

Trends in the incidence of uterine cancer in Niigata, Japan: A population-based study from 1982 to 2007

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Summary

This study investigated trends in the incidence of uterine cancer in Japan. Data from the Gynecological Cancer Registry of Niigata comprising all new cases of uterine cancer registered for the entire female population aged 15 years and over a 25-year period were examined. The age-standardized ratio of carcinoma *in situ* has substantially increased among females < 40 years of age (from 3.8 (in the period of 1982-1989) to 40.9 (2000-2007)). There was a significant trend in increasing incidence of invasive cervical cancer for those < 40 years of age (from 4.7 to 13.1), whereas a significant trend of decreasing incidence for the 50+ year age group. The ratios of corpus cancer were increased approximately two-folds both among the population aged < 50 years and those aged 50+ years and thus becoming equivalent to invasive cervical cancer. This prefecture-wide population-based study shows the practical trend in uterine cancer in Japanese females. The current health service must emphasize education among young adults concerning cervical cancer prevention while concentrating on screening. Avoiding risk factors, such as obesity, and increasing protective factors may lower risk for corpus cancer both in younger and older females.

Key words: Uterine cancer; Carcinoma *in situ*; Cervical cancer; Corpus cancer; Incidence; Population-based study.

Introduction

Uterine cancer is the fourth most common cancer in Japanese females with an estimated 24,240 cases in 2003 including 8,674 invasive cervical cancer, 6,955 carcinoma *in situ*, and 7,430 corpus cancer [1]. There is evidence that the incidence of cervical cancer has decreased in wealthy countries as a combined result of risk reduction from health education, changes in lifestyle, and the beneficial effects of screening programs. These factors have led to females being diagnosed at both an earlier stage of disease and also at a younger age. Moreover the incidence of corpus cancer is likely to increase in such countries, mainly due to the increasing obesity epidemic.

The national cancer incidence in Japan has been estimated by the Research Group for Population-based Cancer Registration in Japan since 1975, based on the data from 5-12 population-based cancer registries [2]. However, there are some biases for estimating the overall incidence in Japan since they use data from only a limited number of registries or limited area of the district (not district-wide). The primary objective of this study was to use data from the prefecture-wide gynecologic cancer registry in Niigata to describe the females diagnosed with cervical and corpus cancer within the prefecture. This analysis evaluated 25 years (1982-2007) of uterine cancer incidence data obtained from the Gynecologic Cancer Registry of Niigata in order to investigate the trend in the incidence of uterine cancer in Japanese females.

Materials and Methods

These analyses were based on cancer cases reported to the Gynecologic Cancer Registry of Niigata between 1982 and 2007. This registry was established in 1982 and is a population-based registry which covers the entire female population in Niigata prefecture of around 1.2 million inhabitants. All information on newly diagnosed gynecologic malignant tumors as well as pre-malignant tumors in females aged ten years and over has been collected. Information sources include all hospitals including gynecologic oncology departments as well as private clinics that diagnose and/or treat cancer patients in Niigata prefecture. This study investigated the trends in uterine cancer (WHO: International Statistical Classification of Disease and Related Health Problems, Tenth Revision, code C53 and 54) incidence in Niigata prefecture, according to the following sub categories: invasive cervical cancer (C53), corpus cancer (C54), and carcinoma *in situ* (D06) between 1982 and 2007.

The trend in uterine cancer incidence in Niigata prefecture from 1982 to 2007 was investigated. Age-standardized incidence rates (ASRs) were calculated with 95% confidence limits, for each disease with the world population as the standard. Patients were divided into three groups based on age: < 40 years, 40-49 years, and 50+ years for carcinoma *in situ* and cervical cancer, and < 50 years and 50+ years for corpus cancer. The change in ASRs in three chronological periods, 1982-1989, 1990-1999, and 2000-2007, were examined. Differences in ASRs between the first period (1982-1989) and the last period (2000-2007) were evaluated using rate ratios (RR) and the corresponding 95% confidence interval (CI).

