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Original Article

Incidence and lifetime risk of uterine corpus cancer in Taiwanese women from 1991 to 2010

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ABSTRACT

Objective: Although uterine corpus cancer has been the most common malignancy of the female genital tract in many countries, the lifetime risk of this cancer has not yet been determined among Taiwanese women. The purpose of the study was to describe the change in incidence and the lifetime risk of uterine corpus cancer over a 20-year period from 1991 to 2010 in Taiwan.
Materials and methods: We conducted a population-based registry study using the released database (available online) from the Taiwan Cancer Registry.
Results: A total of 15,542 women newly diagnosed with uterine corpus cancer were included in this study. The total number of this cancer increased by 5.7-fold from 1991 to 2010. The annual age-specific rate nearly doubled during the past decade (2001–2010) when compared with the previous decade (1991–2000). Incidence rates were highest in women aged 50–59 years, and increasing incidence rates were observed in each age strata starting from 40 years to 85 years and more, after the year 2000. The lifetime risk of being diagnosed with uterine corpus cancer was 0.39% in 1991–1995, 0.54% in 1996–2000, 0.73% in 2001–2005, and 1.12% in 2006–2010 among Taiwanese women.
Conclusion: According to the observed changes in incidence rate, the burden of uterine corpus cancer in the general female population is expected to increase in the near future. From a public-health perspective, care providers should develop strategies for the prevention, early detection, and intervention to reduce the rapidly increasing incidence of uterine corpus cancer in Taiwan.

Introduction

Uterine corpus cancer occurs predominately in postmenopausal women aged 50–60 years [1]. Endometrial carcinoma is the most common histologic type, which accounts for approximately 80% of the corpus malignancy [2]. According to the online GLOBOCAN 2012 database [3], the age-standardized incidence rates (ASR) of uterine corpus cancer are as high as 16.3–19.5 per 100,000 person-years in several Western countries (USA, Canada, and Norway), whereas a low rate of 2–11.2 per 100,000 person-years are seen in many Asian countries (China, Korea, India, Thailand, Malaysia). In the USA, the Surveillance, Epidemiology, and End Results data of nine registries indicate that the incidence of uterine corpus cancer remains relatively stable over the past 30 years (ASR of 20.0 in 1980 vs. 18.3 per 100,000 women/year in 2007) [4]. In contrast, uterine corpus cancer is the most rapidly increasing gynecologic malignancy among Taiwanese women. During the same timeframe, the ASR of uterine corpus cancer has nearly septupled from 1.69 in 1980 to 11.36 per 100,000 women/year in 2010 [5]. In 2010, uterine corpus cancer ranked as the sixth most common cancer in women, and accounted

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for roughly 4.4% of all newly diagnosed female malignancies, with 1752 new cases.

The lifetime risk of developing cancer is commonly used to provide a risk estimate in a population, which renders the proportion of the population expected to develop the disease over the course of a lifetime [6]. Although uterine corpus cancer receives considerable attention in many developed countries, the lifetime risk of this cancer as a whole has not yet been determined among Taiwanese women. The purpose of this study was to describe the change in incidence and the lifetime risk of uterine corpus cancer over a 20-year period from 1991 to 2010 in Taiwan.

Materials and methods

Data on uterine corpus cancer incidence, age-specific, and age-standardized (to the world standard 2000 population) incidence rates per 100,000 women/year were obtained for the years 1991–2010 from the released database (available online) at the official website of Taiwan Cancer Registry (TCR) [5]. All women were diagnosed with uterine corpus cancer (International Classification of Diseases for Oncology, Field Trial 182 and International Classification of Diseases for Oncology-3 C54). The primary site codes were classified according to the International Classification of Diseases for Oncology, Field Trial edition, and shifted to the third edition version (International Classification of Diseases for Oncology-3) in 2002. TCR is a population-based national cancer registry, established by the Ministry of Health and Welfare in 1979 to estimate cancer incidence among all civilian residents in Taiwan. Hospitals with 50 or more beds throughout the country are required to report diagnostic and surgical information on newly diagnosed cases of cancer to the TCR on an annual basis. Since all data used in this study were online, publicly accessible aggregate datasets that were openly available to anyone, Institutional Review Board approval was not required for this study.

