

RESEARCH COMMUNICATION

Cervical Adenocarcinoma and Squamous Cell Carcinoma Incidence Trends among Tunisian Women

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Abstract

Introduction: Uterine cervix cancer is an important public health problem in Tunisia. In this study, we report trends in the incidence of adenocarcinoma and squamous cell carcinoma of the cervix uteri in the central region of Tunisia during 1993-2006. **Design:** Data were obtained from the Cancer Registry of the Center of Tunisia which registers invasive cancer cases by active methods. Five-year age-specific rates, crude incidence rates (CR), world age-standardized rates (ASR), percent change (PC) and annual percent change (APC) were calculated using annual population data. **Results:** Among all women cancers, cervix uteri cancer accounted for 5.9% and ranked the fourth during the study period with an ASR of 6.9 per 100,000. The ASRs decreased notably with an APC of -6.7% over the whole period. However, incidence rates of adenocarcinomas have increased during the last years (APC: +14.4%). **Conclusion:** The introduction of cytological screening programs has led to a marked decrease of the incidence rates of cervix uteri cancer among Tunisian women. The data underline the fact that the population-based cancer registry is an indispensable tool for providing data for planning and evaluation of programs for cancer control.

Keywords: Cervix uteri - cancer - incidence - epidemiology - tunisia

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Introduction

Uterine cervix cancer is the second most common cancer among women worldwide, with estimated 493,000 new cases and 274,000 deaths in the year 2002 (Bray et al., 2005). 83% of cases occur in developing countries where cervix cancer accounts for 15% of female cancers. In developed countries, the cervix cancer accounts for only 3.6% of new cancers (Bray et al., 2005). In these countries, well-developed screening programs had led to an important decline of cervix cancer incidence and mortality rates: the deaths number decreased by half during 40 last years (Dargent, 1999; Arbyn et al., 2007; Mathew and George, 2009). However, in developing countries, organized screening programs of the uterine cervix cancer were absent or limited making it the leading cancer affecting women (Sankaranarayanan et al., 2001; Bray et al., 2005).

The majority of the cervix tumors are squamous cell carcinomas (SCC), whereas adenocarcinomas are relatively rare (Vizcaino et al., 1998). It is quite clear that high-risk human papillomavirus (HPV) are the major etiological agents of the majority of SCC and adenocarcinomas as well as their precursor lesions (Muñoz

et al., 2002; zur Hausen, 2002). The natural history of the cervical cancer takes place according to a continuum of precancerous lesions (cervical intra epithelial neoplasia, CIN) leaving an important place to cancer prevention (zur Hausen, 2002). Epidemiologically, the surveillance of the high-grade precancerous lesions, which are at present more frequent than the invasive cancers, is one of indicators of cancer screening evaluation (zur Hausen, 2002).

Population-based studies describing the uterine cervix cancer incidence were rarely reported from Tunisia (Maalej et al., 2004). In the Sousse region, Tunisia, invasive cervix cancer represented the fourth cancer among women with a world age-standardized incidence rate (ASR) of 7.1 per 100,000 during 1998-2002 (Curado et al., 2007). Considering the incidence, and the feasibility and the profitability of the screening programs, the cervix cancer occupied the first row, with the breast cancer, in the scale of the priorities of the Ministry of Public Health in Tunisia. National strategy of cancers screening has been already fixed in 1998. Since, a program of cervix cancer screening by cervico-vaginal smears practice has been set up by the National Office of the Family and the Population. The Direction of the Basic Health Care of the Ministry of Public Health had affected cytological screening programs

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in fourteen provinces, including the Center of Tunisia. In this work, we reported trends in the incidence rates of adenocarcinoma and SCC of the cervix uteri over 14-year period (1993-2006).

Materials and Methods

A population-based cancer registry, collecting information on cancer in the Center of Tunisia was established in the Pathology Department of Farhet Hached University Hospital of Sousse since 1987. Cancer Registry of the Center of Tunisia includes six provinces (Sousse, Monastir, Mahdia, Kasserine, Sidi Bouzid, and Kairouan) covering a total surface of 28,426 km².

Our cancer registry uses proactive methods of data collection. Primary sources include the Departments of Pathology of the public and private medical centers of the region as well as the Departments of Radiotherapy, Oncology and Hematology. Registration validity and completeness were evaluated using HV% index (the proportion of cases with histological verification of diagnosis). Data of the Cancer Registry of the Center of Tunisia has been judged to be of sufficient quality to appear in "Cancer Incidence in Five Continents (CI5) Vol. IX" (Curado et al., 2007).

