RESEARCH COMMUNICATION

Cancer of Corpus Uteri in Tunisia: Epidemiological and Clinicopathological Features

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Abstract

  <u>Introduction</u>: The aim of this study was to survey for the first time the burden and characteristics of corpus uteri cancers in Central Tunisia. <u>Design</u>: Characteristics of all cancer cases diagnosed during a 15-year period were analyzed based on the data of the Cancer Registry of the Center of Tunisia. Five-year age-specific rates, crude incidence rates, world age-standardized rates (ASR), and annual percent change (APC) were calculated using annual data on population size and its estimated age structure. <u>Results</u>: A total of 218 new cases of corpus uteri cancer were recorded. The ASR was 3.1 per 100,000 with a significant increase over time (APC: +7.1%; 95% CI: 3.1%, 11.1%). The median age at diagnosis was 60 years and only 20.6% of patients were less than 50 years old. The tumor size was higher than 2 cm in 83.5% of cases. Stage I was the most frequent (59.9%) followed by advanced stages (23.2%). Endometrial adenocarcinoma was the most frequent histological type (62.8%) with grade II accounting for 48.5% of cases. <u>Conclusion</u>: Corpus uteri cancer is an important female cancer with increasing trend over time. These findings justify the need to plan and develop effective programs aiming at the control of the spread of cancer in Tunisia.

Keywords: Corpus uteri - cancer - incidence - increasing trend - clinicopathological study - Tunisia

Introduction

Cancer of the corpus uteri is the most common gynecologic malignancy in many Western countries, and some of the highest incidence rates are observed in European populations (Curado et al., 2007; Ferlay et al., 2010). In the United States, cancer of the corpus uteri is the fourth leading cancer in women behind breast, lung and colorectal cancers and accounts for approximately 6% of all cancers with 42,160 diagnosed cases and 7780 deaths annually (Jemal et al., 2009). Some authors recognized that race has an impact on some characteristic features and survival outcomes (Connel et al., 1999). In the United States, incidence rates are higher in whites than in black, Hispanic or Asian/Pacific Islander women (Jemal et al., 2009). The highest incidence rates are seen among United States Hawaiian (25 per 100 000 person-years), nonHispanic whites in Los Angeles (20 per 100 000 person-years), and Jews born in Europe or America (15 per 100 000 person-years) (Parkin et al., 2005). However, mortality is almost twofold higher in blacks than in whites (7.1 versus 3.9 per 100,000 women), likely due to the higher incidence of aggressive cancer subtypes, as well as

issues of access to, and quality of, healthcare services (Yap and Matthews, 2006). Cancer of the corpus uteri happens to be a cancer of post-menopausal women; worldwide 91% of cases of the corpus uteri occur in women aged 50 years and above (Parkin et al., 2005). Monitoring the incidence is important for health care planning purposes and for the identification of risk factors (Armstrong, 1992). Most data on corpus uteri cancer come from more developed regions and Western countries. Therefore, the burden and characteristics of this cancer from Tunisia were rare. The purpose of this study is to report for the first time the epidemiological, clinical and pathological features of corpus uteri cancers diagnosed in the Center of Tunisia during a 15-year period (1993-2007), based on the database of the population-based Cancer Registry of the Center of Tunisia.

Materials and Methods

We carried out a retrospective study of all cases of corpus uteri cancer diagnosed in the Pathology Department of the Farhet Hached University Hospital, Sousse and registered in the Cancer Register of the

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Center of Tunisia during 15-year period time (January 1993 - December 2007). The cancer registry has provided important information on cancer patterns over the previous years (Parkin et al., 2003; Curado et al., 2007; Missaoui et al., 2010; Missaoui et al., 2010; Missaoui et al., 2010). The study was approved by the Human Ethics Committee at the Farhet Hached University Hospital of Sousse (Tunisia) and it conformed to the provisions of the Declaration of Helsinki.

