Excessive pap smears due to opportunistic cervical cancer screening

R.A.P. Freitas, G.A.F. Carvasan, *B.Sc.*; **S.S. Morais,** *B.Sc.*; **L.C. Zeferino,** *M.D., Ph.D.*

[1]*Department of Obstetrics and Gynecology, School of Medical Sciences, State University of Campinas, Cidade Universitária "Zeferino Vaz", Campinas, São Paulo (Brazil)*

Summary

The study aimed to analyze the Pap smears carried out for cervical cancer screening according to Ministry of Health guidelines. All smear tests carried out within the public health system in Campinas in 2003 were analyzed. All tests that did not conform to the guidelines were considered excessive. The guidelines recommend screening once every three years for all women aged 25 to 59 after they have received two negative smears. This study showed that the majority of women initiated screening prior to 25 years of age and the periodicity was predominantly annual, followed by biannual tests. In conclusion, 63.4% of tests were excessive. The screening coverage was 14.76%, but if all the tests had been performed as recommended, the final coverage over three years could have reached 65.4%. Thus it is possible to increase the coverage with the available resources since the screening works like an organized program.

Key words: Cervical cancer screening; Vaginal smear; Public health administration; Women's healthcare; Screening programs.

Introduction

Cervical cancer is the third most common type of cancer among Brazilian women, with only skin (non-melanoma) and breast cancer being more common [1]. This form of cancer is an important public health issue, since its incidence may be reduced through efficient screening programs [2-4].

Cervical intraepithelial neoplasia is a consequence of the action of the human papilloma virus (HPV), and its prevalence is closely associated with early sexual initiation and sexual activity with various partners [5,6]. Cervical epithelial lesions pass through various stages before becoming invasive carcinomas. Early detection may be carried out with the Papanicolaou test, thereby permitting therapeutic measures that may lead to a cure in as many as 100% of cases [7, 8].

Despite the existence of a cervical cancer-screening program, 19,260 new cases are estimated to have occurred in Brazil in 2006 [1]. Moreover, there is no evidence of any reduction in the mortality rate from this type of cancer [9]. The Brazilian program recommends screening women 25-59 years of age once every three years following two negative control tests [1]. Considering that indicators of incidence and mortality suggest that the preventive actions carried out are ineffective, it is possible that the recommended guidelines are not being adequately followed. This study analyzed the age at which women are being screened and the interval between tests. From this data, it is possible to estimate the number of screening tests that are being carried out outside the age group and periodicity established by the Brazilian screening program and, consequently, what constitutes excessive testing.

Revised manuscript accepted for publication February 11, 2008

Materials and Methods

This cross-sectional study included women who were clients of the Brazilian public health system in Campinas, which is composed of 47 healthcare centers in five districts: north, east, south, northwest and southwest. Data from eight referral outpatient departments were also analyzed.

The study population comprised all the women who had been submitted to a Pap smear for cervical cancer screening within the Brazilian public health system in Campinas between January and December 2003. Samples were collected by a nurse or doctor, and were sent to the Cytopathology Laboratory of the Women's Integrated Healthcare Center (CAISM) at the State University of Campinas (UNICAMP).

Exclusion criteria comprised:

Women undergoing follow-up at cervical pathology outpatient departments; those who had undergone Pap smear testing at the outpatient department of UNICAMP's Teaching Hospital or at CAISM; hysterectomized women; those who had previously undergone radiotherapy; those who had been submitted to cauterization; women who had a previous abnormal Pap smear result; and women undergoing post-treatment follow-up. After applying the exclusion criteria, 54,338 Pap smear results were analyzed.

In 2003, regulations in force required that a sample from the cervical canal should be collected using an appropriate brush and a sample from the ectocervix should be obtained using an Ayre spatula. Cytological diagnosis was established according to the Bethesda System [10].

Pap smear results were obtained from the data system of CAISM's Cytopathology Laboratory, which registers the information directly from the request form and the results of the Pap smear. This form was edited to transmit data using barcode scanners. This information system has features that automatically test data consistency. For each cell type, either squamous or glandular, only one diagnosis was accepted.

Calculation of the excessive cytology tests was made by using the study carried out by van Ballegooijen *et al.* [4] as a reference, and adjusting it for the data available in the database

of the Cytopathology Laboratory of UNICAMP. Based on the Ministry of Health guidelines, excessive testing was defined as:

– All tests carried out outside the target age group, i.e. performed in women ≤ 24 or ≥ 60 years of age.

– Whenever the interval between the previous screening control and the current one was less than three years; in these cases, information was recorded on the length of the interval: two years, one year or less than one year.

