Screening Elderly Women for Urogenital Cancers: When Should We Stop Giving Older Women Pap Tests?

Marie-Hélène Mayrand, MD, MSc, FRCSC, *Departments of Oncology and Epidemiology, McGill University, Montreal, PQ.*

Eduardo L. Franco, PhD, *Professor of Epidemiology and Oncology, Director, Division of Cancer Epidemiology, McGill University, Montreal, PQ.*

Introduction

The Canadian population is growing older, and women represent an ever higher proportion among the elderly: 57% of Canadians over 65 years of age are female, and in the "over 85" age group, this proportion reaches 70%.[1] We can expect that specific health care issues that pertain to this segment of the population will receive renewed attention. Understandably, there has been a special interest in identifying preventive health care measures that can effectively prevent disability or premature death in women over age 65.

With the sole exception of cervical cancer, there is no evidence that screening women for urogenital neoplasms, such as endometrial, ovarian and bladder cancers, reduces mortality from these cancers, regardless of age.[2] Therefore, the focus of this article will be on reviewing the basis for practice recommendations concerning screening for cervical cancer. Although essentially preventable, cancer of the uterine cervix continues to be a significant health problem, particularly in older women. In Canada, older women have the highest incidence and mortality rates from cervical cancer when compared to younger age groups.[3] In the United States, 25% of cervical cancers are diagnosed in women over 65, but 40%-50% of the mortality occurs in this age group.[4] This warrants the identification of the most appropriate screening strategy in this group of women.

Cancer of the uterine cervix is one of the most preventable cancer types because of the presence of a long, asymptomatic, precancerous phase and the availability of a relatively simple and specific screening test.[3,5] The Papanicolaou (Pap) test has been the principal screening test for cervical cancer for the last 50 years. New tests are presently under investigation but will not be discussed in the present article because published guidelines are still not available. Although no randomized controlled trials of Pap cytology have ever been performed, other evidence suggests that the Pap test has played a pivotal role in reducing both incidence and mortality from this disease. In Canada, the mortality from cervical cancer was reduced by 80% after the Pap test became widely used.[5] Studies in other countries have yielded similar results.[6-8]

Screening Older Women

Given the recognized value of the Pap smear and the importance of cervical cancer in elderly women, why do we eventually stop cervical screening? There are many reasons why the value of the Pap test is not as widely recognized in older women. One reason is that studies showing the benefits of Pap screening generally have not included older women.[9,10] Moreover, there are certain characteristics of the older population that directly affect the risk / benefit equation of Pap testing:

1. The lower life expectancy of the older population makes it less likely that they will benefit from screening. Indeed, it probably takes at least five years for a screen-detectable asymptomatic cancer to become symptomatic and even longer to cause death, taking into account that the progression of cervical disease may be different in older women, as discussed below (point #4).[10] Finding and treating a cancer precursor that would never have caused the patient any symptoms can be considered a failure of screening, in the sense that it has caused some morbidity and no benefit.[4] Thus, when deciding if a particular woman should be screened, her life expectancy is one of the most important elements to consider.[4] Chronological age alone is a poor indicator of a woman's life expectancy, because the health and functional status of women become more and more heterogeneous as they age.[4,9,11,12] For this reason, it may be useful to consider the distribution of life expectancies, and not just the average value. For example, in the US, although an average 70 year old woman can expect to live an additional 16 years, 25% will live less than nine years and 25 % will live more than 21 years. Similarly, an average 80-year-old will live nine years, but 25% will live less than five and 25% will live more than 13 years. Although the latter examples are for the U.S. population, comparable estimates would apply to the Canadian vital statistics. It is, of course, impossible to evaluate precisely each patient's life expectancy. However, simply considering the presence and severity of comorbidities and the functional status together with the chronological age will help predict a patient's overall life expectancy.[10] This will give a precise enough estimate to make sound screening decisions.[9]

2. The prevalence of serious comorbidities increases with age.[9,13] Frailty may preclude diagnostic or therapeutic measures to be performed if a screening test were positive. Women in whom additional procedures cannot be carried out because of overriding clinical concerns should not be screened.