The International Classification of Diseases, 10th revision (ICD-10) was used for cancer classification (Percy et al., 1992). In the present study, the inclusion criteria were new cases of corpus uteri cancer (C54) diagnosed between the 1st January 1993 and the 31st December 2007. Medical records were reviewed for data on age, origin, delay to diagnosis, signs and symptoms, paraclinical data at time of diagnosis, histopathology, tumor stage and grade, and treatment.

Incidence rates were analyzed during 1993-2007 period. The proportional age distribution of Sousse population for each year between 1993 and 2007 was provided by the National Institute of Statistics in Tunisia. Crude incidence rates (CR) and five-year age-specific rates were calculated using population denominators derived as described (Bray et al., 2002; Curado et al., 2007). Age-standardized incidence rates (ASR) were calculated by the direct method, using the world standard population (Curado et al., 2007). Rates were expressed per 100,000 person-years (Curado et al., 2007). Trends of incidence rates were analyzed during three periods (1993-1997, 1998-2002 and 2003-2007). The annual percent change (APC) was calculated as previously described (Bray et al., 2005; Chen et al., 2006; Missaoui et al., 2010). In brief, the APC is calculated by fitting log-linear regression line to the natural logarithms of the rates using calendar year as the independent variable (Bray et al., 2005). The APC was obtained from the formula $100 \times [e^{\beta} - 1]$, where β is the parameter estimate obtained on fitting period of event as a continuous variable to the logarithm of the rate (Bray et al., 2005). Statistical significance was determined by calculating 95% confidence intervals (95% CI) for the APC (Szklo and Nieto, 2000). In describing the change, the terms "increase" or "decrease" were used when the rate ratio was statistically significant (two-sided *p values* < 0.05); otherwise the term "stable" was used.

Results

Epidemiology

During the study period, 218 patients with corpus uteri cancer were identified. The median age at diagnosis was 60 years with a mean age of 58.9 years (ranging from 14 to 85 years). Among our patients, 79.4% were more than 50 years old (173 cases) and only 45 cases (20.6%) were less than 50 years (Figure 1).

Corpus uteri cancer was accounting for 2.7% of all women cancers during the whole 15-year period. The crude incidence rate (CR) was 2.4 per 100,000 and the age-standardized incidence rate (ASR) was 3.1 per 100,000. Corpus uteri cancer was ranked eighth among all cancers in women after the cancer of the breast, colon-rectum,
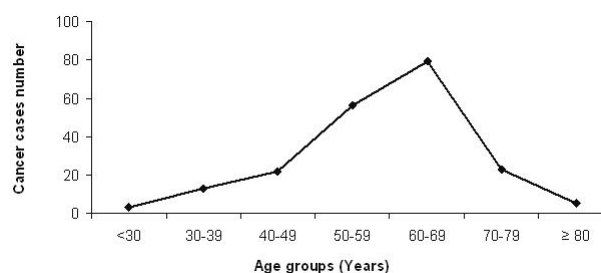

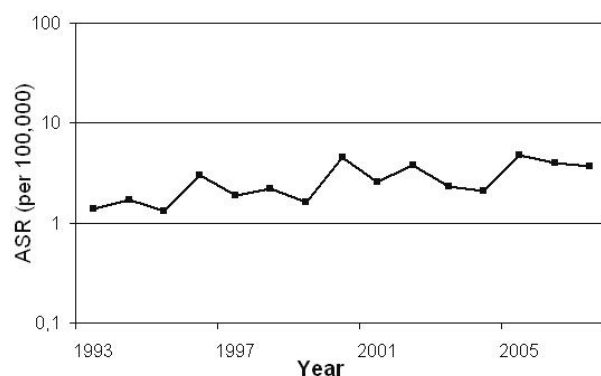**Figure 1. The Distribution of Patients with Cancer of the Corpus Uteri in Central Tunisia, by Age Groups, 1993-2007**

