

Clin-IQ Project

Clinical question: In women with complete hysterectomy and history of cervical cancer how often should a Papanicolaou smear be done to detect early stage recurrence?

Authors: Christine A. Bridges MD, PGY3, Akhil Singhal MD, PGY2

Mentor: Pamela Tietze MD

Program: University of Oklahoma Health Sciences Center Family Medicine Residency Program

Answer: Patients diagnosed at early stages without adjuvant therapies like chemotherapy and radiation should be screened every 6 months for the first 2 years and then annually, while patients with advanced disease and use of adjuvant therapies should receive screening every 3 months for the first year after treatment, then every 6 months for years 2 through 5 returning to annual screening.

Level of evidence: B

Search terms: PubMed Search- "Papanicolaou smear", "cervical cancer", "hysterectomy"

Date of search: 8/5/12

Inclusion and exclusion criteria

Inclusion: humans, women, over age 21, English language, published in last 5 years

Exclusion: men, children

Summary of issues

Cervical cancer, once the leading cause of female deaths from malignancy, fell to number 14 after screening began in the mid-20th century.¹ Screening increased detection of premalignant and early stage malignancies which have a five year survival rate of 92%.¹ As screening has evolved, so has the understanding of the HPV (Human Papilloma Virus) and cervical cancer. HPV may better predict development of Cervical Intraepithelial Neoplasia stage 3+ (CIN 3+) over the next 5-15 years

compared to cytology, and incorporating HPV testing with cytology may in fact lengthen the screening interval and improve disease detection.¹ Despite screening cervical cancer affects many patients. About 12,000 women are diagnosed with cervical cancer annually in the United States. Although 50% are stage 1 at diagnosis, the rate of recurrence remains high at 10-20%.² Approximately three-fourths of recurrence occurs within 2-3 years.² The American Cancer Society (ACS), American Society for Colposcopy (ASC) and Cervical Pathology (ASCCP), and American Society for Clinical Pathology (ASCP) (Figure 1) agree that women from age 21-29 should be screened every three years with cytology alone, then from age 30-65 with HPV and cytology continuing every five years, and no screening for women over age 65 who have had adequate, not otherwise defined, negative prior screening as defined above.¹ More complex algorithms exist once pathology is identified to further screen and perform colposcopy.

Once cervical cancer has been diagnosed many modalities of treatment exist including chemotherapy and radiation, but the definitive cure remains total hysterectomy. After hysterectomy has been performed the question of how best to properly screen patients remains. There is a link between CIN and Vaginal Intraepithelial Neoplasia (VAIN), related to HPV viral integration into surrounding tissues.³ VAIN represents 1% of genital tract malignancies the risk is elevated in women post-hysterectomy after cervical cancer.³

Summary of evidence

Screening tests ideally detect early disease so that intervention can be performed thereby reducing morbidity and mortality from the disease. An expert panel of the ACS, ASCCP, and ASCP performed a systematic review of available evidence from 2009-2011 to make new recommendations regarding cervical cancer screening.¹ This review did not specifically make recommendations regarding Papanicolaou testing in women after hysterectomy for treatment of

cervical cancer, but does discuss detection rates of vaginal cuff cytology. Women with previous history of CIN2+ have a 5-10 fold higher risk of developing cervical cancer and recommendations include screening for 20 years (Figure 1), even if this extends past age 65 but no screening interval was specified.¹ Women who have undergone hysterectomy for benign indications do not require any further screening postoperatively.¹ Evidence for this recommendation was based on a study in the New England Journal of Medicine in 1996 which suggested that 663 tests would be needed to detect one case of vaginal dysplasia in women post hysterectomy for benign reasons.¹ They also report the results of a study from the British Journal of Gynecology which sampled the vaginal cuff of women with CIN at hysterectomy, noting that 2 years post hysterectomy abnormal cytology was 0.7 in 1000.

This systematic review confirms the recommendation to stop screening in women with hysterectomy without malignancy but there still remains the question of how to screen those with history of malignancy. The Society of Gynecologic Oncology (SGO) published a review in 2011 which states that the current recommendations, based on expert opinion and retrospective studies, after hysterectomy divides screening into 2 groups based on extension of disease at time of diagnosis (Figure 2). Patients diagnosed at early stages without adjuvant therapies like chemo and radiation should be screened every 6 months for the first two years, then annually, while patients with advanced disease and use of adjuvant therapies should receive screening every 3 months for the first year after treatment, then every 6 months for years two through 5.² Screening should include cytology; history and physical-emphasizing screening for: pelvic pain, lymphedema in lower extremities, vaginal bleeding, discharge, urinary symptoms, cough, and weight loss.² Symptom history and physical exam (with pelvic) has been shown to detect 29-75% of asymptomatic recurrence compared to cytology alone, with only 0-17%.² They add that previous radiation therapy can make this detection rate lower.² It is recommended to obtain PET-CT if recurrence is suspected,