To calculate the total number of tests in excess, the following formula was constructed: (2/3 (b - a) + $^1/_2$ c + d + e) based on the following assumptions (Table 1). Since a woman's second control should have been carried out one year after the first, to correct the calculation of excessiveness, exams carried out for the first time the previous year were subtracted from the total of all tests carried out at intervals of one year. Since the data regarding the number of tests carried out for the first time in 2002 were unavailable and the data system was unable to identify the tests that represented second screenings, it was assumed that the total number of first tests carried out in 2002 would be the same as the number performed in 2003. Therefore, the calculation of excessive testing was corrected by subtracting the number of tests carried out for the first time in 2003 (a) from the total number of tests performed after an interval of one year (b) in the 25-59 year age group.

Therefore, taking a three-year periodicity as a reference, in three years women should have undergone one screening. In the case of women who underwent screening at an interval of one year, we considered two-thirds of these tests to be excessive after subtracting the cases of second screening [2/3 (b - a)], since in three years three controls would have been carried out, but of these three, only one would have been necessary. In the case of women who underwent screening after an interval of two years (c), we considered 50% of these tests to be excessive, since in three years two screening tests would have been performed, with only one being necessary ($^1/_2$ c). For the purposes of calculation, intervals of less than one year were considered as a year.

Tests carried out at intervals of three years or more were not considered excessive, nor were the tests in which no information was available with respect to periodicity. Tests in which quality was unsatisfactory (d) were included in the sum of tests in excess, since they failed to contribute towards the prevention of cervical cancer and resulted in the test having to be repeated. Finally, the tests performed outside the target age-range were added to the total (e).

Results

The total of studied tests was 54,338. Data showed that 24.6% of women were under 25 years of age, 68.8% were between 25 and 59 years of age, and 6.5% were 60 years of age or older. Of these women, 9.1% had undergone Pap smear testing for the first time. The majority of tests (44.5%) were carried out one year after the previous screening; 25.9% two years afterwards; 8.8% three years later; and 7.2% after four years or more. A further 1.3% of tests had no information with respect to the time since the previous screening.

Of the women who had undergone screening for the first time, 76.2% were under 25 years of age, 8.0% were aged 25-29, and 15.82% were 30 years of age or older.

The quality of the smears was considered satisfactory in 49.8% of cases, and unsatisfactory in 2.1% of samples. The remaining 48.2% of cases were considered satisfactory but with limitations.

Table 1. — *Parameters for the calculation of excessive Pap smears based on the following formula: excessive tests = (2/3 (b – a) + $^1/_2$ c + d + e).*

Equation symbol	Age (years)		Total
a	25 - 59	First screening	939
b	25 - 59	Screening at an interval of ≤ 1 year since previous test	18,507
c	25 - 59	Screening at an interval of 2 years since previous test	10,339
d	25 - 59	Quality of tests unsatisfactory	698
e	< 25 or > 59		16,885

Table 1 shows the parameters comprising the mathematical formula for calculation of the excess cervical smear tests. In the 25-29 year age group, the number of first screening tests was 939. In this same age group, a total of 18,507 tests were found in which the interval since the previous screening was one year or less, and another 10,339 in which the interval was only two years. Quality was unsatisfactory in 698 samples. The number of tests carried out in women ≤ 24 or ≥ 60 years of age was 16,885 (Table 1).

Therefore, of a total of 54,338 tests, 34,465 were considered excessive, corresponding to 63.4%. Based on the data collected for this study, the percentage of the population aged 25-29 covered for cervical cancer screening was 14.76%. If all the tests carried out in 2003 had been performed in women in the age-group recommended by the Ministry of Health, the final coverage in that year would have been 21.8%. If excess testing was eliminated and the same resources were used in accordance with the Ministry of Health guidelines, coverage would have been 65.4% (Table 2).

Table 2. — *Tests in excess and estimated coverage if no excess testing existed.*

Total number of tests	54,338
Tests in excess	34,465
Percentage of the population aged 25-59 covered	14.76%
Percentage of the population that would be covered annually if all tests had been performed in women within the age-group recommended by the Ministry of Health	21.8%
Estimated three-year coverage if all the tests had been carried out within the age-group recommended by the Ministry of Health and no woman had repeated screening within this period	65.40%

Discussion

Cervical cancer begins as a low-grade intraepithelial lesion that may evolve to a more serious lesion over an average period of 10-15 years. This means that the serious lesions are more prevalent in women who have been sexually active for more than ten years, i.e. older women [11]. In young women, low-grade lesions are more prevalent. Moreover, these have a high rate of spontaneous regression. The more severe intraepithelial lesions

have a greater potential to progress to invasive carcinoma; however, they are rare in younger women [12, 13].

