

CERVICAL CANCER IN SINGAPORE – A STATUS CHECK

Clin A/Prof Tay Eng Hseon

ABSTRACT

The incidence of cervical cancer has been declining gently and it now ranks as the 5th most prevalent female cancer in Singapore. About 85 patients die from the disease annually. It is a largely preventable cancer and there are now two preventive measures namely: Pap smear screening and HPV vaccinations.

SFP 2007; 33(3): 32 - 33

STATUS CHECK

1. The incidence of cervical cancer has been declining gently over the last three decades and it now ranks as the fifth most prevalent female cancer in Singapore.
2. The age-standardised rate of cervical cancer incidence has declined from about 18.4 per 100,000 women to 10.6 per 100,000 women, recorded up to the period 1997-2002.
3. An average of about slightly over 200 new cases of cervical cancer are diagnosed every year in Singapore, with about 85 patients dying from the disease annually.
4. The mortality rate is somewhat high (42.5%) indicating that patients are still presenting with latter stages of the disease, where cure rates drop significantly. If detected early, FIGO stage Ia, the cure rate approximates 100%.
5. The treatment for cervical cancers can be largely grouped into four main categories, namely:
 - a. Micro-invasive stage (FIGO Stage Ia) – This stage of cancers is treated largely by surgery, ranging from a simple cone biopsy to a modified radical hysterectomy with pelvic lymphadenectomy.
Five-year survival rate: Approximately 90% and up to 100%.
 - b. Early Localised stage (FIGO Stages Ib – IIa) – Radical Hysterectomy with Pelvic Lymphadenectomy are equally effective as Radical Pelvic Radiotherapy. The bulky diseases are best treated using concurrent pelvic radiotherapy and chemotherapy.
Five-year survival rate: Approximately 65% for bulky disease and up to 90% for small volume diseases.
 - c. Advanced Localised stage (FIGO Stages IIb – IVa) – Concurrent pelvic radiotherapy & chemotherapy is the main stay of treatment for this stage.

Five-year survival rate: Approximately 30% up to 65% depending on the stage of disease.

- d. Metastatic Disease (FIGO Stage IVb) – The aim of treatment for this stage is palliative and employ radiotherapy, chemotherapy and surgery (e.g. bowel diversion) depending on the symptom of the patient.
6. Cervical cancer is highly preventable. There are now two preventive measures, namely: Pap smear screening and HPV vaccinations.
 7. Cervical Screen Singapore was implemented in 2004. This program, as with other countries, will be a relatively costly and labour-intensive exercise for the country, but promises to reduce the incidence and mortality of a largely preventable cancer.
 8. In the Cervical Screen Singapore program, women who ever had sex should routinely have their first Pap test by the age of 25 years old, then repeated every three years thereafter, if no abnormality is detected. The screening may cease at the age of 65 years of age, if the last Pap test and the preceding Pap test (within three years) are normal and there had been no previous diagnosis of pre-cancer.
 9. Women who never had sexual intercourse may be excluded from national screening program. One should consider screening a woman at an earlier age and at more frequent Intervals if she has HIV infection, sexually transmitted diseases or is immunosuppressed (e.g. on steroids therapy).
 10. In women with previous hysterectomy for benign disease and has had normal Pap test results before, need not have any further pap screening. If she never had a pap test before, a baseline Pap test may be performed and cease screening, if the Pap test is found to be normal.
 11. However, the Pap test is by no means a perfect test and its major drawback (3) is a false-negative result. False-negative rates continue to be reported, even recently.
 12. The causes of false negative results include improper sampling, preparation errors and laboratory misinterpretations. The medico legal repercussions of a proven false-negative test can be very costly and has been the cause of extensive efforts to reduce this inherent deficiency of the Pap test.
 13. Adjunctive mechanisms used to enhance Pap testing include: automated slide-handling systems, computerised microscope, automated Pap smear screening, computer-assisted re-screening of conventionally-negative Pap smears, and mono-layer preparation of cervical smears. In addition, non-cytological methods, such as cervicography and microelectrical detection of biophysical changes of

the cervical tissues, have been studied. But such adjunctive mechanisms increase the cost of screening significantly, and have not convinced all governmental agencies to employ them.

