Evaluation of 25 years of Uterine Cervical Cancer Screening at Tokai University Hospital Health Evaluation and Promotion Center

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The total number of persons who underwent uterine cervical cancer screening at the Tokai University Hospital Health Evaluation and Promotion Center during the 25-year period from January 1976 to March 2001 was 30,173 (gross number: 111,181). Since 1995, more than 6,500 females have visited the center annually, and more than 70% were 40-59 years of age. Among these females, 849 exhibited atypical changes higher than class IIIa in the cytological examination (class IIIa: 779, IIIb: 43. IV: 14 and V: 13), and the detection rate was 0.76%. In examining the relationship between the age and number of visits to the center and the detection rate of atypical changes observed in the cytological examination, patients in their 40s exhibited the highest detection rate (1.31%), and the rate at the first screening was 1.19%. Analysis of the age distribution for the detection rate of atypical changes in the cytological examination before 1989 and after 1990 showed that persons in their 40s and 50s had high rates (1.62% and 1.69%, respectively) before 1989, but since 1990 persons in their 20s, 30s and 40s exhibited high rates (2.86%, 2.16% and 2.61%, respectively) ($p < 0.001$). This suggests a lowering of the age at which atypical changes are observed in the cytological examination.

Key words: mass screening, dysplasia, human papilloma virus, uterine cervical cancer

INTRODUCTION

Cancer screening has gradually become more common in Japan since the 1960s. Uterine cervical cancer screening, which is performed using a cytological examination, is an excellent screening method that has been performed on a nationwide scale since 1983 as part of the health care program specified by the Health and Medical Service Law for the Aged. From 1955 to 1965, the mortality of uterine cancer ranked second after gastric cancer among site-specific cancers in females. In recent years, the prevalence rate of uterine cervical cancer has ranked second, after breast cancer, and 5,202 patients died due to this cancer in 2000. Although the mortality of uterine cervical cancer has shown a tendency to decrease over recent years, this cancer still accounts for 4.5% of deaths due to malignant tumors in females [1].

Concordant with the increase in uterine cervical cancer screening, evaluation of the effectiveness of such screening has also been promoted. In 1998, Sato *et al.* published a report on mass screening for uterine cervical cancer performed mainly in the Miyagi Prefecture over 35 years. According to this report, the mortality of uterine cervical cancer was 12.1/100,000 persons before initiation of the screening project, and decreased to 4.0/100,000 due to the mass screening. Therefore, it was concluded that screening is highly effective. In addition, a case-control study on invasive carcinoma concluded that the prevalence of invasive carcinoma was significantly lower in patients who underwent mass screening than in those who were not screened; it was concluded that such screening contributed to a marked decrease in the development of the cancer, although a significant difference in the overall death rate was not observed [2-4].

Previous national and overseas reports have demonstrated that uterine cervical cancer screening enables early detection of the cancer, resulting in a decrease in mortality. In recent years, however, the lowering of the age of the first sexual experience and an increase in the number of people with multiple sexual partners have facilitated an increase in HPV infection in the younger generation, which has been accompanied by an increase in the prevalence of uterine cervical cancer in women in their 20s. Thus, close epidemiological reexamination and a review of the appropriate interval between visits for uterine cervical cancer screening and the target age group for screening is of importance [5-7]. Therefore, the main purpose of the current study was to analyze the results of uterine cervical cancer screening over 25 years in our hospital, and to examine the validity and aims of future mass screening.

SUBJECTS AND METHODS

The Tokai University Hospital Health Evaluation and Promotion Center was established in May 1975, and full-fledged screening of uterine cervical cancer has been performed at the center since January 1976.