but not for routine surveillance.²

The American Journal of Obstetrics and Gynecology published a retrospective analysis of 3030 women with CIN2+ without history of VAIN. Cytology revealed that 7.4% of the women who underwent hysterectomy still had postoperative vaginal cuff smears which later converted to VAIN.³ None of these women were immunocompromised and results were not affected by the method of hysterectomy, vaginal or abdominal.³ Mean time to confirmation of change on biopsy was 45 months post-op, with a median of 35 months.³ This study agrees with the consensus statement from ACS which discussed the increase of VAIN in women with a history of cervical malignancy.

The Journal of Lower Genital Tract Disease also published a study addressing screening modalities in post hysterectomy women. This study was also a retrospective chart review of 64 women, who were divided into two groups based on their indication of post hysterectomy cytology, group A considered to have unnecessary post hysterectomy cytology based on ACS guidelines and group B had risk factors that called for continued surveillance.⁴ Risk factors include DES exposure, history of VAIN, cervical cancer or CIN2+ at time of hysterectomy.⁴ Group A contained 22 women who were referred for 26 total colposcopic exams after abnormal vaginal cuff cytology, while group B contained 42 who were referred for 97 colposcopic exams after abnormal vaginal cuff cytology.⁴ Only one patient in the group A showed High Grade Squamous Intraepithelial Lesion on colposcopy, while in group B, who had risk factors, 19% had VAIN 2- 3 and 2% had Squamous cell carcinoma.⁴ The comparison of these two groups and the disparate rates of abnormal cytology post hysterectomy again confirm current recommendations from SGO to have increased screening for women who have a history of cervical neoplasia.

Figure 1. Cervical Cancer Screening Guidelines: Regular vs History of Cervical Cancer with Hysterectomy¹

