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Editorial

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Trends of uterine cancer incidence: a projection from the past to the future

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> ▶ See the article "Trends in incidence of uterine cancer in Songkhla, Southern Thailand" in volume 30, e22.

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Uterine cancer is the most common malignancy of the female genital tract in more developed countries [1], and is the 2nd most common gynecologic malignancy after cervical cancer in less developed countries including Thailand [1,2]. Most studies in Thailand including our research in uterine cancer reported clinical or pathologic features of both endometrial carcinoma and uterine sarcoma using hospital-based data [3,4]. Except for the report of the National Cancer Institute of Thailand [2], epidemiologic studies investigating the regional or national situation of specific cancer has rarely been reported.

I would like to direct the attention of journal readers to the interesting study by Saeaib and colleagues [5] in this issue of the *Journal of Gynecologic Oncology*. The work is important providing population-based data of uterine cancer. The authors evaluated the trend of uterine cancer incidence in Songkla, the principal province in Southern part of Thailand. Data were collected on uterine cancer cases registered between 1989 to 2016 from the provincial cancer registry and the population census of 1990, 2000, and 2010 reported by the National Statistical Office. Comprehensive statistical analyses using Jointpoint, age-period cohort (APC) method, and Nordpred models were performed.

Several studies from the UK reported the trends of incidence of all cancers including uterine cancer which remained a common malignancy in female over several decades [6,7]. The incidences were found to be slightly increased from 8% in 1984 to 10% in 2007 and projected to be 11% in 2030 in the study by Mistry [6]. Subsequent study by Smittenaar et al. [7] reported 3% in 1993 and 5% in both 2014 and 2035. The differing results may partly lie on the data resources of the country being used and the detail of statistical means used for the analyses: Jointpoint, APC, or cubic splines.

Aside from the studies which projected the trends in the future, one recent study from the US by Henley and colleagues [8] evaluated the actual data of overall incidence (during 1999–2015) and mortality rates (during 1999–2016) of uterine cancer. Subgroup analyses according to the ethnicity, histopathology, and stage of disease were also performed. The incidence rates increased by 12% or about 0.7% per year, with larger increases among non-white women and endometrioid carcinoma [8]. The increased mortality rate of 21% or about 1.1% per year was also observed; however, larger increases were found in Asian-Pacific

islanders, Hispanic and black women. The authors made the observation that the increase of uterine cancer incidence was in contrast to the decrease of other cancers, with many factors contributed to the increased incidence [9].

The study of Saeaib and colleagues [5] estimated the trends of uterine cancer incidence by extrapolating the observed data of each year including the annual percentage change by each age group of 742 patients. The results showed an increased incidence of uterine cancer: 8 per 100,000 women in 2030 compared to 1.54 per 100,000 women in 1989 and 5.30 per 100,000 women in 2016. The trends would be steady by Jointpoint and APC models but increasing with the Nordpred analysis. Subgroup analyses demonstrated higher incidences in the urban than the rural areas and Buddhists than Muslims; however, with a slower increased rate in the urban and among the Muslims.

Few issues were to be noted. One, not specific to this study, was the International Classification of Diseases (ICD) or ICD-10 codes used for data collection in epidemiologic studies. Unlike some other malignant neoplasms, e.g., skin cancer which has distinctive codes for specific histopathology (carcinoma of basal cell, squamous cell, sebaceous cell, Merkel cell, or melanoma), this is not for uterine cancer. Uterine cancer has been included in a C54 category and specified only by various anatomical sites (isthmus, endometrium, myometrium, fundus, overlapping sites, and unspecified sites of corpus uteri) and C55 category (malignant neoplasm of uterus, part unspecified). The codes for major pathologic types of uterine cancer (endometrial carcinoma and uterine sarcoma) which have different predisposing risk factors and clinico-pathologic features are not described. Unless separated by subgroup analysis, the genuine incidence and mortality rates of each type of uterine cancer cannot not be accurately estimated.

Second, the death rate was not included in this report because the authors were aware of the other causes of deaths in uterine cancer patients. Instead, the authors planned to detail the cancer-specific survival in a subsequent study. This seemed to be a reasonable approach based on several reports including our study which demonstrated that approximately 37% of deaths were due to other non-endometrial cancer causes including medical illnesses [10]. The US has already used ICD-10 including the cause of death on death certificates since 2015; although it may be difficult to extract the exact data from other databases especially in the remote past, the lack of such mortality data would leave a question to the readers. Hence, a big picture of overall deaths could be given along with the incidence to make their epidemiologic study more complete.

Another issue concerns the findings in **Table 1**. The authors fractioned the incidence by a 5-year period from 1989–2016 and noted the peak incidence between 55 to 64 years of age. One additional observation could be made. The sharp rise of the incidence over 10% during 2007–2011 compared to 2002–2006 was demonstrated among women aged 55 to 69 years. Aside from the possibility of the expanding growth of an aging population, the other specific risk factors/behavior or medical practice changes should be explored.

And lastly, the authors nicely discussed in detail the many recognized risk factors of uterine cancer, endometrial carcinoma in particular. Another risk factor of genetic predisposition, particularly MMR gene mutation found in the Lynch syndrome, could be added. Such risks are well recognized in Western populations [11]. Notably, only few studies in Asia have been published [12-15]. Our study found the prevalence of MMR gene defect in Thai patients as

high as 55% [15]. This should alert the gynecologic oncologist to assess this particular risk by comprehensive history taking focused on previous and family history. Appropriate pathologic evaluation is warranted [11]. Although this genetic factor is not modifiable and the data are generally not available in the cancer registry, information of genetic risk factors would be valuable to raise an awareness and appropriate screening for other cancers in the patients with endometrial cancer, and all related cancers in other family members.

In conclusion, the incidence and natural history of cancers in any country provide vital knowledge for rational national health care management. The data will guide sound health budget allocation, medical education and patient-based health programs. This important analysis by Saeaib and colleagues [5] found a trend of increased incidence of uterine cancer in one region of Thailand. Such findings should alert the national epidemiologists/ gynecologic oncologists to study the trends in other parts of the country as well. Aside from the established factors of age and religious background; ethnicity, histologic subtype, stage, dietary behavior, medication and alternative compound usage, environmental influences and genetic aspects should be more closely examined. If data from all over the country confirm the findings of this research, current health programs will have to be modified. Recognized risk factors, such as, inappropriate exogenous hormonal therapy, diabetes mellitus, and obesity are generally addressed by health care systems. Perhaps, more novel approaches to reach an optimal goal are needed?

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