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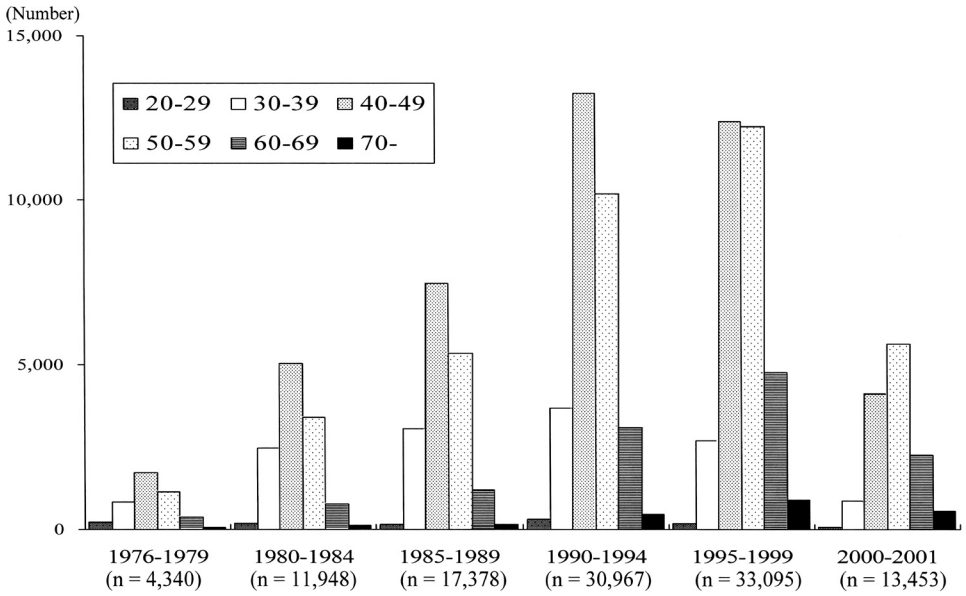

Fig. 1 The relationship between age and number of women screened from 1976 to 2001.

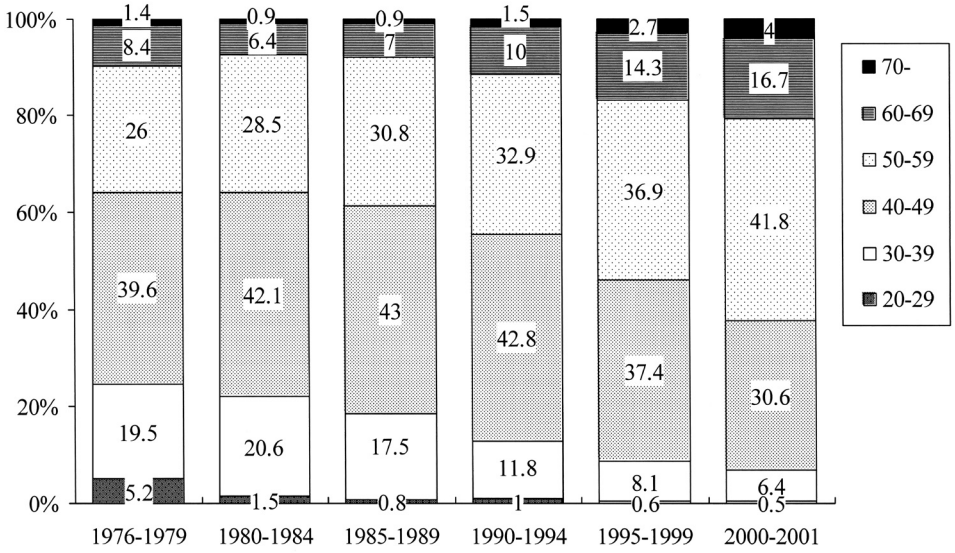

Fig. 2 The relationship between age and detection rate from 1976 to 2001.

In this study, an analysis was performed on 30,173 persons (gross number: 111,181) who underwent uterine cervical cancer screening during the 25-year period from January 1976 to March 2001. Changes in the number and age of persons who underwent screening, the detection rate of atypical changes in the cytological examination, and the age at which cancer developed were examined.

Uterine cervical cells were collected using cotton swabs by obstetricians and gynecologists. These cells were smeared evenly on a glass slide and fixed with 95% ethanol for Papanicolaou staining. Diagnosis based on the cytological examination was performed by screeners and advising pathologists, and the samples were divided into six groups according to the following classification: class I: no abnormal findings; class II: abnormal findings but benign changes; classes III and IIIa: mild to moderate dysplasia; class IIIb: severe dysplasia; class IV: carcinoma *in situ*; and class V: invasive carcinoma. For samples that were class III or higher, colposcopy was performed during a secondary examination in the outpatient gynecological tumor department at our university hospital, and punch biopsy was performed on abnormal lesions observed in the colposcopy. Statistical analysis was performed using a Chi-square test, with $p < 0.05$ regarded as significant.