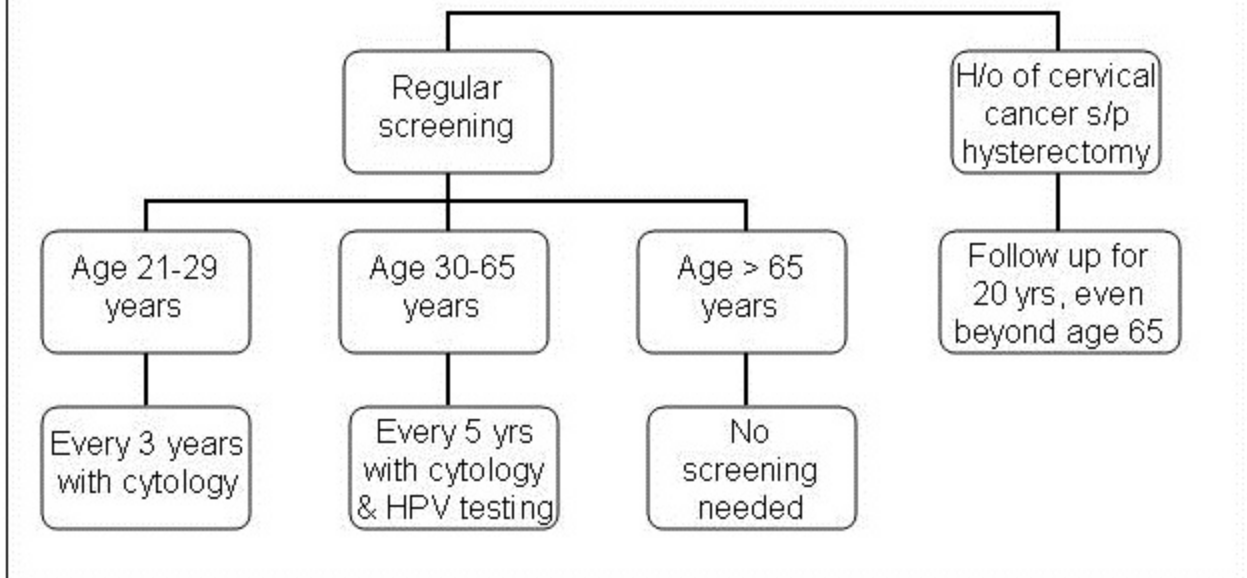
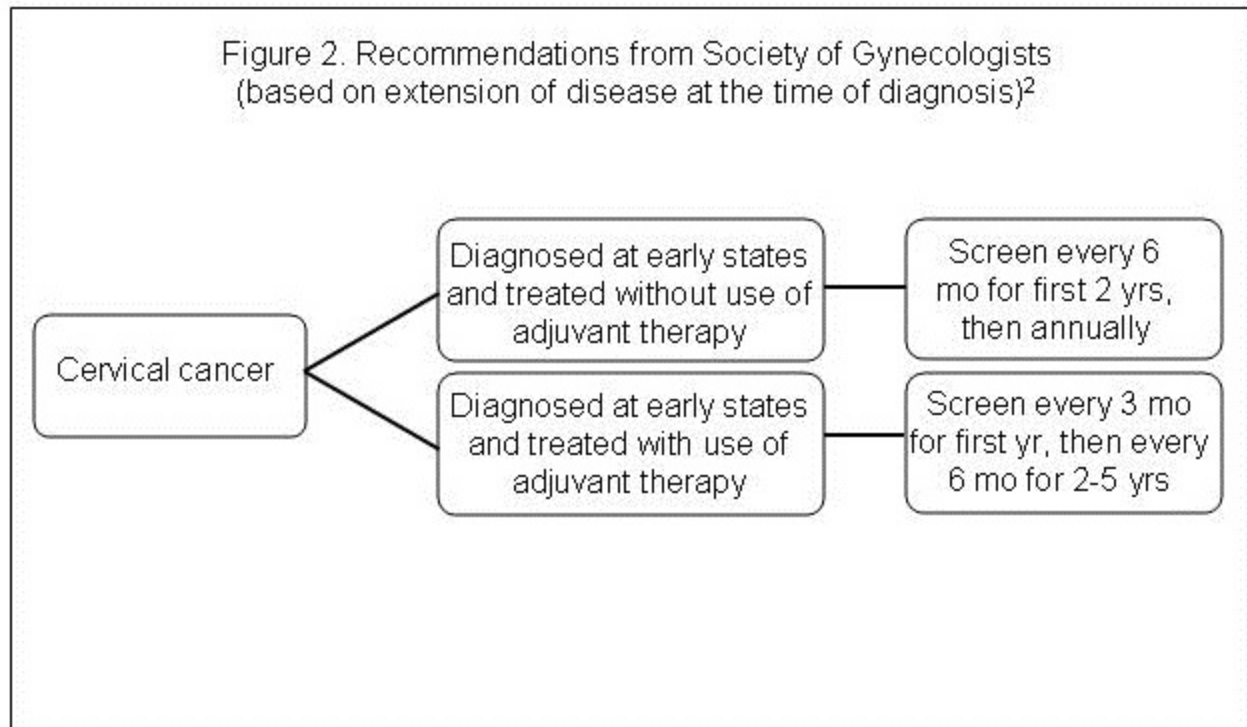


Figure 2. Recommendations from Society of Gynecologists (based on extension of disease at the time of diagnosis)²



Conclusion

As supported by the studies published in Journal of Lower Genital Tract Disease and

American Journal of Obstetrics and Gynecology, there is enough evidence to support the recommendations set forth by Society of Gynecologic Oncologist for screening in post hysterectomy patients who have history of CIN. In the future, we plan to screen patients diagnosed at early stages without adjuvant therapies like chemotherapy and radiation every 6 months for the first 2 years and then annually, while patients with advanced disease and use of adjuvant therapies should receive screening every 3 months for the first year after treatment, then every 6 months for years 2 through 5.

References

1. Saslow D, Solomon D, Lawson H, et al. American Cancer society, American Society for Colposcopy and cervical pathology, and American society for clinical Pathology screening guidelines for the Prevention and early detection of cervical cancer. Journal of Lower Tract Disease, Vol 16, Number 3, 2012-0-0.
2. Salani R, Backes F, Fung M, Holschneider C, et al. Posttreatment surveillance and diagnosis of recurrence in women with Gynecological Malignancies: Society of Gynecologic Oncologist Recommendations. American Journal of Obstetrics and Gynecology. Vol 3, Number 8, 466-478.
3. Schockaert S, Poppe W, Arbyn M, et al. Incidence of Vaginal and Intraepithelial Neoplasia after hysterectomy for cervical intraepithelial neoplasia: A retrospective study. American Journal of Obstetrics and Gynecology. Vol 199, Issue 2 (August 2008).
4. Parva M, Nicholas V, Holtz D, et al. Posthysterectomy Cytology Screening: Indications and Clinical Complications. Journal of Lower Genital Tract Disease. Vol 16 Number 1, 2012, 45-48.