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## Original article

# Sex differences in incidence and mortality of bladder and kidney cancers: National estimates from 49 countries

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#### **Abstract**

**Objectives:** In the United States, among patients diagnosed with bladder cancer (BC), women have increased disease-specific mortality compared with men. The main objective of this study was to determine whether this pattern is also present in other countries. For comparison, similar analyses were performed for kidney cancer (KC).

Methods and materials: Data for this study were obtained from the GLOBOCAN 2008 database. A total of 49 countries with available information on BC and KC incidence and mortality were included in the analysis, representing all major geographic regions except Africa. For each country, we computed the sex-specific ratio of the total number of deaths from a given cancer to the total number of diagnoses in the year 2008 (the mortality-to-incidence ratio [MIR]). The relative MIR was computed for each country as a ratio of MIR in women to MIR in men. A relative MIR of more than 1 would indicate that the number of cancer-specific deaths relative to the number of cancer-specific diagnoses is greater in women than in men.

**Results:** For BC, the relative MIRs were significantly more than 1 in 26 countries (53%), significantly less than 1 in 2 countries (4%), and not significantly different from 1 in 21 countries (43%). The median relative MIR was 1.21 (interquartile range: 1.04–1.41). For KC, the relative MIRs were significantly more than 1 in 4 countries (8%), significantly less than 1 in 3 countries (6%), and not significantly different from 1 in 42 countries (86%). The median relative MIR was 1.00 (interquartile range: 0.94–1.06).

**Conclusion:** Among BC patients, increased disease-specific mortality in women compared with men appears to be a common (although not a universal) phenomenon. This pattern may potentially be explained by differences between the sexes in the biology of disease, time to diagnosis, treatment decisions, and other factors. In contrast, among KC patients, no significant differences in disease-specific mortality were seen between the 2 sexes in the overwhelming majority of the countries. © 2014 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Kidney cancer; Incidence; Mortality

#### 1. Introduction

In the United States, women have a lower life-time risk of bladder cancer (BC) than men; however, among patients diagnosed with BC, women tend to have less favorable outcomes in terms of BC-specific mortality, relative survival, and years of potential life lost [1,2]. Specifically, according to data from the US Surveillance, Epidemiology, and End Results program, men diagnosed with BC on average lose approximately one-third (33%) of their expected remaining years of life to BC, whereas for women, the respective estimate is close to one-half (47%) [2]. These patterns could not be completely explained by differences in

stage or other tumor characteristics at presentation or variation in treatment modalities [1,2]. Among patients diagnosed with BC in Europe, women also seem to have increased disease-specific mortality compared with men, at least according to data reported from some cohorts [3,4]. In the present study, we aimed to examine this question on a larger scale, by analyzing national estimates from different countries. The main objective of the present study was to examine the total number of deaths from BC relative to the total number of diagnoses in men and in women in different countries. For comparison, we also performed similar analyses for kidney cancer (KC).

# 2. Methods

Data were obtained from the GLOBOCAN 2008 database, maintained by the International Agency for Research

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on Cancer. This public access database contains information on cancer incidence and mortality in 182 countries in the year 2008. A detailed description of the GLOBOCAN 2008 can be found in the study by Ferlay et al. [5]. For the current analyses, country-specific inclusion criteria were (1) availability of direct estimates of BC and KC incidence and mortality separately for men and women and (2) at least 100 BC and 100 KC diagnoses in each sex in the year 2008. Direct cancer-specific estimates for a particular country are estimates based on data reported from this country. For many developing countries, no incidence data were available and the incidence reported in GLOBOCAN 2008 was estimated based on incidence in the neighboring countries. Similarly, for countries without vital registration, cancerspecific mortality documented in GLOBOCAN 2008 was estimated indirectly based on cancer-specific mortality from other countries. Although such indirect estimates are better than no information at all, we decided to exclude from the current analyses countries with indirectly estimated incidence or mortality or both. After application of these inclusion criteria, data from 49 countries were available for analysis, representing all major geographic regions except Africa.

For each country, we computed the sex-specific ratio of the total number of deaths from a given cancer to the total number of diagnoses in the year 2008 (the mortality-toincidence ratio [MIR]). The relative MIR was computed for each country as a ratio of MIR in women to MIR in men. A relative MIR more than 1 would indicate that the number of cancer-specific deaths relative to the number of cancerspecific diagnoses is greater in women than in men. We also computed the male-to-female incidence ratio for each country by dividing the number of new cases in men by the number of new cases in women. Confidence intervals for country-specific relative MIRs and incidence ratios were constructed using the Poisson model for occurrence of BC diagnoses and BC deaths [6], which is a reasonable approximation given that both types of events are rare in the general male and female populations.

#### 3. Results

#### 3.1. BC

Sex-specific data on BC incidence and mortality for the 49 countries are summarized in Table 1. In this table, countries are ordered according to the magnitude of the relative MIR. The relative MIRs were significantly more than 1 in 26 countries (53%), significantly less than 1 in 2 countries (4%), and not significantly different from 1 in 21 countries (43%). The median relative MIR was 1.21 (interquartile range: 1.04–1.41 and absolute range: 0.73–1.99). Male-to-female incidence ratios for BC are shown in Table 2. In all 49 countries, BC was significantly more common in men than in women, with a median incidence

ratio of 3.05 (interquartile range: 2.84–3.91 and absolute range: 1.31–6.30).

#### 3.2. KC

Sex-specific data on KC incidence and mortality for the 49 countries are summarized in Table 3. The relative MIRs were significantly more than 1 in 4 countries (8%), significantly less than 1 in 3 countries (6%), and not significantly different from 1 in 42 countries (86%). The median relative MIR was 1.00 (interquartile range: 0.94–1.06 and absolute range: 0.72–1.30). The male-to-female incidence ratios for KC are shown in Table 4. In 46 of 49 countries (94%), KC was significantly more common in men compared with women. The median male-to-female incidence ratio was 1.59 (interquartile range: 1.51–1.79 and absolute range: 0.70–2.22).

### 4. Discussion

The main objective of the present study was to examine the total number of deaths from a given urologic malignancy (BC or KC) relative to the total number of diagnoses in men and in women in different countries. Our findings indicate that among BC patients, increased disease-specific mortality in women compared with men is a common phenomenon, certainly not limited to the United States or selected European countries. This pattern was also seen in most other countries of the American Continent, as well as in Israel, Japan, Australia, and New Zealand, and to a lesser extent in China. Interestingly, in most countries of the Eastern Europe, the relative MIRs tended to be of smaller magnitude compared with those seen in Western Europe, whereas in Russia and the Ukraine, the relative MIRs were significantly below unity, indicating increased incidenceadjusted BC mortality in men. The reasons for this apparent regional variation are unclear. Regarding the male-to-female incidence ratios for BC, the findings were as expected. In all 49 countries, BC was more common in men than in women, with the highest male-to-female incidence ratio seen in Spain (Table 2), which is consistent with previous reports [7].

For KC, no significant differences in incidence-adjusted disease-specific mortality were seen between the 2 sexes in the overwhelming majority (42 of 49 or 86%) of the countries. Only in 4 countries (Finland, France, Sweden, and Japan) were the relative MIRs significantly more than unity, indicating increased mortality in women, whereas they were less than unity in 3 countries (Romania, Russia, and Ukraine), indicating increased mortality in men. The incidence of KC was significantly increased in men in 46 of 49 countries (94%). Only in 1 country (Vietnam) was KC significantly more common in women.

The current analyses have several limitations that must be carefully considered. First, it should be noted that MIR,

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