Short Communication

Time Trends in the Incidence of Testicular Cancer in Childhood and Young Adulthood

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Abstract

Background: There has been a steep increase in the incidence of adult testicular cancer in many populations, but in spite of numerous studies, the etiology of testicular cancer remains elusive. The time trends of childhood testicular tumors are less clear and have been studied in a few populations. To further evaluate whether or not adult and childhood cancers share trend determinants and whether future adult testicular cancer incidences can be predicted through childhood testicular cancer incidences, their rates were compared.

Method: Data on testicular cancer incidence in childhood and in young adulthood were extracted from the IARC Cancer Incidence in the Five Continents Database limited to two 10-year time periods (1967-1976 and from 1987-1996) to allow for truncation-free analyses within the same birth cohort.

Results: Childhood testicular cancer incidence varied 3- to 4-fold, whereas adult testicular cancer incidence varied 10- to 11-fold between the studied populations. No positive correlation between childhood and adulthood incidence of testicular cancer was found.

Conclusion: These data indicate that the incidence of testicular cancer in adulthood is influenced by factors, either prenatal or postnatal exposures different than those determining the trends among children.

Introduction

There has been a steep increase in the incidence of adult testicular cancer in many populations ever since cancer registries accrued data and trends could be ascertained (1-3). With an age peak at 30 years of age and only few cases before puberty, it has been concluded that tumor development is initiated prenatally, but despite numerous studies of prenatal and perinatal exposures, the etiology of testicular cancer remains elusive.

In contrast to the established increase in adult testicular cancer, time trends in childhood testicular tumors are less clear and have been studied in a few populations; i.e., from the Scandinavian countries, England, and the United States (4-7). It is not known to what extent adult and childhood testicular cancer share etiology. To further evaluate whether or not they share determinants of trend and whether future adult testicular cancer can be predicted through childhood testicular cancer, we used data from Cancer Registries established before 1967 to compare the incidence rates of testicular cancer in children and young adults.

We ran time trend analyses separately for two 5-year age groups, i.e., 0- to 4-year-old for childhood cancer and 20- to 24-year-old for cancer in young adulthood, as well as a birth cohort analysis.

Populations and Methods

Incidence Data. Data on testicular cancer incidence (ICD-10: C62) selected on the basis of defined validity criteria (see Population selection criteria) were obtained from the IARC CI5 I-VIII: Detailed Database (8), which contains age- and site-specific annual incidence for a number of selected population-based cancer registries included in the Cancer Incidence in Five Continents (CI5) series. Cancer registries participating in the CI5 series adhere to common protocols and standards of proportion of completeness. Thus, the registries included in this study are able to provide high-quality data. On-line information on morphology is not available in the database (8).

Population Selection Criteria. We restricted our study to two 5-y age groups: patients 0- to 4-year-old for childhood cancer and 20- to 24-year-old for cancer in young adulthood. We chose the former age class because childhood testicular cancer rarely occurs after the age of 4 y, and we selected the 20- to 24-y-old age group for comparability purpose because the predominant subtype of testicular cancer in children as well as young adults in their early 20s is nonseminoma (5, 9).

Data were obtained from two 10-y time periods, from 1967 to 1976 and from 1987 to 1996, to allow for...
truncation-free analyses within the same birth cohort (i.e., those ages 0-4 y in the 1967-1976 period were ages 20-24 y in the 1987-1996 period). All Cancer Registers contributing to the IARC CIS I-VIII: Detailed Database after 1967 were thus excluded from this study. Data were obtained for the following regions: Manitoba (Canada), Osaka (Japan), Israel (Jews only), Denmark, Finland, Iceland, Norway, South Thames Region (England/United Kingdom), Slovenia, and Sweden. Iceland and Slovenia were later withdrawn because of the lack of childhood cases during the study period.

Data Analysis. We estimated the percentage change in incidence with 95% confidence intervals (95% C.I.) from 1967 to 1976 and from 1987 to 1996 for children and adults separately. We evaluated the correlation between childhood and adulthood incidence within the same birth cohort both visually using a scatter plot, and by estimating the Spearman correlation coefficient ($r_s$). Log-transformed incidence rates were analyzed using Pearson correlation ($r$) to check for the effect of weighting by the size of the population.

Results

Childhood testicular cancer incidence varied 3- to 4-fold across populations, with the highest incidence occurring in Osaka (Japan) and the lowest occurring in Israel for both time periods (Table 1). The incidence increased by 43% (95% C.I., 23-60) in Denmark, 33% (95% C.I., 23-56) in Finland, and 37% (95% C.I., 23-58) in Norway, remained stable in Osaka (Japan) and the South Thames Region (England/United Kingdom), and decreased by 25% (95% C.I., 14-35) in Israel during the study period (Table 1).