In the eighties, a study carried out by the International Agency for Research on Cancer (IARC) found that initiating screening at 20 years of age leads to a reduction of 1-2% in the accumulated rate of invasive carcinoma compared to screening from 25 years of age [14]. Therefore, beginning screening prior to age 25 means diagnosing predominantly less severe lesions, the majority of which regress spontaneously, consequently leading to a system that is poorly effective in reducing mortality rates from invasive cancer. Moreover, the rare cases of invasive carcinoma that occur in this age-group are normally very aggressive and very probably would occur irrespective of screening [15].

The same occurs in the case of screening at close intervals, since less severe lesions remain for less time. Therefore, repeating the test annually leads to the detection of predominantly low-grade lesions [13]. On the other hand, the more severe precursor lesions may take more than ten years to progress, therefore, women who undergo periodic screening will have various opportunities at which to detect these lesions. These were the conclusions reached in the IARC study, which showed that the reduction in the incidence of cervical cancer does not vary significantly when controls are annual or triennial, 93% and 91%, respectively; not justifying, therefore, the implementation of an annual screening program [14].

From the point of view of public health, the effectiveness of a cervical cancer-screening program is known to depend on the percentage of the population covered by the program. To achieve coverage of 80%, for example, 27% of women in the target age-group would have to be submitted to a Pap smear in one year, while in the following two years, the tests would be carried out in different women, attaining 80% of the total female population over a three-year period. However, this is not what is occurring. According to the results of this study, 73.6% of tests were carried out less than three years after a previous screening test, not including first screenings, i.e. there is a large contingency of women who undergo Pap smears every year.

In Campinas, the percentage of the population covered in 2003 was 10.19%, well below the expected rate for effective screening. Moreover, the age group with greatest coverage was between 20 and 34 years of age, an age at which less severe lesions are the most common.

Analysis of the age distribution of the women who carried out tests for the first time showed that the majority were 15 to 19 years of age, followed by the 20 to 24-year age-group, i.e. below the age recommended by the Ministry of Health [1].

Another important finding from this study refers to the quality of smears. Quality was found to be satisfactory but with some restrictions in 48% of all tests carried out, while a further 2% of smears were unsatisfactory. This results in an important waste factor, as well as additional discomfort to the women, since tests often have to be repeated. It is a fact that the low quality of smears is prejudicial to the performance of cervical cancer screening, since it leads to a greater rate of false-negative results and, consequently, a greater risk for the population [16].

A total of 54,338 tests were carried out of which 63.4% were considered in excess, i.e. a further 34,465 women from the target population could have been screened if the Ministry of Health guidelines had been followed. This would increase screening coverage and lead to a more effective control of this form of cancer with less need to increase healthcare resources.

The number of tests carried out in women 25-59 years of age, excluding those in which quality was unsatisfactory, was 36,755. The population in Campinas in this age group was 249,062; therefore, the percentage of the population covered by screening was 14.76% in 2003. If all the tests carried out in 2003 had been performed in the age bracket recommended by the Ministry of Health, the final coverage in that year would have been 21.8%. Thus, over three years, this coverage could have reached 65.4% if no woman had repeated the test in that period of time. This would be considered a high rate since it did not include tests carried out in the private sector.

Nevertheless, the situation of the city of Campinas may be considered privileged compared to the rest of the country, since specific data for Campinas show a reduction of 37.5% in the mortality rate for cervical cancer in the periods 1992-1993 and 1997-1998 [17].

The results of this study show that cervical cancer screening in Campinas does not adhere to the guidelines of the Ministry of Health. The majority of women began screening before reaching 25 years of age and most women carried out the test annually or biannually. With respect to the number of tests performed, annual screening coverage was low.

Therefore, to optimize cervical cancer screening, the best solution would not be to reduce the frequency of Pap smears, but to redistribute these tests to women who have not been reached by the program.

Acknowledgments

This work was supported by the São Paulo Foundation for the Support of Research (FAPESP) through Scientific Initiation Grant # 04/00921-0.

References

[1] Brasil Ministério da Saúde. Programa Nacional de Controle do Câncer do Colo do Útero e de Mama - Viva Mulher. Rio de Janeiro (Brasil): Instituto Nacional de Câncer. [cited 2007 Feb 24]. Available from: http://www.inca.gov.br/prevencao/programas/viva_mulher/

[2] Ferlay J., Bray F., Pisani P., Parkin D.M., GLOBOCAN 2000: "Cancer incidence, mortality and prevalence worldwide". Version 1.0., Lyon; IARC Press; 2001. (IARC Cancer Base No. 5).