All rates were expressed as per 100,000 women/year (over 1 year of observation) or per 100,000 person-years (over several years of observation). We compared the age-specific rate, estimated annual percent change (EAPC), and the lifetime risk of four calendar periods (1991–1995, 1996–2000, 2001–2005, and 2006–2010). Since the age-specific rate was not available for the period 2006–2010, it was calculated using stratified procedure counts (by 5-year age groups) and corresponding population denominators (from the National Statistics, Republic of China) [7]. In 2010, 49.8% of the Taiwan population (or 11.5 million civilian residents) were women. The EAPC was used to describe the annual percentage change of age-specific rate for each calendar period. By fitting a regression line to the natural logarithm of age-specific rate using calendar year as a regression variable, EAPC was calculated using the exponential formula [$EAPC = 100^{*}(\exp^{m}-1)$], where "m" was the slope parameter of the regression line and "exp" was the exponential function. Although the cumulative risk calculation proposed by Day (1987) [8] was not directly equivalent to the lifetime risk of developing cancer over a lifetime [6], by setting the truncated upper age band to the average life expectancy in Taiwanese women, the calculated cumulative risk was approximately equivalent to the lifetime risk. Since the average life expectancy among Taiwanese women increased from 76.76 years in 1991 to 82.47 years in 2010 [9], an average of 79 years was used as the average life expectancy of the female population in Taiwan between 1991 and 2010 for the cumulative risk calculation. The cumulative rate expressed as a percentage was first calculated from the cross-sectional age-specific rate until age 79 years. The cumulative risk was then calculated from the cumulative rate using the exponential formula [$\text{cumulative risk} = 1\text{-}\exp^{-\text{cumulative rate}}$)] as proposed by Day (1987) [8]. All calculations were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC, USA). All reported *p*-values were based on two-sided tests at the 0.05 level of statistical significance.

Results

A total of 15,542 women were newly diagnosed with uterine corpus cancer in Taiwan between 1991 and 2010 (Table 1). The numbers of uterine corpus cancer increased by 5.7-fold from 262 cases in 1991 to 1752 cases in 2010 (1.4-fold from 1991 to 2000; 1.5-fold from 2001 to 2010). The EAPC from 2001 to 2010 was 14.25 [95% confidence interval (CI): 4.91–24.43], which was almost twice the estimated annual rate between 1991 and 2000. Although the annual increase in rates for the 1991–1995 period (5.01%/year) was not statistically significant (95% CI: 1.56–8.58), there was a significant increase in the EAPC for the other three calendar periods [9.62% (95% CI: 5.54–13.86) in 1996–2000; 8.67% (95% CI: 6.97–10.39) in 2001–2005; and 10.23% (95% CI: 7.13–13.42) in 2006–2010)].

The age-standardized incidence rate of uterine corpus cancer increased by 2.8 times from 3.02 cases in 1991 to 11.36 cases per 100,000 women in 2010 (Figure 1). Figure 2 demonstrates a shift in the age distribution of uterine corpus cancer risk between the periods 1991–1995 and 2001–2005. The risk increased with age and peaked at women aged 50–59 years for all periods. However, the next highest peak was at women aged 75–79 years during the period 1991–1995, but shifted to those aged 80–84 year after year 2000. In other words, more elderly women were diagnosed of uterine corpus cancers in the periods 2001–2005 and 2006–2010 than during the periods 1991–1995 and 1996–2000. In 2010, approximately 65% of all incident cases were diagnosed among women aged 40–59 years (41.4% among women aged 50–59 years and 23.5% among those aged 40–49 years), followed by 26.7% among women aged 60 years or above, and the remaining 8.4% in women aged less than 40 years.