As summarized in Table 2, adult testicular cancer incidence varied 10- to 11-fold between the studied populations. Incidence increased markedly from 1967 to 1976, to 1987 to 1996 (Table 2). Finland, Israel, Norway, Sweden, and Manitoba (Canada) experienced an increase of well over 100%, whereas the rates in Osaka (Japan), Denmark, and the South Thames Region (England/United Kingdom) rose by ~50%. In general, the rates in the lower incidence populations increased more modestly than those of higher incidence populations.

Table 1. Testicular cancer incidence rate (per 10^5 person-year), ranking and percentage change of a cohort analysis of two 10-y calendar-period intervals

<table>
<thead>
<tr>
<th>Registries</th>
<th>0- to 4-y-old</th>
<th>1967-1976</th>
<th>Rate (95% C.I.)</th>
<th>Rank</th>
<th>1987-1996</th>
<th>Rate (95% C.I.)</th>
<th>% Change (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada*</td>
<td>2</td>
<td>0.4 (0.2-1.0)</td>
<td>6°</td>
<td>2</td>
<td>0.5 (0.1-1.1)</td>
<td>5°</td>
<td>25 (8-98)</td>
</tr>
<tr>
<td>Japan†</td>
<td>47</td>
<td>1.2 (0.8-1.5)</td>
<td>1°</td>
<td>28</td>
<td>1.2 (0.7-1.6)</td>
<td>1°</td>
<td>0 (−6 to 16)</td>
</tr>
<tr>
<td>Israel‡</td>
<td>6</td>
<td>0.4 (0.1-0.7)</td>
<td>6°</td>
<td>5</td>
<td>0.3 (0.1-0.5)</td>
<td>6°</td>
<td>25 (−7 to −35)</td>
</tr>
<tr>
<td>Denmark</td>
<td>14</td>
<td>0.7 (0.3-1.1)</td>
<td>4°</td>
<td>15</td>
<td>1 (0.5-1.5)</td>
<td>3°</td>
<td>43 (23-60)</td>
</tr>
<tr>
<td>Finland</td>
<td>15</td>
<td>0.9 (0.4-1.3)</td>
<td>2°</td>
<td>19</td>
<td>1.2 (0.7-1.7)</td>
<td>1°</td>
<td>33 (23-56)</td>
</tr>
<tr>
<td>Norway</td>
<td>13</td>
<td>0.8 (0.4-1.2)</td>
<td>3°</td>
<td>17</td>
<td>1.1 (0.5-1.6)</td>
<td>2°</td>
<td>37 (23-58)</td>
</tr>
<tr>
<td>Sweden</td>
<td>20</td>
<td>0.7 (0.4-0.9)</td>
<td>4°</td>
<td>16</td>
<td>0.6 (0.3-0.9)</td>
<td>4°</td>
<td>−14 (−6 to −26)</td>
</tr>
<tr>
<td>UK³</td>
<td>12</td>
<td>0.5 (0.2-0.8)</td>
<td>5°</td>
<td>12</td>
<td>0.5 (0.2-0.8)</td>
<td>5°</td>
<td>0 (−4 to 2)</td>
</tr>
</tbody>
</table>

NOTE: Age period: ages 0 to 4 y.
*Canada/Manitoba.
†Japan/Osaka Prefecture.
‡Israel/Jews.
§United Kingdom, England/South Thames Region.

Table 2. Testicular cancer incidence rate (per 10^5 person-year), ranking and percentage change of a cohort analysis of two 10-y calendar-period intervals

<table>
<thead>
<tr>
<th>Registries</th>
<th>20- to 24-y-old</th>
<th>1967-1976</th>
<th>Rate (95% C.I.)</th>
<th>Rank</th>
<th>1987-1996</th>
<th>Rate (95% C.I.)</th>
<th>% Change (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada*</td>
<td>22</td>
<td>5.1 (3.0-7.2)</td>
<td>3°</td>
<td>45</td>
<td>10.4 (7.4-13.4)</td>
<td>3°</td>
<td>104 (91-136)</td>
</tr>
<tr>
<td>Japan†</td>
<td>38</td>
<td>0.9 (0.6-1.2)</td>
<td>7°</td>
<td>49</td>
<td>1.3 (0.9-1.6)</td>
<td>8°</td>
<td>44 (34-66)</td>
</tr>
<tr>
<td>Israel‡</td>
<td>27</td>
<td>2.1 (1.3-2.9)</td>
<td>5°</td>
<td>97</td>
<td>5.9 (4.7-7.1)</td>
<td>6°</td>
<td>181 (162-224)</td>
</tr>
<tr>
<td>Denmark</td>
<td>186</td>
<td>9.1 (7.8-10.4)</td>
<td>1°</td>
<td>289</td>
<td>14.5 (12.8-16.2)</td>
<td>1°</td>
<td>59 (45-78)</td>
</tr>
<tr>
<td>Finland</td>
<td>33</td>
<td>1.5 (1.0-2.0)</td>
<td>6°</td>
<td>88</td>
<td>5.2 (4.1-6.3)</td>
<td>7°</td>
<td>247 (223-298)</td>
</tr>
<tr>
<td>Norway</td>
<td>99</td>
<td>6.3 (5.1-7.5)</td>
<td>2°</td>
<td>233</td>
<td>13.8 (12.0-15.6)</td>
<td>2°</td>
<td>119 (101-146)</td>
</tr>
<tr>
<td>Sweden</td>
<td>137</td>
<td>4.3 (3.6-5.0)</td>
<td>4°</td>
<td>282</td>
<td>9.3 (8.2-10.4)</td>
<td>4°</td>
<td>116 (98-142)</td>
</tr>
<tr>
<td>UK³</td>
<td>122</td>
<td>5.1 (4.2-6.0)</td>
<td>3°</td>
<td>187</td>
<td>7.4 (6.3-8.5)</td>
<td>5°</td>
<td>45 (33-63)</td>
</tr>
</tbody>
</table>