Results

The trends in the age-standardized incidence rates are illustrated in Figure 1. A total of 9,605 females with uterine cancer including carcinoma *in situ* of the cervix, invasive cervical cancer, and corpus cancer cases were diagnosed between 1982 and 2007. The ASRs of carci-

Fig. 1

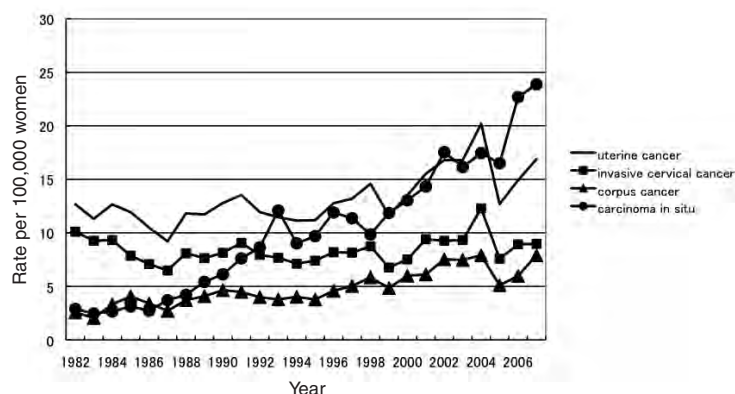


Fig. 3

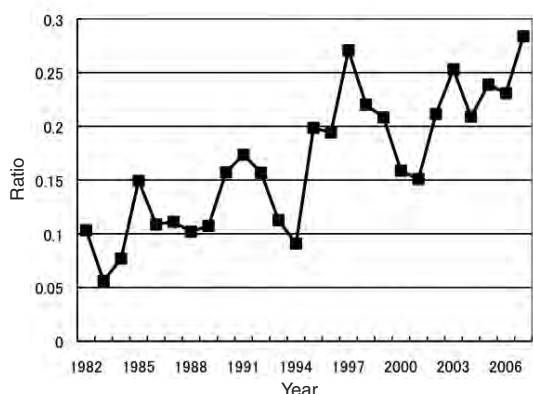


Fig. 2

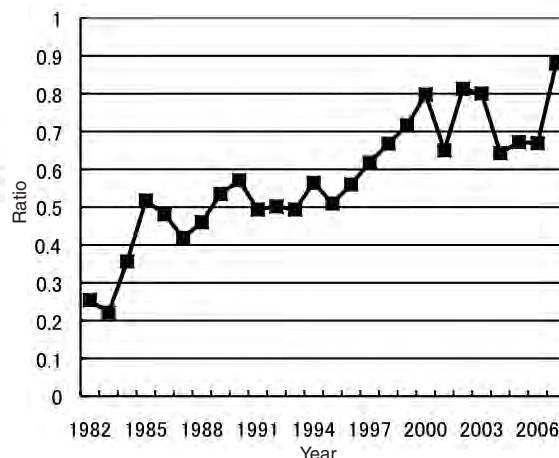


Figure 1. — Trends in the age-standardized incidence rates of uterine cancer. The incidence of “uterine cancer” is a combined incidence of invasive cervical cancer and corpus cancer. Standard population: world standard population.

Figure 2. — Trends in corpus/invasive cervical cancer ratio.

Figure 3. — Trends in invasive cervical adenocarcinoma/squamous carcinoma ratio “adenocarcinoma” includes adenocarcinoma and adenosquamous carcinoma.

noma *in situ* dramatically increased by approximately eight-fold from 2.9 (in 1982) to 23.9 (in 2007) per 100,000 females. The incidence rates of uterine cancer (C53 and C54) increased from 12.7 to 16.9 reflecting the increased incidence rate in corpus cancer with an approximately three-fold increase from 2.6 to 7.9. Conversely, the invasive cervical cancer incidence rate slightly decreased from 10.1 to 9.0. The ratio of corpus cancer to invasive cervical cancer incidence increased steadily from 0.3 to 0.9 (Figure 2).

The trends in the ASRs of carcinoma *in situ* and invasive cervical cancer by age group and the period of diagnosis are shown in Table 1. The incidence rates of both carcinoma *in situ* and invasive cervical cancer among females aged < 40 years and 40–49 years significantly increased during the period from 2000–2007 in comparison to the period from 1982–1989. The ASRs for carcinoma *in situ* have increased substantially among those aged < 40 years (approximately 11-fold, from 3.8 to 40.9), whereas the ASRs increased moderately among those aged 40–49 and age 50+ years, approximately three-fold and two-fold, respectively. There was a significant trend in increasing incidence of invasive cervical cancer in the < 40 years population, whereas a significant trend in decreasing incidence was observed for the 50+ year age group. The incidence rate was almost stable among those aged 40–49 years.