Figure 3 shows the lifetime risk (cumulative risk before age 79 years) of incident cases of uterine corpus cancer in the 1991–1995, 1996–2000, 2001–2005, and 2006–2010 periods, based on the cross-sectional age-specific incidence rates in Table 1. The lifetime risk of being diagnosed with uterine corpus cancer was 0.39%, 0.54%, 0.73%, and 1.12% for 1991–1995, 1996–2000, 2001–2005, and 2006–2010 periods, respectively. In 2010, the lifetime risk of uterine corpus cancer was 1.25% for a 79-year-old woman and 1.35% for women aged $\geq$85 years (Figure 4).

Discussion

This study investigated the changes in incidence and the lifetime risk of uterine corpus cancer in the general female population in Taiwan from 1991 to 2010. Our findings suggested that the incidence of uterine corpus cancer increased by 5.7-fold during the study period. The annual age-specific rate nearly doubled during the past decade (2001–2010) when compared with the previous decade (1991–2000), particularly in the latest period from 2006 to 2010. Incidence rates were highest in women aged 50–59 years, and increasing incidence rates were observed in each age strata starting from 40 years to 85 years and more, after the year 2000. The lifetime risk of being diagnosed with uterine corpus cancer was 0.39% in 1991–1995, 0.54% in 1996–2000, 0.73% in 2001–2005, and 1.12% in 2006–2010 among Taiwanese women.

The majority of endometrial cancers (70–80%) are estrogen-related malignancies [10]. The rapid increase in the incidence and the lifetime risk of uterine corpus cancer are most likely attributed to the increasingly prevalence of both exogenous and endogenous estrogen sources among Taiwanese women over the past 20 years

Table 1
Estimated numbers and rates of age-specific incidences of uterine corpus cancers among Taiwanese women by calendar periods (1991–1995, 1996–2000, 2001–2005, and 2006–2010).

1991–1995			1996–2000			2001–2005			2006–2010		
Y	No.	Rate[a]	Y	No.	Rate[a]	Y	No.	Rate[a]	Y	No.	Rate[a]
1991	262	2.63	1996	399	3.81	2001	714	6.51	2006	1,184	10.49
1992	311	3.09	1997	495	4.68	2002	786	7.12	2007	1,192	10.50
1993	325	3.20	1998	549	5.14	2003	815	7.35	2008	1,438	12.60
1994	327	3.18	1999	553	5.13	2004	921	8.26	2009	1,522	13.25
1995	343	3.31	2000	627	5.76	2005	1,027	9.16	2010	1,752	15.20
Total	1,568	3.03		2,623	4.87		4,263	7.54		7,088	12.51
EAPC		5.01			9.62*			8.67*			10.23*
EAPC (1991–2000)			7.29								
EAPC (2001–2010)			14.25*								

Data Source: Taiwan Cancer Registry.
* $p < 0.05$.
EAPC = estimated annual percentage change.
[a] Age-specific incidence rate per 100,000 women.