14. The factors critical to having a successful Pap smear screening program include achieving a wide coverage of women screened in the community, the sensitivity and specificity of the Pap test and the prompt effective management of pre-cancerous cervical abnormalities detected through screening.
15. Coverage is still a limiting factor in Cervical Screen Singapore. In the Singapore Health Survey, 70% of women have had a least one pap test in their lifetime and only 50% of women had a pap test within the preceding three years.
16. The discovery of the central etiologic role of genital human papilloma virus (HPV) in cervical carcinogenesis led to the employment of HPV vaccines to prevent cervical cancer.
17. The HPV vaccines (quadrivalent and bivalent vaccines) have been demonstrated to have high level of efficacy with minimal side effects. Their protective effects have been sustained since its use in the studies, for the last five to six years.
18. However, prophylactic cervical cancer vaccines does not eliminate the requirement for a cervical screening till the incidence of cervical cancer is reduced significantly such that having a national screening program would not be cost-effective.
19. The feasibility of HPV testing has not been demonstrated in the setting of a low-resource, developing country.

REFERENCES

1. Chia KS, Seow A, Lee HP, Shanmugaratnam K. Singapore Cancer Registry Report No. (5). Trends in Cancer Incidence in Singapore 1993-7.
2. Anttila A, Pukkala E, Soderman B, Kallio M, Nieminen P, Hakama M. Effect of organised screening on cervical cancer incidence and mortality in Finland, 1963-1995: recent increase in cervical cancer incidence. *Int J Cancer* 1999;83:59-65.

3. Wain G, Hacker NF. Pitfalls in the screening and early diagnosis of cervical cancer. *Curr Opin Obstet Gynecol* 1990;2:74-9.
4. Mubiayi N, Bogaert E, Boman F, Leblanc E, Vinatier D, Leroy JL, Querleu D. Cytological history of 148 women presenting with invasive cervical cancer. *Gynecol Obstet Fertil* 2002;30:210-7.
5. *Acta Cytologica* Volume 40, Jan-Feb 1996 (1).
6. Coppleson M, Reid BL, Skladnev VN, Dalrymple JC. An electronic approach to the detection of pre-cancer and cancer of the uterine cervix: a preliminary evaluation of Polarprobe. *Int J Gynecol Cancer* 1994;4:79-83.
7. Broadstock M. Effectiveness and cost effectiveness of automated and semi-automated cervical screening devices: a systematic review of the literature. *N Z Med J*. 2001 Jul 13;114(1135):311-3.
8. Bosch FX, Manos MM, Munoz N, Sherman M, Jansen AM, Peto J, Schiffman MH, Moreno V, Kurman R, Shah KV. Prevalence of human papillomavirus in cervical cancer: A worldwide perspective. *J Natl Cancer Inst* 1995;87:796-802.
9. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz N. Human papilloma virus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999;189:12-9.
10. Cox JT. Clinical Role of HPV Testing. *Obstetrics & Gynecology Clinics of North America* Volume 23 Number 4, December 1996 : 811-51.
11. ASCUS-LSIL Triage Study (ALTS) Group. Results of a randomized trial on the management of cytology interpretations of atypical squamous cells of undetermined significance. *Am J Obstet Gynecol*. 2003;188:1383-92.
12. Koutsky LA, Ault KA, Wheeler CM, Brown DR, Barr E, Alvarez FB, Chiacchierini LM, Jansen KU. A controlled trial of a human papilloma virus type 16 vaccine. *N Eng J Med* 2002;347:1645-51.
13. Harper DM et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial. *Lancet*. 2004 Nov 13;364(9447):1757-65.
14. Diane M Harper et al. *Lancet* 2006; 367: 1247–55. Sustained efficacy up to 4-5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial.
15. Quadrivalent Vaccine against Human Papillomavirus to prevent High-Grade Cervical Lesions. The FUTURE II Study Group. *New England Journal of Medicine* 2007;356:1915-27.
16. Effect of prophylactic human papillomavirus L1 virus-like-particle on risk of cervical intra-epithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. The FUTURE II Study Group. *Lancet* 2007; 369:1861-8.
17. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. HPV PATRICIA Study Group. *Lancet*. 2007 Jun 30;369(9580):2161-70.

LEARNING POINTS

- o Cervical cancer is a largely preventable cancer.
- o Pap smear screening and HPV vaccinations are two strategies to prevent cervical cancer.
- o A successful Pap smear screening programme, such as the Cervical Screen Singapore, depends on a wide coverage of women screened in the community, the sensitivity and specificity of the Pap test, and the prompt effective management of pre-cancerous cervical abnormalities detected through screening.
- o Presently, prophylactic cervical cancer vaccines does not eliminate the requirement for a cervical screening.