Trends in the incidence according to the histological type of cervical cancer are illustrated in Figure 3. The

ratio of adenocarcinoma incidence (including adenocarcinoma and adenosquamous carcinoma) to all invasive cervical cancers steadily increased from 6% (in 1982) to 25% (in 2007). The trends in the ASRs of cervical cancer according to the histological type by age and period of diagnosis are shown in Table 2. The incidence of squamous cell carcinoma was significantly increased in the < 40 age group whereas it was significantly decreased in the 50+ age group. Significant increases (approximately two-fold) of ASRs for adenocarcinoma were observed in all age groups.

Trends in the ASRs of corpus cancer by age group and period of diagnosis are shown in Table 3. The rates increased approximately two-fold both among the population aged < 50 years and that aged 50+ years.

Discussion

This study investigated evolution of trends in the incidence of uterine cancer in Japanese females during the last 25 years using data from the prefecture-wide gynecologic cancer registry in Niigata. There was a significant and striking increase in the incidence of carcinoma *in situ* and a significant increase in the incidence of invasive cervical cancer in the < 40 age group. Whereas the incidence of invasive cervical cancer appeared to be more or less stable or to show a marginal significant increase in the 40–49 age group and a significant decrease in the 50+ age group. The incidence rate of corpus cancer has been

Table 1. — Trends in the ASRs of carcinoma *in situ* and invasive cervical cancer by age group and the period of diagnosis.

Time period	15-39	Age group 40-49	50+
Carcinoma <i>in situ</i>			
1982-1989	3.8 (2.8-4.9)	11.5 (9.2-13.9)	4.7 (3.7-5.7)
1990-1999	18.6 (14.8-22.4)	25.2 (22.7-27.8)	7.9 (7.1-8.8)
2000-2007	40.9 (34.4-47.5)	36.8 (29.9-43.8)	9.1 (8.5-9.7)
Rate ratio* (95% CI)	11.2 (9.6-12.8)	3.3 (2.8-3.7)	2.1 (1.6-2.6)
Invasive Cervical Cancer			
1982-1989	4.7 (4.0-5.4)	17.5 (14.8-20.1)	24.2 (20.1-28.2)
1990-1999	9.3 (7.9-10.7)	18.9 (17.1-20.7)	15.3 (13.5-17.0)
2000-2007	13.1 (10.7-15.4)	21.3 (18.6-24.0)	14.8 (13.2-16.3)
Rate ratio* (95% CI)	2.8 (2.5-3.2)	1.3 (1.0-1.5)	0.6 (0.5-0.8)

*Rate ratio: 2000-2007 versus 1982-1989.

Gray boxes show statistically significant different compared with 1982-1989. Values are incidence rate (95% confidence interval).

Incident rates are per 100,000 and age-adjusted to the World standard population.

Table 2. — Trends in the ASRs of cervical cancer according to the histological type by age and period of diagnosis.

Time period	15-39	Age group 40-49	50+
SCC			
1982-1989	3.8 (3.5-4.2)	15.2 (13.8-16.5)	22.9 (21.1-24.7)
1990-1999	7.1 (6.4-7.8)	16.0 (14.7-17.4)	12.8 (11.8-13.8)
2000-2007	10.0 (9.8-10.0)	14.5 (13.3-15.7)	10.9 (9.5-12.4)
Rate ratio* (95% CI)	2.7 (2.1-3.3)	0.9 (0.6-1.2)	0.5 (0.3-0.8)
Adenocarcinoma[#]			
1982-1989	0.8 (0.6-1.1)	2.2 (1.6-2.8)	2.1 (1.7-2.5)
1990-1999	1.1 (0.7-1.5)	4.7 (3.2-6.3)	3.0 (2.3-3.7)
2000-2007	1.8 (1.1-2.5)	5.7 (2.6-8.8)	3.2 (2.3-4.1)
Rate ratio* (95% CI)	2.2 (1.3-3.2)	2.4 (1.1-3.8)	1.6 (1.1-2.2)

*Rate ratio: 2000-2007 versus 1982-1989.

Gray boxes show statistically significant different compared with 1982-1989. Values are incidence rate (95% confidence interval).

Incident rates are per 100,000 and age-adjusted to the World standard population.

[#] adenocarcinoma includes adenocarcinoma and adenosquamous carcinoma.

Table 3. — Trends in the ASRs of corpus cancer by age group and period of diagnosis.

Time period	15-49	Age group 50+
1982-1989	2.4 (1.9-2.8)	11.5 (9.6-13.4)
1990-1999	3.2 (2.8-3.7)	16.1 (14.3-17.8)
2000-2007	5.3 (4.2-6.5)	23.1 (20.3-25.9)
Rate ratio* (95% CI)	2.3 (1.9-2.6)	2.1 (1.7-2.4)

*Rate ratio: 2000-2007 versus 1982-1989.