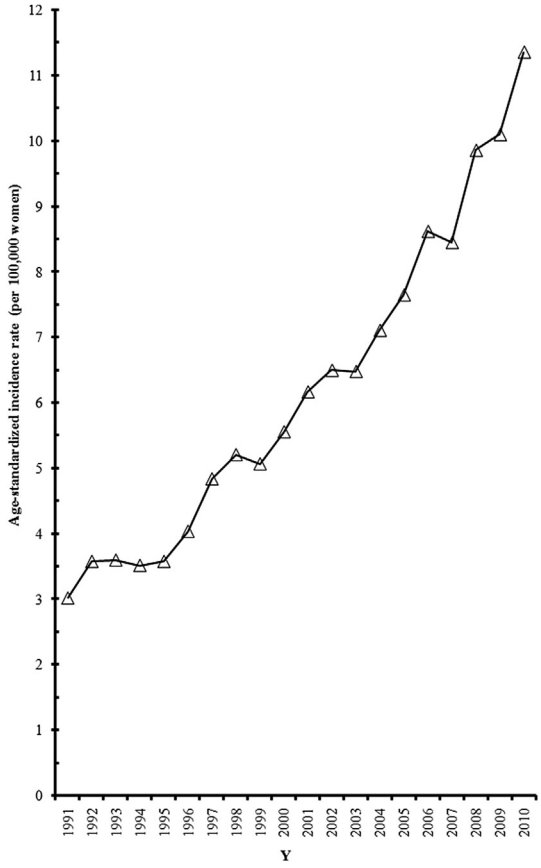

Figure 1. The age-standardized incidence rates of uterine corpus cancer per 100,000 women/year in Taiwan, 1991–2010. (direct method, world standard 2000 population).

(1991–2010). Ever since the increasingly industrialization in Taiwan starting from the 1960, there has been an impact of westernization on Taiwanese lifestyles, including a sedentary life pattern, high-caloric, high-fat, and low-fiber dietary habits, declines in fertility rates, and delayed childbearing [11–14]. These lifestyle choices can increase estrogen levels in the body and induce chronic estrogen dominance in women. The long-term stimulation of the endometrium by excessive unopposed endogenous estrogen secretion allows continued proliferation of the endometrial tissues and can increase the risk of estrogen-responsive uterine disorders such as uterine corpus cancer [15,16]. Moreover, the high prevalence of metabolic risk factors such as obesity and diabetes [17], an increase in the proportion of elderly population aged 65 years and above (7% in 1993, 10.2% in 2007, and a projected 20% in 2025) [18], and the high overall use of hormonal replacement therapy among postmenopausal women (34.7–56.2% in 2002–2007) [19] are also important risk factors, which may partially explain the elevated incidence and the increased risk of uterine corpus cancer in Taiwan. Furthermore, the increasing industrialization since 1960 has brought forth not only westernized lifestyles, but also a cumulative exposure to nonylphenol, bisphenol A, and phthalates in the surrounding environments. Lu et al [20] reported that the average daily intake of nonylphenol (due primarily to rice consumption) in Taiwan is 4 and 8.5 times higher than in Germany and New Zealand, respectively. On top of that, bisphenol A and phthalates in the plastic bottles and food containers, which are used extremely heavily in Taiwan, can easily leach out and contaminate the food and beverage they contain [21]. In addition, high concentrations of polycyclic aromatic hydrocarbons and related compounds are detected in ambient air in Taiwan [22]. Estrogenic steroid hormones are also found in river water and wastewater treatment plant effluents of Taipei City [23]. Consequently, the adoption of westernized lifestyles, the high prevalence of metabolic risk factors, the high overall use of hormonal replacement therapy, and the cumulative exposure of environment pollutants with estrogenic effect might explain the substantial increase in the incidence and the lifetime risk of uterine corpus cancer among the female population in Taiwan over the study period.

Although the lifetime risks of developing uterine corpus cancer vary considerably by country, it is considered the most common gynecologic cancer in developed countries. Figure 5 compares the lifetime risk (cumulative risk before age 75 years) of this disease in Taiwan in 2010 (from Figure 4) with the 2012 rates of the selected Western and Asian countries from the online GLOBOCAN 2012 database [3]. Cumulative risks were highest (greater than 2) in USA, Poland, Norway, and Canada, which represented roughly twice the risk observed in Asian countries such as Japan and China, and four times the risk in Malaysia, Korea, Thailand, and India. The cumulative risk of 1.15 in Taiwan was similar in magnitude to the risks reported for Japan and China. The variation of lifetime risk for this disease between the Asian and Western countries could be attributed to differences in health-care systems, screening, lifestyle factors, and gene-by-environment interactions in these countries [24], which might have protected Asian women from uterine corpus cancer development.