The International Classification of Diseases, 10th revision (ICD-10) was used for cancer classification in the Cancer Registry of the Center of Tunisia (Percy et al., 1992). The inclusion criteria were cancer of the uterine cervix (C53) (Percy et al., 1992) diagnosed between January 1993 and December 2006 (recurrences and metastases of an anterior diagnosed cancer were not recorded). Trends of the incidence rates were analyzed during three time periods (1993-1997, 1998-2002 and 2003-2006). The data used in this article may not exactly correspond to those published in the same periods of Vol. IX of "Cancer Incidence in Five Continents (CI5)" (Curado et al., 2007) and "Cancer in Africa, Epidemiology and Prevention" (Parkin et al., 2003), because of subsequent additions or corrections of the dataset.

Crude incidence rates (CR) and five-year age-specific rates were calculated for the three time periods, 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 (Chen et al., 2006). The percent change (PC) in rate and the annual percent change (APC) were calculated as previously described (Chen et al., 2006).

Results

A total of 15 523 cases were registered in the Cancer Registry of the Center of Tunisia during the 14 years, of which, 86.4% had been histologically verified (HV%). Cancer Registry of the Center of Tunisia counted 6 913 cancers among women, of which, 410 cancers were of the cervix uteri (5.9%). The HV% was higher than average for all cancers (94.6%). The mean age at diagnosis was 52.1 years during the whole period (23-85 years) with 33.4%

of patients were aged 40-49 years; only 2.7% were aged 20-30 years.

The most represented histological type was the SCC (90.5%) followed by the adenocarcinoma (7.3%). The proportion of patients with adenocarcinoma increased from 1993 to 2006. The relative proportion of this histological type increased from 2.8% (1993-1997) to 7.9% and 7.8% during 1998-2002 and 2003-2006, respectively.

Cervix uteri was accounting for 5.9% of all women cancers during the whole 14-year period. The crude incidence rate (CR) was 5.8 per 100,000 and ASR was 6.9 per 100,000. Cervix uteri cancer was ranked fourth among all cancers in women after the cancer of the breast, other skin (other than melanoma, C44) and colon-rectum.

Between 1993-1997, cervix cancer took the fourth place (7.8%) after the cancer of the breast, other skin and colon-rectum. The CR was 8.4 per 100,000 and the ASR was 9.9 per 100,000. During the years 1998-2002, incidence rates decreased with an ASR of 7.4 per 100,000 without any rank change. During 2003-2006, the ASR was 5.3 per 100,000. Thus, the cancer of the cervix uteri has shown a significant decline in incidence during the observation period with an APC of -6.7% (Figure 1). The decline of the incidence rate has concerned mainly the SCC of the cervix uteri. However, the adenocarcinoma incidence increased by +14.4%. The ASR was markedly increased from 0.08 per 100,000 between 1993-1997 to 0.23 per 100,000 during 2003-2006.

Figure 2 shows the age-specific incidence rates of the cervix cancer during the whole 14-year period. Rates were highest for patients aged 60-65 years (34.6 per

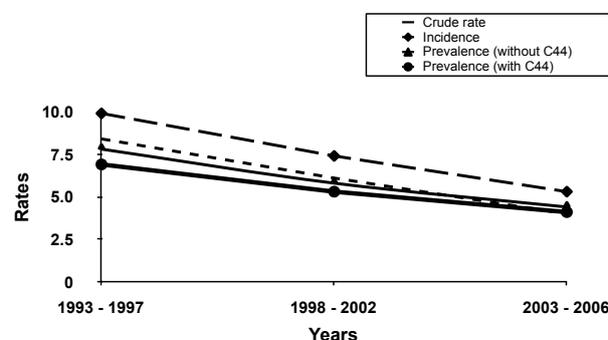


Figure 1. Trends of the Incidence of the Cervix Uteri Cancer in the Center of Tunisia, 1993-2006 CR: crude incidence rate per 100,000; ASR: world age-standardized incidence rate per 100,000.

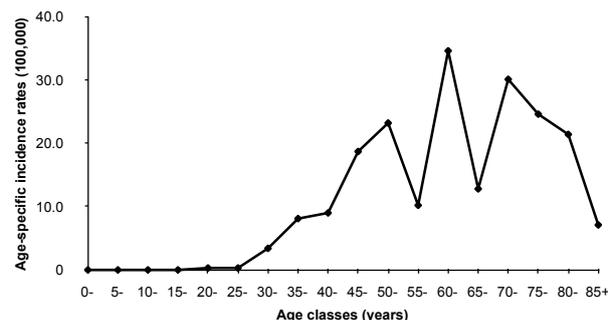


Figure 2. Age-specific Incidence Rates of the Cervix Uteri Cancer in the Center of Tunisia, 1993-2006

100,000). Two lower peaks were reached for patients aged 70-75 years (30.1 per 100,000) and 50-55 years (23.2 per 100,000).

Discussion

In the Center of Tunisia, the mean age of patients with cervix uteri cancer was close to that described since 1984 in the North Tunisia (51.3 years) (Ben Youssef et al., 1987) and that reported in 1994 in global Tunisian population (53.7 years) (Maalej et al., 2004). The predominant histological type was SCC; adenocarcinoma represented only 7.3%. Our data joined those already described with the dominance of the SCC (Vizcaino et al., 1998), but with lower rate.