Gray boxes show statistically significant different compared with 1982-1989. Values are incidence rate (95% confidence interval).

Incident rates are per 100,000 and age-adjusted to the World standard population.

steadily increasing in all age groups and reached almost the same incidence rate as that for cervical cancer.

The incidence of invasive cervical cancer has been decreasing in many countries as a combined result of risk reduction from health education and the beneficial effects of screening programs [3]. However, it is interesting to note that the young adult group (< 40 years) clearly showed an increasing trend in invasive cervical cancer while the older age group (over 50 years) showed a decreasing trend. These changes in trends may be attributed to changes in sexual lifestyle and resultant higher prevalence of HPV infection in the younger generation of

Japanese females. The age at the time of first intercourse in Japanese girls has recently sharply decreased. In 2000, 79% of Japanese girls reported having the first sexual intercourse between the ages of 16 and 19 [4]. On the other hand the married age has been reported to be increasing with the estimated mean age for marriage reaching 29.6 years in 2006 [5]. The prevalence of high-risk HPV infection was higher in young Japanese females at 23.1% among those aged 20-29, and 7.9% for those aged 30-49 in 2003 [6].

The significant increasing trend of carcinoma *in situ* in the young adult age group was a remarkable finding in this study. This increasing trend may partly reflect changes in cervical cancer screening practices. The Japanese government revised the legislation in 2005 and lowered the starting age of the screening from 30 to 20 years of age. However nationwide screening coverage for cervical cancer is still low in Japan with only 14% of one-year coverage [7]. Older females tend to demonstrate continued participation, but remarkably fewer younger females participate in such screening programs, and this finding highlights the need to optimize the coverage of the invited population.

Recently, many studies have shown a constant or increased incidence of adenocarcinoma with a decrease in the incidence of squamous carcinoma [8-10]. The relative frequency of adenocarcinoma increased from 12.4% of all cervical cancers during the period 1973-1976, to 24.9% during the period 2001-2004 in the US [11]. This study showed almost the same trend in the incidence of cervical adenocarcinoma with the increased incidence rates in all age groups. High-risk HPV infection is a significant cause of adenocarcinoma similar to squamous cell carcinoma, and therefore the increasing trend in adenocarcinoma may also be attributed to changes in sexual lifestyle and the resultant higher prevalence of HPV infection in Japanese females. Females with adenocarcinoma had a poorer prognosis than those with squamous cell carcinoma, especially in advanced stage cancer. Therefore, cancer screening is more important for adenocarcinoma to improve the prognosis.

The incidence of corpus cancer varies widely among countries, tending to be higher in Western countries and lower in the countries of Africa and Asia including Japan. Corpus cancer is both the most common type of uterine cancer and the most common cancer of the female reproductive system in the US [12]. In general, corpus cancer tends to be a disease of affluent societies and countries with Westernized lifestyles. Recent epidemiological studies show that the incidence rate of corpus cancer is steadily increasing in Japan and the current study is also consistent with those findings [13]. The magnitude of the increasing incidence rate was higher in females over 50 years than those under 50 years. This increased incidence has been due to certain factors; the greater longevity of the population, better nutrition, improved health care and living conditions have led most females to live long enough to develop corpus cancer. Although the exact cause of corpus cancer is still unclear, several major risk

factors for the development of corpus cancer include nulliparity, early menarche, late menopause, obesity, diabetes mellitus, hypertension, family history, tamoxifen therapy, and unopposed estrogen therapy. Of these risk factors, obesity may play the largest role with a recent study indicating that almost 40% of corpus cancer cases are secondary to obesity [14]. A steadily increasing trend in Japan suggests that corpus cancer will become the most common gynecological cancer in Japan in the near future.

The incidence rate of uterine cancer varies within Japan; however, the trend in the incidence rate in this prefecture-wide study is similar with the estimated trend of uterine cancer in Japanese females by the Japanese National Cancer Center. Since nationwide tumor registration has not yet been established in Japan, this prefecture-wide study gives the practical trend in uterine cancer in Japanese females.

The detection of carcinoma *in situ* or early stage invasive cervical cancer in young adults will be more important for female health in the future. Public information on the importance of regular cervical Pap smear screening must be continuously offered to all females, especially young adults, as an integral part of a nation's health service. Finally, avoiding risk factors, such as obesity, and increasing protective factors may lower the risk for corpus cancer both in younger and older females.

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