RESULTS

Number and age of persons who underwent uterine cervical cancer screening

Uterine cervical cancer screening was initiated in January 1976, and 4,340 persons underwent screening during the four-year period from 1976 to 1979: an annual average of 1,085. Since then, the number of persons undergoing screening has increased gradually: 29,329 from 1980 to 1989, and 64,064 from 1990 to 1999; since 1995, the annual average has been more than 6,500 (Fig. 1). In addition, persons of 40-50 years

Table 1 Data for 849 women with atypical neoplasia in the uterine cervix.

class	women (%)	average of age
IIIa	779 (91.8)	47.2
IIIb	43 (5.1)	43.4
IV	14 (1.7)	45.1
V	13 (1.5)	55.5

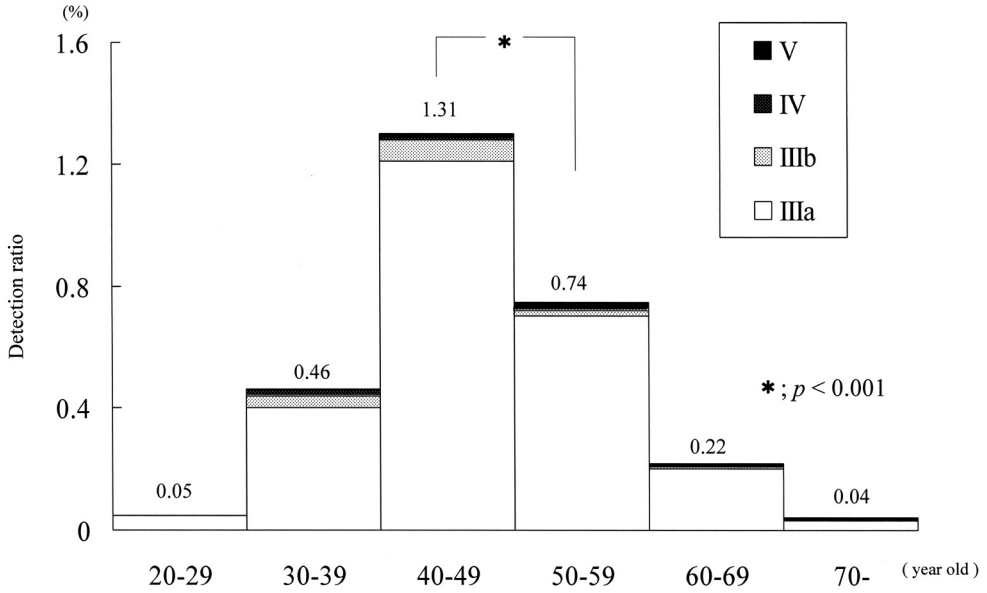

Fig. 3 The relationship between age and detection rate of atypical changes.

of age accounted for 70% or more (70.6-75.7%) of those screened annually from 1980 onwards. Persons aged 60 years or older initially accounted for 7.3-9.8% of those screened annually, and this percentage increased to higher than 10% after 1990, and to higher than 20% after 2000. On the other hand, persons in their 20s-30s initially accounted for more than 20% of those who underwent screening, but this percentage has decreased gradually to 8.7% for the period of 1995-1999, and to 6.9% from 2000-2001 (Fig. 2).

Age and detection rates of atypical changes in the cytological examination

Over 25 years, 849 persons (gross number: 1,003) were categorized with a smear of class III or higher, due to atypical changes observed during cytological examination of the uterine cervix, giving a detection rate of 0.76%. The number (rate, %) and average age of the persons in individual classes were 779 (91.8%) and 47.2 years old in class IIIa, 43 (5.1%) and 43.4 in class IIIb, 14 (1.7%) and 45.1 in class IV, and 13 (1.5%) and 55.5 in class V, respectively (Table 1). By age, the detection rates of atypical changes in the cytological examination were 1.31%, 0.74% ($p < 0.001$), 0.46%, 0.22%, 0.05% and 0.04% in patients aged 40-49, 50-59, 30-39, 60-69, 20-29 and 70 years old or older, respectively (Fig. 3).