Figure 2. Trends in Age-standardized Incidence Rates (ASR) of the Corpus Uteri Cancer in Central Tunisia, 1993-2007
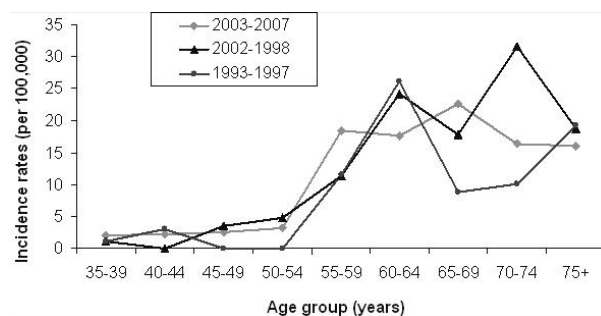

Figure 3. Age-specific Incidence Rates of the Corpus Uteri Cancer in Central Tunisia during Three Time-Periods

other skin (other than melanoma, C44), cervix uteri, non-Hodgkin lymphomas, ovary, and leukemias. Over time, incidence rate (ASR) increased significantly by +7.1% (95% CI: 3.1%, 11.1%) (Figure 2). Figure 3 shows the age-specific incidence rates of the corpus uteri cancer during the three periods.

Clinical features

The mean diagnostic time was 5.8 months and 35.8% of the patients consulted after a time interval of 6 months. Seven patients had been treated for breast cancer. Aside from the past history of breast cancer, a history of ovarian cancer (two patients), colon cancer (two patients) and invasive cervical cancer treated with radiation therapy (one patient) were also revealed. Four patients had other medical illness. Twelve patients reported history of maternal endometrial cancer (six patients), breast cancer (four patients) or ovarian cancer (two patients), the remaining patients had no records regarding family history of cancers.

Pathology

The tumor was more frequently located in the endometrium (81.2%) followed by contiguous localizations of the corpus uteri (31 cases) and the myometrium (7 cases). The tumor size was higher than 2 cm in 83.5% of cases and than to 5 cm in 33.9% of cases.

Tumors classified as adenocarcinoma comprised 62.8% of all cancers of the corpus uteri. Of these, the most common sub classification was adenocarcinoma, NOS, which accounted for 46.7% of all adenocarcinomas registered. Endometrioid adenocarcinoma was the next most common adenocarcinoma, at 41.6% followed by papillary (8%), papillary serous cystadenocarcinoma (2.2%), squamous metaplasia (0.7%), and tubular (0.7%). Sarcomas and Other Specified Types comprise 37.2% of the total. Of these 40.7% are leiomyosarcoma, 16% Mullerian, and 8.6% endometrial stromal sarcoma.

Non invasive tumor represents only 0.4% of cases. Histologically, 48.5% of corpus uteri cancers were intermediate-differentiated, followed by well-differentiated tumors (44 cases) and poorly-differentiated tumors (26 cases). According to the Federation Internationale de Gynecologie et d'Obstetrique (FIGO, 1989) and the American Joint Committee on Cancer (AJCC) staging system, stage I was the most frequent (59.9%) followed by advanced stages (stages III and IV) with 23.2% of cancer cases. Only one tumor was at stage 0.

Therapeutics

Among our patients, 90.8% received a surgical treatment (198 cases). For 82 patients (41.4%), adjuvant treatment (radiation therapy, chemotherapy, and/or hormone therapy) had been indicated. Among these patients, only one patient was handled by the three adjuvant modalities; two patients received chemotherapy associated to radiation therapy; 7.1% of cases received chemotherapy and 34.3% received radiation therapy. Surgery was the only treatment for 116 patients. An exclusive chemotherapy and an exclusive radiation therapy have been indicated for only one patient, respectively. Unfortunately, 20 patients had received no treatment. Among our patients, eight patients were dead and 27 patients have recurrent tumors.