NOTE: Age period: ages 20 to 24 y.
*Canada/Manitoba.
†Japan/Osaka Prefecture.
‡Israel/Jews.
§United Kingdom, England/South Thames Region.
As shown in Fig. 1, birth cohort scatter plot analysis and the determination of the Spearman’s rank correlation coefficient ($r_s = -0.34; P = 0.41$) revealed no correlation between childhood and adulthood incidence of testicular cancer. When Manitoba (Canada) and Israel (Jews) registries were left out of the analysis, the correlation coefficient became 0.0 ($P = 1.00$). Pearson correlation of log-transformed incidence rates was also used to check the effect of weighting by the size of the population. After the exclusion of Japan, the nonweighted Pearson correlation was 0.16 ($P = 0.73$) and 0.26 ($P = 0.57$) after weighting.

Discussion

We studied eight populations with a long history of cancer registration and found that the incidence of adult testicular cancer doubled in 20 years, whereas no substantial increase in childhood testicular tumors occurred over the same period. In addition, incidence rates of testicular cancer did not correlate between children and adults when analyses were carried out in a single birth cohort.

Several previous studies have shown a secular increase in the incidence of adult testicular cancer (2-4, 10-15). Childhood testicular cancer has been less studied, but the incidence has been reported to be constant over time in Denmark, Norway, and Sweden between 1960 and 1985 (4) and in the United States between 1973 and 2000 (6). A third study estimated an annual increase in incidence of 1.3% between 1962 and 1995 in England and Wales compared with an annual change of 3.4% among young adults (5).

Unfortunately, information on tumor histology was lacking and analyses were therefore not restricted to germ-cell testicular cancers. However, the majority of testicular cancers are of germ-cell origin not only in adults (9) but also in children (5, 6), and the influence of other tumor types is limited. For example, in the population-based Piedmont Childhood Cancer Registry, we identified 15 cases of testicular cancer in 1964 to 2005, 13 of which (87%) were nonseminomas (data not shown; ref. 16). In addition, because most of childhood germ-cell testicular tumors are nonseminomas, we analyzed the incidence of adult testicular cancer in the 20 to 24 age groups in which most of the germ-cell tumors are of nonseminoma type. Another limitation is that only eight countries fulfilled the inclusion criteria for our study. However, these countries are scattered throughout the world, and there is limited evidence of geographic heterogeneity in our results. As a third weakness, we acknowledge that the completeness and validity of cancer registration, especially in children, might have improved over time. Such detection improvement, however, should bias our results toward an increasing trend in incidence and could not explain the relative lack of trend among children in our data.

Wide periods (10 years) were used for comparison to avoid small numbers of childhood testicular cancer. However, this approach combined together different birth cohorts and the year of birth is an established determinant of the lifetime risk of adult testicular cancer. Furthermore, it is known that the rates in most of the countries involved in this study were rapidly increasing with year of birth among young adults (2, 17). Therefore, our estimate of testicular cancer incidence rate of young adults is an average incidence rate comprising different birth cohorts characterized by somewhat different rates. Although this approach increased the power of the analyses on childhood testicular cancer, given its rarity, their numbers remained small and dictated the wide 95% C.I. for the trends and possibly the apparent lack of correlation between the two sets of rates. Sensitivity analysis conducted by leaving out small populations (Manitoba/Canada and Israel/Jews) or Japan, which was an outlier and, by population weighted Pearson correlation of log-transformed incidence rates, showed that these populations are unlikely to affect the correlation.

In conclusion, only the causes of testicular cancer in adults have been increasing in prevalence over the last hundred or so years and these data indicate that the incidence of this cancer in adults is to a significant extent influenced by factors other than those determining the trends in children (7). Although research on the etiology of adult testicular cancer in the last decades focused mostly on prenatal exposures, additional postnatal environmental exposures may be temptingly invoked to explain the difference between adults and children.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

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