Over the past 40 years, multiple reports have documented the increase in relative distribution of adenocarcinoma compared to SCC in developed countries (Eifel et al., 1995; Smith et al., 2000; Sasieni and Adams, 2001; Wang et al., 2004). We observed an increase in relative distribution of adenocarcinoma compared to SCC during the period study. In the United States, from 1973 to 1977, the proportions of SCC and adenocarcinoma were 88% and 12%, respectively; however, from 1993 to 1996, the proportions were 76% and 24%, respectively (Smith et al., 2000). Eifel et al. have reported that between 1960 and 1989, the proportion of patients with adenocarcinoma has increased 24% to 49% (Eifel et al., 1995).

During the observation period, the ASR of the cervix uteri was weak and similar to rates observed in Spain (Navarra), Australia (Western) and USA (Michigan) (Curado et al., 2007). Incidence rates reported in this study were widely weaker than the rates observed in the most developing countries such as Southern and Central America, Eastern and Southern Africa, and the Caribbean Islands, where the incidence rates exceeded 40 per 100,000 (Curado et al., 2007).

Cancer of the cervix uteri has shown a marked decline in developed countries over the past 40 years, due to wider implementation of cytological screening and increased detection of precancerous lesions (Smith et al., 2000; Vizcaino et al., 2000; Wang et al., 2004; Belot et al., 2008). The decline is mainly attributable to a decrease in incidence of the most common histological variant, the SCC (Vizcaino et al., 2000). In our study, incidence rates decreased progressively from 1993 to 2006 failing down to 5.3 per 100,000 (2003-2006). The decline of incidence rates could be the result of the introduction of cytological screening programs in the Center of Tunisia since 1998 by the Ministry of Public Health and the National Office of the Family and the Population. In France, the incidence rates of the cervix uteri cancer did not stop decreasing between 1980 and 2005; the annual average decline rate was 2.9% (Belot et al., 2000). Similar findings were observed in USA and in most European countries (Bergström et al., 1999; Arbyn and Geys, 2002; Taylor et al., 2006; van der Aa et al., 2008), with the possible exception of Ireland (Levi et al., 2000). The absence of a cervix cancer screening program in Ireland was the most feasible explanation of this difference (Comber and Gavin, 2004). The decrease of incidence and mortality rates of the cervix

uteri cancer was also described in Asian countries (Jin et al., 1999; Chen et al., 2006; Murthy et al., 2005), but with weaker proportions compared with the Western countries. Screening practice, as well as the changes of life style, the dramatic changes of socioeconomic circumstances and other environmental exposures during the last two decades could explain the declining trends in these countries (Jin et al., 1999; Yang et al., 2003).

However, there has been an increase in relative and absolute incidence of adenocarcinomas compared to SCC over the past 40 years in developed countries, especially among younger women (Sasieni and Adams, 2001; Wang et al., 2004; Bray et al., 2005; Castellsagué et al., 2006; Howlett et al., 2007). In our study, the incidence rates of adenocarcinoma were very weak; however, there was an increasing trend in spite of the presence of cytological screening programs. Increase of the incidence and mortality rates of adenocarcinomas has in fact been observed in several countries (Sasieni and Adams, 2001; Visioli et al., 2004; Howlett et al., 2007). A statistically significant increase of adenocarcinomas incidence, by at least 3% per year, has been reported in Europe, particularly among younger women (Sasieni and Adams, 2001; Bulk et al., 2005). In the United States, Smith et al. reported an increase of the adenocarcinoma incidence by 29% from 1973 to 1996 (Smith et al., 2000). Possible reasons include the increased prevalence of risk factors such as obesity, nulliparity, or HPV18 (Eifel et al., 1990; Castellsagué et al., 2006; Gien et al., 2010). Another possible explanation includes increased detection of precursor lesions with screening programs which are more effective in detecting SCC than adenocarcinoma (Krane et al., 2001; Sherman et al., 2005; Howlett et al., 2007; Gien et al., 2010). The cytological screening of invasive adenocarcinoma and its precursors is affected by a high rate of false negative reports as a result of sampling errors and interpretation problems, which especially influence the diagnosis sensitivity of Papanicolaou smears (Krane et al., 2001; Howlett et al., 2007). New technologies will clearly have to take into account the requirement for more sensitive methods for the detection of adenocarcinomas in particular.

In conclusion, the incidence of the cervix uteri cancer decreased progressively during the study period, following the introduction of cytological screening programs by the Ministry of Public Health in the Center of Tunisia. However, adenocarcinomas were diagnosed more frequently during last years. Available screening programs appear less effective for the detection of adenocarcinomas and their precursor lesions; thus, they need more sensitive methods. The population-based cancer registry is an indispensable tool for providing data for planning and evaluation of programs for cancer control in all societies.

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