Number of visits and detection rates of atypical changes in cytological examination

In evaluating the relationship between the detection rate of atypical changes in cytological examination and the number of visits by persons classified as class III, the highest rate (1.19%) was observed during the first screening, followed by a rate of 0.37% in the second screening ($p < 0.001$). Except for those cases in which the cancer was detected after screening for more than 11 times, the detection rates decreased with an increase in the number of visits for screening (Fig. 4).

Atypical changes in cytological examination before and after 1989, and age upon development of cancer

The relationship between atypical changes observed during the cytological examination and the age at which development of cancer occurred were compared for the periods before and after 1989. Almost no changes were observed in the detection rates for persons aged 50-59, 60-69 and 70 years old or older in the 1976-1989 and 1990-2001 periods. However, an increase in the detection rate was observed in persons aged 20-29 (from 0.38% to 2.82%, a 7.4-fold increase; $p < 0.001$), 30-39 (from 1.26% to 2.16%, a 1.7-fold increase; $p < 0.001$), and 40-49 years old (from 1.62% to 2.61%, a 1.6-fold increase; $p < 0.001$). The statistically significant increases in persons aged 20-29, 30-39 and 40-49 years old suggest a lowering of the age at which

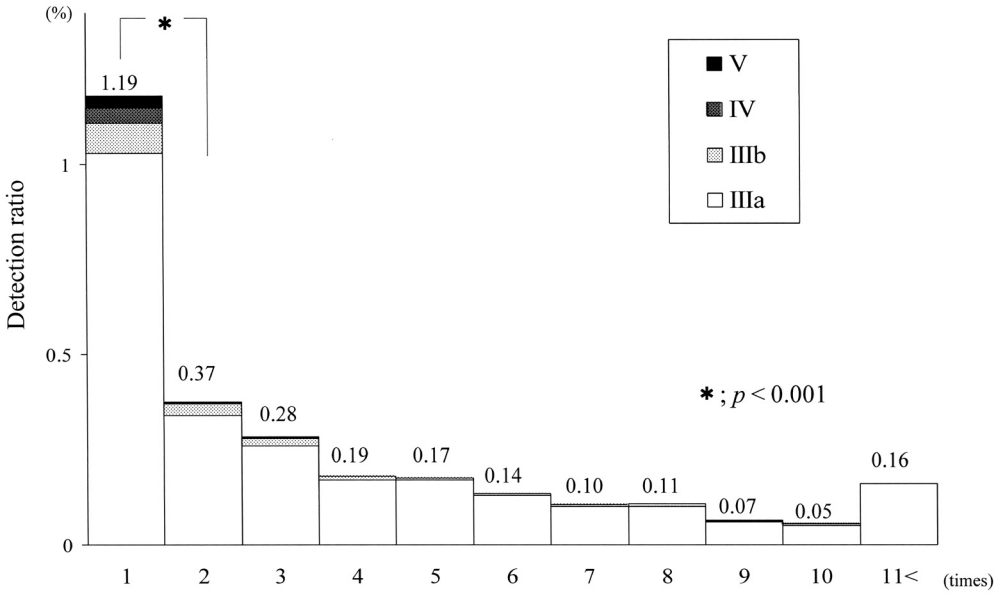

Fig. 4 The relationship between screening time and detection rate of atypical changes.

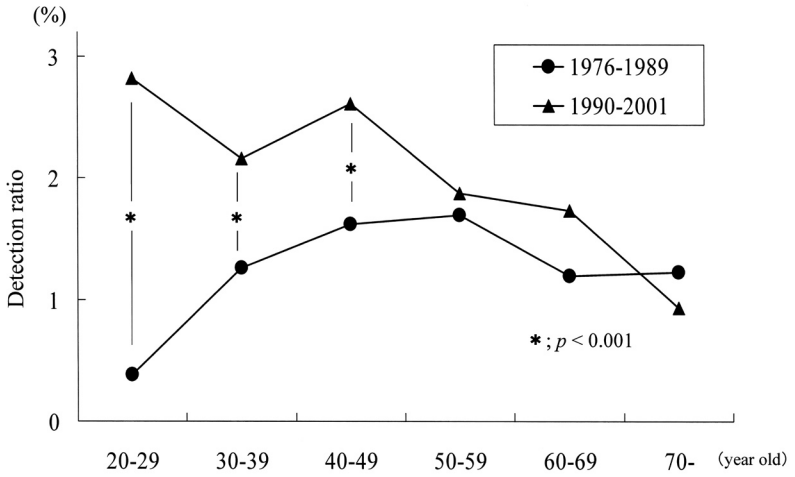

Fig. 5 The relationship between age and percentage of atypical changes.

atypical changes were detected in cytological examinations (Fig. 5).