3. The screening test performance tends to be different in the older population.[13] To be effective, the Pap smear must sample the transformation zone of the cervix, which is the junction between the squamous epithelium and the columnar epithelium, where cancer precursors arise. In the postmenopausal woman, this zone tends to recede to the cervical canal, and may not be as effectively sampled.[11,14,15] This is a valid but theoretical concern, since no study has yet shown that the Pap smear is less sensitive in older women. However, there is some evidence that the Pap smear may be less specific in older women. Indeed, atrophic changes can be mistakenly interpreted as dysplasia and lead to unwarranted additional tests. There is conflicting evidence as to the benefit of hormonal supplements to increase the test's specificity.[16,17] Sawaya *et al.* have suggested that the positive predictive value of the Pap smear is close to zero in postmenopausal women who have previously been repeatedly screened with normal results. This is due both to the test's lack of specificity, and to the low prevalence of cervical cancer precursors in a population that has been repeatedly screened.

4. The natural history of cervical cancer may be different in older women. Some have suggested that the progression from a preinvasive to an invasive lesion may happen more frequently as women age. Some evidence also suggests that when progression does occur, it may be faster. The fact that cervical cancer precursor rates, such as *in situ* cancer rate, fall with age, but that the incidence rate of invasive cancer increases with age, lends support to this theory.[15,18] If this is true, then the time window when the Pap test may prevent invasive cervical cancer is shorter for older women.

Various groups have tried to evaluate the benefit of Pap testing in women over 50. Retrospective studies in European populations have concluded that preinvasive lesions are infrequently diagnosed through Pap testing in women older than 50 years of age, if they have been adequately screened through an organized program.[15,19-21] These studies have suggested that women older than 50 should be released from screening programs so that resources may be more efficiently allocated.

These studies provide guidance on screening decisions among older women who have repeatedly received normal results in the context of an organized screening program. Unfortunately, this is of limited help in the Canadian setting. Canada is among the industrialized countries that have not implemented a national, organized, screening program; only a few provinces have benefited from population-based cervical screening. In most regions, we rely on opportunistic screening, with the result that low risk women are over-screened and high risk women are under-screened or not screened at all.[22] Canadian data show that older women are the most non-compliant group in terms of cervical cancer screening. Over 40% of women aged 60–69 have either never had a pap smear, or had the last one more than three years ago. This proportion increases to 69% in women older than 70. This is probably part of the reason why, in Canada, the probability of developing cervical cancer in the next 10 years is highest in the 70–79 age group.[18] Because of lack of screening, older women are also more often diagnosed at a later stage of disease, when treatments are much less effective.[11] There is strong evidence that screening elderly women with an inadequate screening history is beneficial both in terms of reducing mortality and saving money to the health care system.[23] Thus,

Table 1
Selected Practice Recommendations Concerning Age to Discontinue Pap Test Screening of Older Women[14,26-29]

