of the studies available reflect the 1990's and does not reflect the better understanding of Pap smear testing today. New technologies have risen with Gardasil, Thin Prep cervical smears, and digital colposcopies. Some of the studies were performed before colposcopies were routinely done and available. Babarinsa et al. (19) suggested a lack of colposcopies could cause residual disease suggesting incomplete removal of the original disease.

CONCLUSION

Healthcare cost savings are increasingly important. Limiting the amount of inappropriate use of Pap smears could have a substantial cost-saving effect on health care. Given the lack of recent evidence available as to how often patients be screened after a hysterectomy for CIN, no recommendations can be made for screening women who had a hysterectomy for CIN. Only a few women developed vaginal cancer in the research available. Requiring women to continue frequent Pap smears may seem unjustified. Following ACOG (4) recommendations of three consecutive negative tests may seem appropriate until more research is available. Continuing to follow ACOG recommended guidelines includes annual gynecologic pelvic examinations regardless of cervical cancer screening.

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References

1. Saraiya M, Lee, N.C., Blackman, D., Smith, M-J., Morrow, B., and McKenna, M.T. Observations from the CDC. An assessment of Pap Smears and hysterectomies among women in the United States. J of Womens Health Gend Based Med 2002;11(2):103-9.
2. American Cancer Society (ACS). Guidelines for the early detection of cancer [database on the Internet]. 2009 [cited August 18, 2009]. Available from: http://www.cancer.org/docroot/ped/content/ped_2_3x_acs_cancer_detection_guidelines_36.asp
3. USPSTF. Screening for cervical cancer: Recommendations and rationale [database on the Internet]. 2003 [cited August 18, 2009]. Available from: http://www.ahrq.gov/clinic/3rduspstf/cervcan/cervcanrr.htm.
4. ACOG. Cervical cancer screening: Testing can start later and occur less often under new ACOG recommendations [database on the Internet]. 2003 [cited August 18, 2009]. Available from: http://www.acog.org/from_home/publications/press_releases/nr07-31-03-1.cfm.
5. Jemel A, Siegel, R., Ward, E., Hao, Y., Xu, J., Murray, T., et al. . Cancer statistics. Cancer J Clin 2008;58(2):71-96.
6. Parkin DM, Bray, F., Ferlay, J., and Pisani, P. Global cancer statistics, 2002. Cancer J Clin 2005;55(2):74-108.
7. Saslow D, Runowicz, C.D., Solomon, D., Moscicki, A-B., Smith, R.A., Eyre,H.J., et al., for the American Cancer Society. American Cancer Society guidelines for the early detection of cervical neoplasia and cancer. J Low Genit Tract Dis 2002;7(2):67-86.
8. Wright TC, Massad, S., Dunton, C.J., Spitzer, M., Wilkinson, E.J., Solomon, D, Conference ftASfCaCPC. 2006 consensus guidelines for the management of women with cervical intraepthelial neoplasia or adenocarcinoma in situ. Am J Obstet Gynecol 2007;197(4):340-5.
9. McCredie MR, Sharples, K.J., Paul, C., Baranyai, J., Medley, G., Jones, R.W., and Skegg, D.C. Natural history of cervical neoplasia and risk of invasive cancer in women with cervical intraepithelial neoplasia 3: A retrospective cohort study. Lancet Oncol 2008;9(5):425-34.
10. Edgren G, Sapren, P. Risk of anogenital cancer after diagnosis of cervical intraepithelial neoplasia: A prospective population-based study. Lancet 2007;8(4):311-6.
11. Hellman K, Silfversward, C., Nilsson, B., Hellstrom, A.C., Frankendal, B., & Pettersson, F. Primary carcinoma of the vagina: Factors influencing the age at diagnosis. The Radiumhemmet series 1956-1996. Int J Gynecol Cancer 2004;14(3):491-501.
12. ACS. Detailed guide: Vaginal cancer. What are the risk factors for vaginal cancer [database on the Internet]. 2009 [cited August 18, 2009]. Available from: http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_What_are_the_risk_factors_for_vaginal_cancer_55.asp.
13. Dodge JA, Eltabbakh, G.H., Mount, S.L., Walker, R.P., and Morgan, A. Clinical features and risk of recurrence among patients with vaginal intraepithelial neoplasia. Gynecol Oncol 2001;83(2):363-9.
14. Wu XM-G. Descriptive epidemiology of vaginal cancer incidence and survival by race, ethnicity, and age in the United States. Cancer 2008;113(S10):2873-82.
15. Castle PE, Schiffman M, Bratti MC, Hildesheim A, Herrero R, Hutchinson ML, et al. A Population-Based Study of Vaginal Human Papillomavirus Infection in Hysterectomized Women. J Infect Dis 2004;190(3):458-67.
16. Wiener JJ, Sweetnam, P.M., & Jones J.M. Long term follow up of women after hysterectomy with a history of pre-invasive cancer of the cervix. Brit J Obstet Gyneco 1992;99(11):907-10.
17. French DM. Psychological costs of inadequate cervical smear test results. Brit J Cancer 2004;91(11):1887-92.
18. Schockaert S, Poppe, W., Arbyn, M., Verguts, T., and Verguts, J. Incidence of vaginal intraepithelial neoplasia after hysterctomy for cervical intraepithelial neoplasia: A retrospective study. Am J Obstet Gynecol 2008;199(2):113.e1-.e5.
19. Babarinsa I, Mathew, J., Wilson, C., and Oladipo, A. Outcome of vaginal intraepithelial neoplasia following hysterectomy for cervical intraepithelial neoplasia. J Obstet Gynaecol 2006;26(2):157-8.
20. Kalogirou D, Antoniou, G., Karakitsos, P., Botis, D., and Papadimitriou, A. Vaginal intraepithelial neoplasia (VAIN) following hysterectomy in patients treated for carcinoma in situ of the cervix. Eur J Gynecol Oncol 1997;18(3):188-91.
21. Gemmell J, Holmes, D.M., & Duncan, I.D. How frequently need vaginal smears be taken after hysterectomy for cervical intraepithelial neoplasia? Br J Obstet Gynecolo 1990;97(1):58-61.
22. Hellberg DaN, S. 20-year experience of follow-up of the abnormal smear with colposcopy and histology and treatment by conization or cryosurery. Gynceolo Oncolo 1990;38(2):166-9.
23. van Nagell J, J., Hanson, M.B., Donaldson, E.S., & Gallion, H.H. Treatment of cervical intraepthelial neoplasia III by hysterectomy without intervening conization in patients with adequate colposcopy. Cancer 1985;56(12):2737-9.
24. Fawdry RD. Carcinoma-in-situ of the cervix: Is post-hysterectomy cytology worthwhile? Br J Obstet Gynecol 1984;91(1):67-72.

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