[3] Parkin D.M., Bray F.I., Devesa S.S.: "Cancer burden in the year 2000. The global picture". *Eur. J. Cancer,* 2001, 37 (suppl. 8), S4.

[4] van Ballegooijen M., Marle E., Patnick J., Lynge E., Arbyn M., Anttila A. *et al.*: "Overview of important cervical cancer screening process values in European Union (EU) countries, and tentative predictions of the corresponding effectiveness and cost-effectiveness". *Eur. J. Cancer*, 2000, *36,* 2177.

[5] Atalah E., Urteaga C., Rebolledo A., Villegas R.A., Medina E., Csendes A.: "Alimentación, tabaquismo e historia reproductiva como factores de riesgo del cáncer de cuello del útero. [Diet, smoking and reproductive history as risk factor for cervical cancer]". *Rev. Med. Chile*, 2001, *129,* 597.
[6] Kjellberg L., Hallmans G., Johansson R., Bergman F., Wadell G., Angström T. *et al.*: "Smoking, diet, pregnancy, and oral contraceptive use as risk factors for cervical intra-epithelial neoplasia in relation to human papillomavirus infection". *Br. J. Cancer,* 2000, *82,* 1332.
[7] Brasil Ministério da Saúde. Prevenção do Câncer do Colo do Útero. Manual Técnico para Laboratórios. Brasília, DF: Ministério da Saúde; 2002.
[8] Elovainio L., Nieminen P., Miller A.B.: "Impact of cancer screening on women's health". *Int. J. Gynaecol. Obstet.,* 1997, *58,* 137.
[9] Brasil Ministério da Saúde. Atlas de mortalidade por cancer no Brasil 1979-1999. Rio de Janeiro (Brasil): Instituto Nacional de Câncer. [cited 2007 Feb 24]. Available from: http://www.inca.gov.br/atlas/docs/seriestemp_BR.pdf (Série temporal das taxas de mortalidade, brutas e ajustadas por idade pelas populações mundial e brasileira, para topografias selecionadas, entre 1979 e 1999).
[10] Solomon D., Davey D., Kurman R., Moriarty A., O'Connor D., Prey M. *et al.*: "Forum Group Members; Bethesda 2001 Workshop. The 2001 Bethesda System: terminology for reporting results of cervical cytology". *JAMA,* 2002, *287,* 2114.
[11] Wright V.C., Riopelle M.A.: "Age at beginning of coitus versus chronologic age as a basis for Papanicolaou smear screening: An analysis of 747 cases of preinvasive disease". *Am. J. Obstet. Gynecol.,* 1984, *149*, 824.
[12] Östör A.G.: "Natural history of cervical intraepithelial neoplasia: a critical review". *Int. J. Gynecol. Pathol*., 1993, *12,* 186.
[13] d'Ottaviano-Morelli M.G., Zeferino L., Cecatti J.G., Terrabuio D.R., Martinez E.Z.: "Prevalence of cervical intraepithelial neoplasia and invasive carcinoma based on cytological screening in the region of Campinas, Brazil". *Cad. Saude Publica,* 2004, *20,* 153.
[14] I.A.R.C. working group on evaluation of cervical cancer screening programmes: "Screening for squamous cervical cancer:duration of low risk after negative results of cervical cytology and its implications for screening policies". *Br. Med. J.* (Clin. Res. Ed.), 1986, *293,* 659.
[15] Datta N.R., Pasricha R., Singh U., Srivastava A.: "Predictors of survival end points in patients with cancer of the cervix on long-term follow-up: inferences and implications from an audit of patients treated with a specific radiotherapy protocol". *Clin. Oncol. (R. Coll. Radiol.),* 2004, *16*, 536.
[16] Amaral R.G., Zeferino L.C., Hardy E., Westin M.C., Martinez E.Z., Montemor E.B.: "Quality assurance in cervical smears: 100% rapid rescreening vs 10% random rescreening". *Acta Cytol.,* 2005, *49,* 244.
[17] Zeferino L.C., Pinotti J.A., Jorge J.P., Westin M.C., Tambascia J.K., Montemor E.B.: "Organization of cervical cancer screening in Campinas and surrounding region, Sao Paulo State, Brazil". *Cad Saude Publica*, 2006, *22,* 1909.

Address reprint requests to:
L.C. ZEFERINO, M.D., Ph.D.
Rua Alexander Fleming, 101,
Cidade Universitária "Zeferino Vaz",
13083-970 Campinas, São Paulo (Brazil)
e-mail: zeferino@hc.unicamp.br