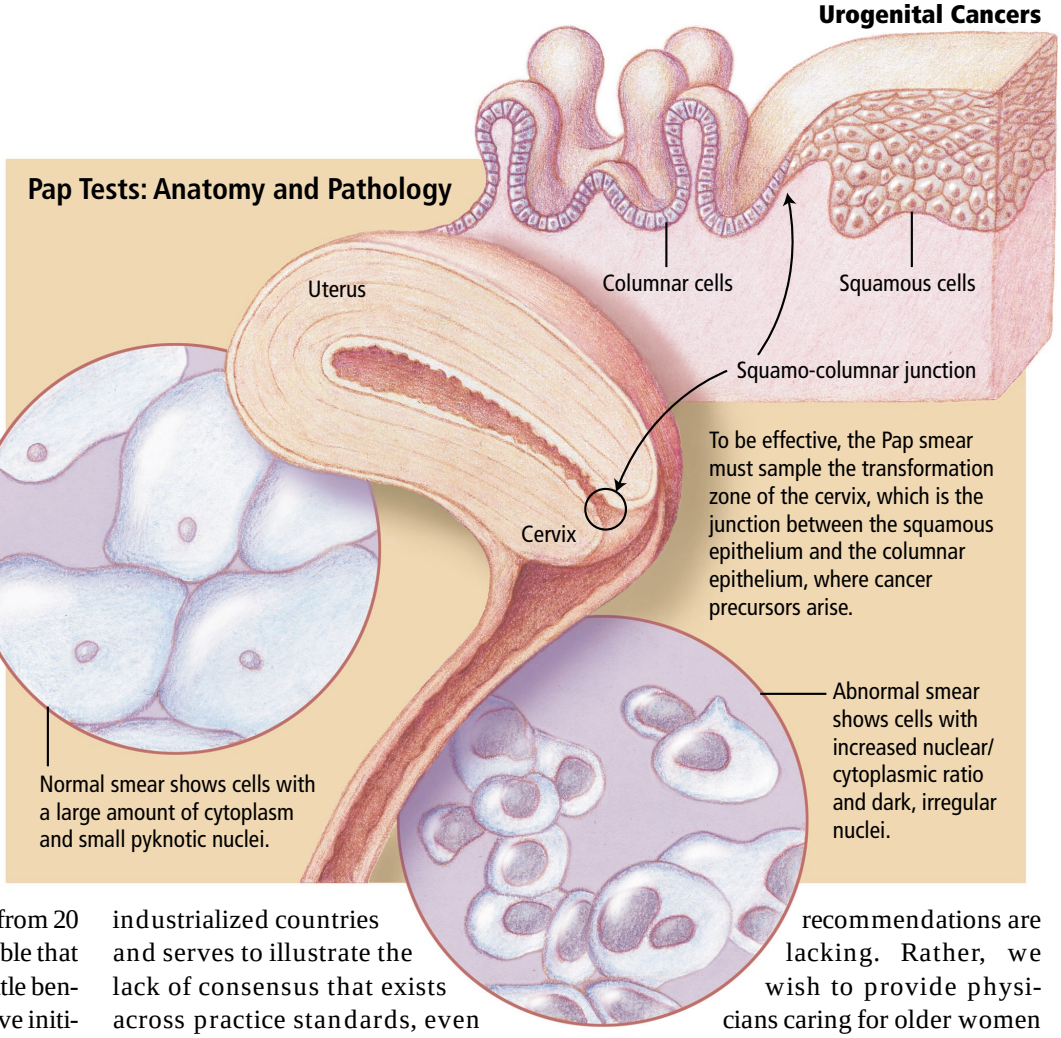
Country	Recommended age to discontinue screening
Sweden	– Between 50 and 60, depending on region
Denmark	– Stop every third year screening at 59 – Screen women 60-74 years of age, once
Finland, Ireland, Netherlands, Scotland	– 60
Belgium, Greece*, Italy*, United Kingdom (except Scotland)	– 64
France*, Portugal*, Spain*	– 65 (except Isère Department, France: 60)
Canada*	– 69 (70 in British Columbia) – If woman over 67 has never been screened, 2 smears, at least 6 months apart, should be taken before discontinuing screening
Australia	– 70
Germany, Austria*, Luxembourg	– No upper age limit
United States**: – U.S. Preventive Task Force – American Geriatrics Society – ACS, ACOG, AMA, NIH	 – 65 – At least until 70 – Individualized after 70 (no evidence for or against) – If never been screened, at least 2 negatives – No upper limit

* limited screening programs
** no organized screening programs

Abbreviations: ACS: American Cancer Society; ACOG: American College of Obstetricians and Gynecologists; AMA: American Medical Association; NIH: National Institute of Health

considering the screening history of a woman is probably as important as considering her estimated life expectancy when deciding whether or not she should be screened.