Discussion

The current study investigated epidemiological and clinicopathological features of corpus uteri cancer in Central Tunisia using the data provided by the population-based cancer registry of the Center of Tunisia. The cancer of the corpus uteri was within the 10 leading sites of cancer among women during the study period. Nevertheless, the Tunisian female population has a lower incidence than other parts of the world. The highest incidence rates (ASR) were in the United States (16.5 per 100 000 women, rank order 4) and Northern Europe (12.4 per 100 000, rank order 4) (Ferlay et al., 2010). In Japan, the rates were nearly half that of the United States (7.6 per 100 000, rank order 6). Incidence rates were low in the Southern and East Asia region (2.6 per 100 000, rank order 11) and Eastern Africa (2.4 per 100 000, rank order 8) (Ferlay et

al., 2010). In India, cancer of the corpus uteri is one of the most common cancers among women and occupied the 5th to 10th rank among cancers occurring in women during the year 2004-2005 among various Indian registries (Ferlay et al., 2010; Murthy et al., 2011).

In this study, time trends in the incidence of cancer of the corpus uteri have been examined and showed significant increase during a 15-year period time. Trends in the incidence of cancer may occur as a result of a variety of factors such as initiation of screening programs, changes in diagnostic methods, completeness and reliability of data, changing profile of risk factors in the population, or as a consequence of better health awareness (Murthy et al., 2011). In Tunisia, no organized mass screening program exists for any of the anatomical sites of cancer (Until 2010). Therefore, no changes have been made in the diagnostic methods for cancer of the corpus uteri. Microscopic verification of the disease has been the main diagnostic approach adopted for diagnosis of the disease. The increase in the incidence over time suggests that there has been an increasing exposure to risk factors for the disease. Early age at menarche, nulliparity, late menopause, unopposed postmenopausal estrogen replacement therapy, postmenopausal obesity, polycystic ovary syndrome, and feminizing ovarian tumors are described as the important risk factors for the development of cancer of the uterine corpus (Beral et al., 1999; Bakken et al., 2004; Murthy et al., 2011). The estrogen use was described as a possible explanation for the increasing incidence of cancer of the corpus uteri in Danish women aged 55–64 years (Ewertz and Jensen, 1984). The main risk factors for cancer of the corpus uteri are broadly similar to those for cancers of the breast and ovary (Beral et al., 1999; Murthy et al., 2011). Interestingly, we reported recently significant increasing trends of the incidence rates of cancers of the breast and ovary in Central Tunisia (Missaoui et al., 2010; Missaoui et al., 2010). Risk factors for cancer of the corpus uteri include also a large reduction in physical activity and large increase in prevalence of obesity (Key et al., 2002; Marthy et al., 2011). The energy intake, energy expenditure, and the body mass index (BMI) have been shown to be independent risk factors influencing the risk of cancer of the corpus uteri (Furberg and Thune, 2002; Marthy et al., 2011).

Recently, in Norway, the incidence trends of the cancer of corpus uteri revealed interesting patterns from 1953 through 2007 that may be useful in generating hypotheses that are relevant for primary prevention (Lindemann et al., 2010). In women at postmenopausal age (55 years or older), there was a general increase in incidence over the entire period. Whereas, in women younger than 55 years, there was a general incidence increase until around 1980 that was followed by a decline until 1998, after which the rates again have increased until 2007 (Lindemann et al., 2010). The prediction for the next 20 years suggests that incidence rates of cancer of the corpus uteri will dramatically increase unless effective preventive strategies are implemented in Norway (Lindemann et al., 2010). In India, a steady increase of the incidence has been shown ranging from 0.88 to 6.88% per year in the five registries that showed an increasing trend (Murthy et al., 2010).

These incidence trends appeared to result from an increase in the prevalence of risk factors and in improvement in diagnostic procedures. However, in Italy, and according to the Italian Network of Cancer Registries database, corpus uteri cancer incidence rates were stable during the period 1986-1997 (Zambon and La Rosa, 2004).

In conclusion, corpus uteri cancer affects Tunisian women at an early stage with increasing incidence trends over time. Most cancer of the corpus uteri is environmental in origin. Limiting fat consumption and avoiding excess energy intake may result in some reduction in the incidence of cancer of the corpus uteri. Our findings justify the need to plan and develop effective programs aiming at the control and prevention of the spread of cancer amongst Tunisian population.

Acknowledgments

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