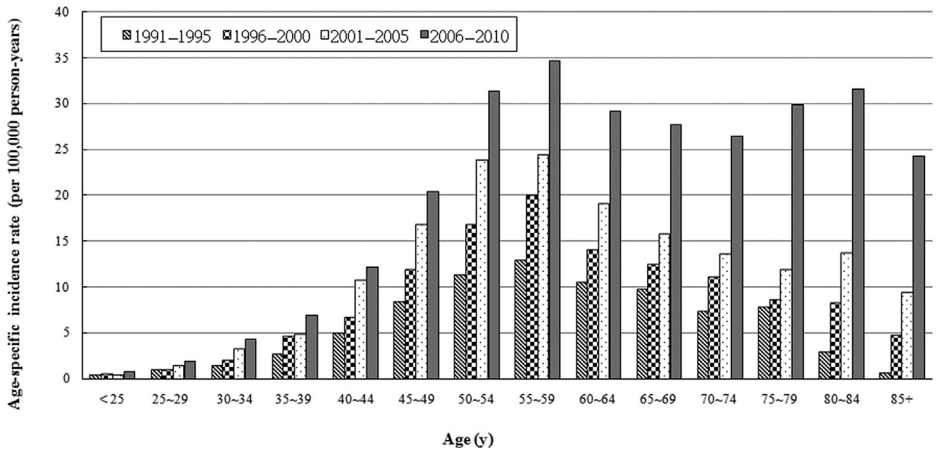

Figure 2. The age-specific incidence rates of uterine corpus cancer per 100,000 person-years in Taiwan for the periods 1991–1995, 1996–2000, 2001–2005, and 2006–2010.

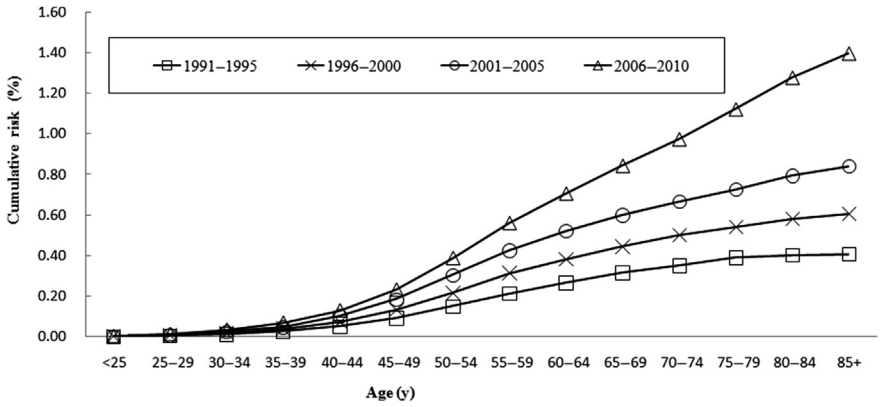

Figure 3. Lifetime risk (cumulative risk before age 79 years) of developing uterine corpus cancer in Taiwan for the periods 1991–1995, 1996–2000, 2001–2005, and 2006–2010.

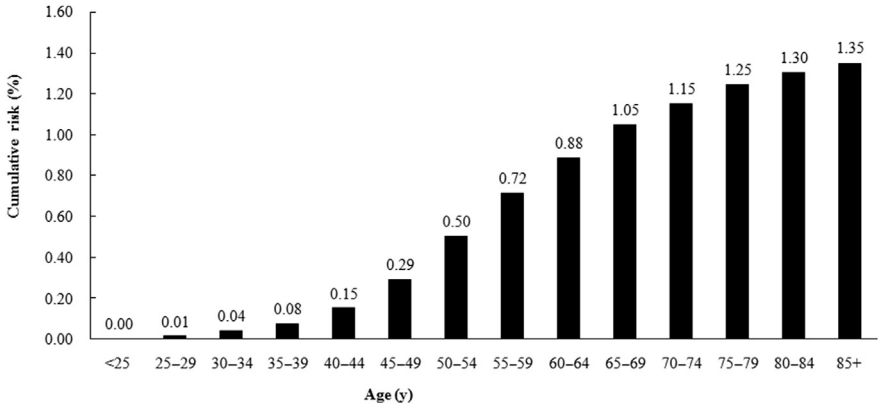

Figure 4. Lifetime risk (cumulative risk before age 79 years) of developing uterine corpus cancer in Taiwan in 2010.

