

Is the incidence of invasive vulvar cancer increasing in the United States?

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Abstract

Objective To document incidence rates of vulvar cancer, specifically invasive vulvar cancer, from 1973 to 2004 in the US.

Methods Nine US cancer registries from the Surveillance, Epidemiology, and End Results (SEER) databases were used to identify women 15 to 84 years of age who were first diagnosed with vulvar cancer during 1973-2004. Age-adjusted incidence rates and annual percentage changes were calculated for different time periods, stage of the disease, age, race, and geographic area.

Results During 1973-2004, the incidence of in situ vulvar tumors increased an average of 3.5% per year (95% CI: 2.9%, 4.1%), while the incidence of invasive tumors increased 1.0% per year (95% CI: 0.6%, 1.4%). An increasing incidence was observed for localized and regional invasive tumors. To at least some degree, the rise of incidence rates of incidence tumors was evident in every age category, race, and geographic region.

Conclusions Incidence rates of invasive vulvar cancer have increased in the US during the last three decades. The reasons for this increase are unknown.

Introduction

While the reported incidence of *in situ* vulvar neoplasia in the US has increased several-fold during the past few decades [1], it is uncertain whether there has been a corresponding change in the incidence of invasive vulvar tumors. Using data from the US Surveillance, Epidemiology, and End Results (SEER) program [2], Judson *et al.* noted a 20% increase in incidence between 1973 and 2000, but it is not clear whether age-adjustment had been performed, given that they did not observe any appreciable change in age-specific incidence rates in their study. Another analysis of this same data source suggested no change over time, but the inadvertent use of an erroneous denominator of the rate limits its usefulness [3]. Because of this ambiguous state of affairs, we sought to tabulate the age-adjusted incidence of invasive vulvar cancer in the US during the past several decades, extending the period of observation through 2004.

Methods

Data for this study were obtained from the SEER network of population-based cancer registries. These registries have served the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah as well as the metropolitan areas of San Francisco-Oakland, and Detroit (beginning in 1973); 13 counties in the Western Washington region (beginning in 1974); and the metropolitan area of Atlanta (beginning in 1975). We included in the numerator of the incidence rates those females who were 15 to 84 years old at the time they were first diagnosed with vulvar carcinoma (either *in situ* or invasive) during the period 1973-2004. The denominator was composed of women from the same regions who were at risk.

Using SEER*Stat software (Surveillance Research Program, National Cancer Institute (seer.cancer.gov/seerstat) version 6.4.4), incidence rates were computed and adjusted to the age

distribution of the 2000 US standard population. They were calculated for the entire period of 1973-2004 as well as for four 8-year periods (1973-1980, 1981-1988, 1989-1996, and 1997-2004). Rates were obtained separately for in situ and invasive tumors and, for the latter, within categories of stage (localized, regional distant), age (15-34, 35-54, 55-74, and 75-84 years), race (white, black, and other), and geographic area (the 9 areas with registries included above). The annual percentage change (APC) in incidence (and corresponding 95% confidence intervals) was computed, also using the SEER*Stat software.

Results

There were 11,079 new in situ and 6,532 new invasive cases of vulvar cancer in the SEER population during 1973-2004 (Table 1). The age-adjusted incidence rates of vulvar carcinoma by stage of the disease during 1973-1980, 1981-1988, 1989-1996, and 1997-2004 are shown in Table 2. The APC of the incidence of in situ tumors was 3.5% per year (95% CI: 2.9%, 4.1%) during that period of time. The incidence of invasive vulvar carcinoma also increased, but to a much smaller degree (APC of 1.0% per year, 95% CI: 0.6%, 1.4%). An increase was evident for both localized and regional invasive tumors, but not for those with evidence of metastatic disease at the time of diagnosis. To at least some degree, the incidence of invasive vulvar carcinoma rose in every age category in each of the four periods (Table 3). The rise in incidence rates was most evident in white women (Table 4). The incidence of invasive vulvar carcinoma rose to at least some extent in each of the populations that comprised the SEER program (Table 5).

Discussion

We observed a rising trend in the age-adjusted incidence of invasive vulvar tumors in the US during the past three decades. This trend was present among women of all ages and in all geographical areas.

Several risk factors for vulvar carcinoma are known [3]. Infection with an oncogenic human papillomavirus (HPV) increases the risk of vulvar neoplasia, particularly infection with HPV16 [4], and about 40% of vulvar cancers are HPV-associated [5]. Recent estimates of the prevalence of HPV infection are about 26.8% among US women 15-59 years, with HPV16 being the most common type [6]. Whether a rise in the prevalence of vulvar HPV infection in US women accounts for the rise in their incidence of invasive vulvar is unknown, since there are no long-term data on HPV prevalence in this population.

Studies of immunocompromised patients have indicated that a weakened immune system is associated with an increased risk of vulvar cancer [7-9]. HIV infection is associated with lowered T cell activity and HIV positive women are at increased risk of HPV-related cancers [9]. Since the introduction of antiretroviral therapies, the mortality rates of HIV infected individuals have become similar to those of the general population [10], suggesting that the prevalence of the HIV-infected population has increased. A suppressed immune system also characterizes persons who have received an organ transplant, and it is estimated that there has been a 1.6-fold increase in the occurrence of transplantation in the US between 1997 and 2005 [11]. European studies have observed that this group is also at increased risk of vulvar and vaginal cancers [12]. Lastly, women who smoke have been found to be at strongly increased risk of developing *in situ* vulvar cancer [13, 14]. However, there appears to have been a decrease in the prevalence of smoking among US women during 1965-2006 [15]. Another possible reason for the change of rates is the way in which invasive vulvar cancers have been coded. Vulvar disease is often multifocal and

may sometimes be classified as anal or vaginal cancer. It is unlikely, however, that any such misclassification would have increased steadily over time

Increased numbers of women who are immunosuppressed may account for some of the increase in invasive vulvar cancer incidence rates. Future studies will be needed to understand the degree to which the increase in the incidence of invasive vulvar carcinoma observed in the US is explained by change in the prevalence of immunosuppression.

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