Short Communication

Alcoholism and Risk for Cancer of the Cervix Uteri, Vagina, and Vulva

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Abstract
We conducted a population-based cohort study to analyze the risk of developing cancers of the female genitals among 36,856 patients with a hospital discharge diagnosis of alcoholism (ICD-7: 307, 322; ICD-8: 291, 303; ICD-9: 291, 303, 305A) in Sweden between 1965 and 1995. The follow-up was done by linkages of national registries. Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) were computed based on nationwide specific cancer rates. The first year of follow-up was excluded from all analyses to minimize the impact of selection bias.

We found that alcoholic women had excess risks for in situ cervical cancer (SIR, 1.7; 95% CI, 1.6–1.9), for invasive cervical cancer (SIR, 2.9; 95% CI, 2.4–3.5), and for cancer of the vagina (SIR, 4.6; 95% CI, 2.2–8.5) but not for cancer of the vulva (SIR, 1.0; 95% CI, 0.4–2.0). The fact that alcoholics had an excess risk also for the in situ cancer suggests that the observed excess in invasive cervical cancer may not only be attributable to less use of Pap smear screening among them. The alcoholic women may be at higher risk for the progression from human papillomavirus infection to a malignant lesion for lifestyle-related reasons (promiscuity, smoking, use of contraceptive hormones, and dietary deficiencies). We conclude that alcoholic women are at high risk for in situ and invasive cervical cancer and for cancer of the vagina.

Introduction
The few published studies on the association between alcohol consumption and risk of cancers of the cervix uteri, vulva, and vagina presented contradictory or inconclusive results (1–5). We conducted a large retrospective cohort study among women with alcoholism in Sweden aiming to compare the incidence of these cancers among alcoholics and the general population.

Materials and Methods
Our methods have been described in detail previously (6). We identified our cohort in the Swedish Inpatient Register, held by the National Board of Health and Welfare since 1964. In Sweden, there is virtually no private inpatient treatment; thus hospital-provided medical services are population based and referable to the county in which the patient lives. In addition to national registration numbers (unique personal identifiers assigned to all Swedish residents), each record contains administrative and medical data, such as hospital department and discharge diagnoses. The diagnoses are coded according to the seventh revision of the ICD (ICD-7) through 1968, the eighth revision (ICD-8) until 1986, and the ninth revision (ICD-9) thereafter. The number of hospitals delivering data to the register has increased steadily; the register covered 60% of the Swedish population in 1969, 75% in 1978, and 85% by the end of 1983 (7). From 1987, the register attained complete nationwide coverage.

After exclusion of records with erroneous national registration numbers and patients with a prevalent cancer, our cohort consisted of 36,856 women, registered at least once with a hospital discharge diagnosis of alcoholism (ICD-7: 307, 322; ICD-8: 291, 303; ICD-9: 291, 303, 305A) between 1965 and 1994. Record linkage of this cohort to the nationwide registers of Causes of Death, Emigration and Cancer, allowed complete follow-up through 1995. We calculated the expected number of cancers by multiplying the observed number of person-years in 5-year age and calendar year strata with stratum-specific cancer incidence rates in Sweden and subsequently the corresponding SIRs and 95% CIs. We excluded the person-time and events during the first year of follow-up to avoid bias attributable to increased likelihood of hospitalization for alcoholism in the presence of a yet undetected malignancy (8).

Results
The women’s mean age at enrolment was 42.7 years, and the mean duration of follow-up was 9.4 years. We found a moderate excess risk for in situ cervical cancer and for invasive cervical cancer (Table 1) and a marked excess risk for cancer of the vagina (Table 2). This increased risk was fairly constant during the entire follow-up. For cancer of the vagina, and to a lesser extent cancer of the cervix, the SIRs increased with age at follow-up (that means, age at cancer diagnosis). Among the vaginal cancers, one was an adenocarcinoma (SIR, 4.1; 95% CI, 0.1–22.9), 8 were squamous cell cancers (SIR, 4.7; 95% CI, 2.0–9.2), whereas 1 had unknown histology. Vulvar cancer was...
detected among 8 women, all of them squamous cell cancers, yielding an overall SIR of 1.0 (Table 2).

For in situ cervical cancer, the SIRs increased with increased age at follow-up. This trend of increasing SIRs with age at follow-up was not evident for invasive cervical cancer (Table 1).

Discussion
To our knowledge, this is the largest prospective study on alcoholism and cancer of the cervix, vagina, and vulva published to date. In our population-based, prospective cohort study design, selection and information bias, as well as differential misclassification of the alcoholism diagnosis, are unlikely. If misclassification occurred, it should have been non-differential (for patients that develop cancer and those who do not) and, therefore our point estimates could have been biased toward the unit.

The incidence of reported cancer in situ in Sweden increased rapidly during 1958–1967, and since then it has been quite stable (9). Although we cannot measure the completeness of registration of cancer in situ of the cervix (i.e., the proportion of occurring in situ cancers that are actually detected and registered), it is known that the registration of detected and diagnosed cancers in situ is >90% (10). To access whether we had variations in the registration of in situ lesions during the study period, we performed a stratified analysis by age and calendar year at diagnosis. We observed no remarkable differences in the association between alcoholism and in situ cervical cancer over time or by age groups (data not shown).

Among women alcoholics, the excess risk for invasive cervical cancer may not arise only because they get fewer Pap smears, because we found also an excess of carcinoma in situ/H11022 among 36,856 women who were hospitalized between 1965 and 1994 for alcoholism in Sweden.

Table 1  SIR with 95% CI of developing cancer of the cervix during 1–28 years of follow-up among 36,856 women who were hospitalized between 1965 and 1994 for alcoholism in Sweden

<table>
<thead>
<tr>
<th>Age at follow-up</th>
<th>Observed</th>
<th>SIR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>502</td>
<td>1.7</td>
<td>1.6–1.9</td>
</tr>
<tr>
<td>&lt;35</td>
<td>180</td>
<td>1.5</td>
<td>1.3–1.8</td>
</tr>
<tr>
<td>35–49</td>
<td>246</td>
<td>1.8</td>
<td>1.6–2.0</td>
</tr>
<tr>
<td>50–59</td>
<td>55</td>
<td>2.4</td>
<td>1.8–3.1</td>
</tr>
<tr>
<td>60+</td>
<td>21</td>
<td>2.7</td>
<td>1.7–4.2</td>
</tr>
</tbody>
</table>

* Age at cancer diagnosis.

Table 2  SIR with 95% CI of developing cancer of the vagina and vulva during 1–28 years of follow-up among 36,856 women who were hospitalized between 1965 and 1994 for alcoholism in Sweden

<table>
<thead>
<tr>
<th>Age at follow-up</th>
<th>Observed</th>
<th>SIR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>8</td>
<td>1.0</td>
<td>0.4–2.0</td>
</tr>
<tr>
<td>&lt;50</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>50+</td>
<td>8</td>
<td>1.2</td>
<td>0.5–2.4</td>
</tr>
</tbody>
</table>

*a Using expected rates specifically for vulva squamous cell carcinoma, the overall SIR was 1.1 (95% CI, 0.5–2.2).

References


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