There are a number of limitations that should be considered when interpreting our study results. First, we were unable to verify the validity of our incidence data in the TCR registry prior to 2005 due to the lack of information on the percentage of cases that were diagnosed with uterine corpus cancer by death certificate only. However, the low percentage of death certificate only (0.06–0.33%) for uterine corpus cancer between 2005 and 2010 as well as the high percentage of morphological verification (90.3–93.4% confirmed microscopically) for all cancers in women during the same period warrant the inherent validity of our study results [5]. Moreover, a traceback procedure was simultaneously implemented by the TCR Task Force to double-check all received data from the medical providers, which markedly enhanced the completeness and validity of the cancer registry. Second, we were unable to account for mortality as a competing risk in our lifetime risk approximation due to the use of aggregate data in our study. Since

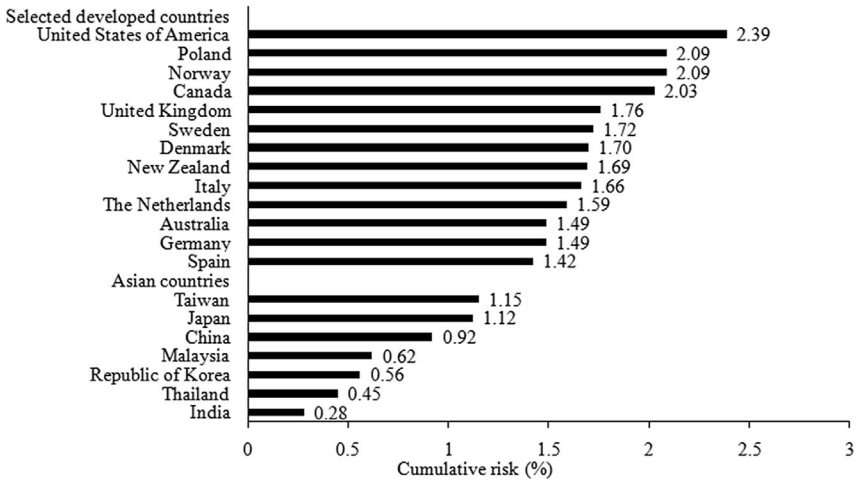

Figure 5. Lifetime risk (cumulative risk before age 75 years) of developing uterine corpus cancer for selected Western and Asian countries in 2012 compared with the risk in Taiwan in 2010 (Source: online GLOBOCAN 2012, except 2010 Taiwan data from Taiwan Cancer Registry).

not all women live to the age of 79 years, we might have overestimated the probability of developing uterine corpus cancer over a Taiwanese woman's lifetime.

The present study describes the rapid increase in the incidence and the lifetime risk of uterine corpus cancer from 1991 to 2010. Although the overall risk of this cancer is still lower than those reported in many developed countries, Taiwan's risk for this cancer is currently among one of the highest among Asia countries, along with Japan and China. According to the observed changes in incidence rate, the burden of uterine corpus cancer in the general female population is expected to increase in the near future. The results of this study can be generalized to other Chinese population of similar composition, but do not apply to high-risk individuals with certain risk factors such as obesity, family history, tamoxifen users (due to breast cancer), environmental exposures or hereditary diseases that predispose them to an increased risk of the disease [25]. From a public-health perspective, care providers should develop strategies for the prevention, early detection, and intervention to reduce the rapidly increasing incidence of uterine corpus cancer in Taiwan.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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