Also, the above-mentioned studies were conducted in birth cohorts with more conservative sexual practices. In this population, HPV infections, the cause of most cervical cancers, tended to be acquired when a woman was in her 20s, with the initiation of sexual activity, with one of the few partners the woman would have in her lifetime. This would lead to preinvasive lesions developing when the woman was in her 30s and 40s, and invasive cancer when she is over 50. Given that most invasive cancers arise from preinvasive lesions, and that those women were screened intensively from 20 to 50 years of age, it is understandable that screening past the age of 50 adds little benefit. However, later generations have initiated intercourse earlier, are more likely to switch partners at any age and have on average a higher number of sexual partners. This changes the risk profile of HPV infection. For this reason, it is possible that we will see changing patterns of cervical cancer precursor incidence, even in women who have had multiple normal Pap smears. For example, there is new evidence that a second peak in HPV infection occurs in the 40-year-old age group. Even though little is known about the natural history of such infections in older women, it is reasonable to suspect that there could eventually be a second incidence peak in precursor lesions in women over 50.



Existing Practice Standards

Since there is no randomized controlled trial to address the issue of when to stop screening for cervical cancer, and since the results of most epidemiological studies are difficult to generalize to our population, we may wish to base our decision on clinical practice guidelines. Table 1 summarizes existing recommendations from different industrialized countries and serves to illustrate the lack of consensus that exists across practice standards, even among different organizations within a country, on when to stop screening for cervical cancer using the Pap smear. It is noteworthy that, to some extent, the heterogeneity in guidelines reflects the fact that some of the countries have some form of organized screening programs and that recommendations pertain to the inclusion of women in said program. While it may not be cost effective to screen all 70-year-old women who have had multiple normal screens in their lifetime, it does not follow that no 70-year-old women would benefit from screening.

We have seen that cervical cancer remains a significant health problem for older women in Canada. This is mostly because this age group has not been as intensively screened as younger women have, but also possibly because of worse screening test performance in this population and different disease biology. It is beyond the scope of the present article to suggest at what age an organized screening program in Canada should stop including women because evidence-based recommendations are lacking. Rather, we wish to provide physicians caring for older women in regions where no such program exists, with a framework that can assist them in deciding whether or not a particular woman should be screened.

Conclusions

Considering the available evidence there seems to be no justification to stop opportunistic screening before the age of 70, unless specific problems exist that shorten life expectancy or would preclude further diagnostic or therapeutic action. Because of a shorter life expectancy and frequent comorbid conditions, few women over 80 will benefit from screening. For women between the ages 70 and 80, the decision to screen or not to screen will need to be addressed individually, taking into account the factors that affect the probability that the woman will benefit from screening. Although not specific to the older population, it is worth mentioning that women who have not had sexual intercourse and women who had a total hysterectomy for a benign condition and no history of biopsy-proven high

grade cervical intra-epithelial neoplasia or cervical cancer do not need to be screened. Both the removal of the cervix and benign pathology should be documented.[24,25] In summary, we propose the following framework as shown in Table 2.

The future holds many challenges in the area of cervical cancer screening for older women. Studies should focus on the value of the Pap test in the older population of Canadian women and on factors that may affect the test's performance. A better understanding of the natural history of the disease in this population would no doubt help to design tailored screening strategies. Efforts should also be made to identify ways to successfully reach under-screened older women. This information will be essential if an evidence-based organized screening program is to be implemented in Canada. ◆

Table 2

General Proposed Framework for Screening Women for Cervical Neoplasia

Women in whom cervical cancer screening may be safely discontinued:
- Women over 70 who have had at least three normal screens in the last 10 years and no history of biopsy-proven, high-grade cervical intra-epithelial neoplasia or cervical cancer
- Women with a life expectancy lower than 5–7 years
- Women in whom a positive Pap test cannot be followed up by a diagnostic work-up and/or therapeutic procedures (because of comorbidity or other clinical reasons)

Women in whom cervical cancer screening should probably go on indefinitely (at least until the residual life expectancy is lower than 5–7 years or comorbidity would prevent further tests or treatment):
- Women with a history of biopsy proven intra-epithelial neoplasia grade 2 or higher or cervical cancer
- Immunosuppressed women, including HIV-positive women and women on immunosuppressive drug therapy

Women in whom cervical cancer screening is most likely to be useful:
- Women who have never been screened
- Women who have not been screened in the previous five years

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