DISCUSSION

The Tokai University Hospital Health Evaluation and Promotion Center has a thorough medical evaluation system that includes uterine cervical cancer screening. The annual number of persons who underwent screening was initially approximately 1,000, but increased to 3,400 after 1985, and to 6,500 after 1995. Evaluation of the age at the time of screening showed that persons aged 40-59 years old accounted for more than 70% of the total and that those aged 30-39 years old accounted for 17-20% during the initial phase of screening. Persons aged 60-69 years old accounted for 10% after 1990, and this percentage increased to 16.7% after 2000, while those aged 30-39 years old accounted for 8.1% initially, with this percentage decreasing gradually to 6.4% after 2000 (Figs. 1 and 2). These results depended largely upon the background of people who visited our hospital: at our center, employees of nearby companies that had a contract for screening accounted for approximately 70-80% of the total; the fee for screening was subsidized by the companies. These cases initially accounted for approximately 65% of all persons undergoing screening, but this proportion increased to 75% after 1990. The target age of screening for company employees was 40-50 years old, and this may be the cause of the large number of persons in this age range who visited our hospital for screening. This caused a decrease in the proportion of patients aged 20-29 who underwent screening, as shown in Figure 1. Many of these persons continued to regularly undergo screening, even after retirement from the company, which may have caused the recent increase in the percentage of persons aged 60 years or older. In a report of mass screening of 150,000 persons in Tokyo, the consultation rate was highest for patients

aged 40-50 years, followed by those aged 35-40 years; these results are consistent with our data [8].

The detection rate for uterine cervical dysplasia differs between reports: detection rates of 0.17-0.43% have been found in screening of more than 30,000 persons [8-10]. Compared to these data, the detection rate in the current study was relatively high (0.76%), indicating that early detection was achieved because colposcopy was used in the primary screening [11].

The detection rates of atypical changes by cytological examination according to age were 1.13% in persons aged 40-49 years old, 0.74% in those aged 50-59, 0.46% in those aged 30-39, 0.22% in those aged 60-69, and 0.04-0.05% in those aged 20-29 and 70 years old or more. Oda *et al.* reported these rates as 1.81% in persons aged 30-39 years old, 1.09% in those aged 40-49, and 0.74% in those aged 50-59, showing a peak at an age 10 years younger than that in our data [8]. After 1990, atypical changes in the cytological examination were observed at higher rates, i.e., 2.82% in persons aged 20-29 years old, 2.16% in those aged 30-39, and 2.61% in those aged 40-49, demonstrating a trend towards a lowering of the age at which atypical changes were found in the cytological examination. In mass uterine cervical cancer screening performed mainly in Ibaraki Prefecture from April 1996 to December 1998, 2,491 cases showed changes of class IIIa or higher upon cytological examination [8]. In addition, 9 (5.05%) out of 135 persons aged 10-19 years old exhibited atypical changes during examination, suggesting increased occurrence of atypical changes in younger women and girls, consistent with our data [12].

Human papilloma virus (HPV) infection has been shown to be related to the development of uterine cervical cancer, and more than 70 types of HPV have been confirmed to date. In particular, type 16 and type 18 HPV are considered to be in the high-risk group for dysplasia of the uterine cervical epithelium. In a random sampling survey performed for subjects aged 17-65 years old in the Ishikawa Prefecture, Sasagawa *et al.* reported that 51% of those aged 10-19 years old and 50% of those aged 20-24 years old had HPV-positive DNA tests [5, 13]. In addition, a follow-up survey of HPV-positive subjects demonstrated that dysplasia developed in the uterine cervix at a high rate within three years [13, 14]. Although there was a difference in local characteristics and statistical procedures, it is certain that the HPV-positive rate has increased among the younger generation, which may be due to an increase in their sexual activity. Therefore, it is of importance that gynecologists emphasize the importance of uterine cervical cancer screening to younger women.

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