Incidence of Adenocarcinoma of the Esophagus Among White Americans by Sex, Stage, and Age

Linda Morris Brown, Susan S. Devesa, Wong-Ho Chow

Rapid increases in the incidence of adenocarcinoma of the esophagus have been reported among white men. We further explored the temporal patterns of this disease among white individuals by sex, stage, and age by use of data from the Surveillance, Epidemiology, and End Results program. We identified 22759 patients from January 1, 1975, through December 31, 2004, with esophageal cancer, of whom 9526 were diagnosed with adenocarcinoma of the esophagus. Among white men, increases in the incidence of esophageal cancer were largely attributed to a 463% increase in the incidence of adenocarcinoma over this time period, from 1.01 per 100 000 person-years (95% confidence interval [CI] = 0.90 to 1.13) in 1975–1979 to 5.69 per 100 000 person-years (95% CI = 5.47 to 5.91) in 2000–2004. A similar rapid increase was also apparent among white women, among whom the adenocarcinoma rate increased 335%, from 0.17 (95% CI = 0.13 to 0.21) to 0.74 per 100 000 person-years (95% CI = 0.67 to 0.81), over the same time period. Adenocarcinoma rates rose among white men and women in all stage and age groups, indicating that these increases are real and not an artifact of surveillance.

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Total esophageal cancer incidence and mortality have been increasing among white men, stable among white women, and decreasing in black men and women (1). It is projected that there will be 16470 new patients diagnosed with esophageal cancer and 14280 deaths from it in 2008 (2). Rapid increases in the incidence of adenocarcinoma of the esophagus have been reported in the United States, with rates highest among white males (3–6). These patterns are in contrast to those for squamous cell carcinoma of the esophagus, for which rates have been considerably higher among blacks than whites and have been declining in recent decades. To better understand the temporal patterns and to assess the potential influence of heightened surveillance for adenocarcinoma we performed a detailed examination of the temporal trends among white individuals by sex, stage, and age. Esophageal adenocarcinoma cases among blacks (211) and other races (185) were too few for in-depth analyses.

Data from nine population-based registries in the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program (1) were used to calculate incidence rates of primary invasive esophageal cancer (International Classification of Diseases for Oncology, 3rd edition, topography codes 150–159) for 22759 white patients diagnosed during the period from January 1, 1975, through December 31, 2004, in six 5-year time periods (ie, 1975–1979 through 2000–2004) (7). The nine registries, accounting for approximately 10% of the US population, are located in the metropolitan areas of Atlanta, Detroit, San Francisco–Oakland, and Seattle–Puget Sound and the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah. All SEER Registries annually meet the Gold Standard Registry Certification from the North American Association of Central Cancer Registries, Inc, for completeness (at least 95%), accuracy (<3% of cases identified through death certificates only), and timeliness of data. Age-adjusted rates (using the 2000 US standard) and 95% confidence intervals (CIs) were calculated by sex and histological type (adenocarcinoma, morphology codes 8140–8575; squamous cell carcinoma, codes 8050–8084) by use of SEER*Stat software (8). Age-adjusted rates by stage (local, regional, distant, and unknown, as indicated by SEER historic stage A) and age-specific rates (age groups 25–44, 45–54, 55–64, 65–74, and ≥75 years) were calculated for adenocarcinoma by sex. All rates were expressed per 100 000 person-years, and only data points with at least 10 observations were presented. Temporal trends were plotted so that a slope of 10 degrees represented a change of 1% per year (ie, 40 years on the horizontal axis is the same length as one logarithmic cycle on the vertical axis) (9).

During the time period 1975–2004, 22759 white patients were diagnosed with esophageal cancer (16493 men and 6266 women), of whom 9526 were diagnosed with adenocarcinoma (8128 men and 1398 women). Among white men, total age-adjusted esophageal cancer rates increased steadily from 5.76 per 100 000 person-years (95% CI = 5.49 to 6.03) during 1975–1979 to 8.34 per 100 000 person-years (95% CI = 8.08 to 8.60) during 2000–2004, largely because of a 463% increase in adenocarcinoma rates from 1.01 (95% CI = 0.90 to 1.13) to 5.69 (95% CI = 5.47 to 5.91) (Table 1 and Figure 1). The incidence of squamous cell carcinoma decreased 50% across the study period, from 3.81 per 100 000 person-years (95% CI = 3.59 to 4.03) in 1975–1979 to 1.90 per 100 000 person-years (95% CI = 1.77 to 2.03) in 2000–2004. With the decreases in squamous cell carcinoma and the increases in adenocarcinoma, the rate for adenocarcinoma among white men surpassed that for squamous cell carcinoma around 1990. Among white women, total esophageal cancer rates remained constant at around 2.0 per 100 000 person-years during the time period 1975–2004, attributable to a 29% decrease in squamous cell carcinoma from 1.38 per 100 000 person-years (95% CI = 1.28 to 1.50) during 1975–1979 to 0.98 per 100 000 person-years in 2000–2004 (95% CI = 0.90 to 1.06) and a 335% increase in adenocarcinoma from 0.17 per 100 000 person-years (95% CI = 0.13 to 0.21) in 1975–1979 to 0.74 per 100 000 person-years in 2000–2004 (95% CI = 0.67 to 0.81). The gap between squamous cell...
**CONTEXT AND CAVEATS**

**Prior knowledge**
Rapid increases in the incidence of adenocarcinoma of the esophagus have been reported among white men.

**Study design**
Registry study in which data from the Surveillance, Epidemiology, and End Results program from January 1, 1975, through December 31, 2004, was used to explore the temporal patterns of this disease among white individuals by sex, stage, and age.

**Contribution**
Adenocarcinoma incidence rates rose from 1975 through 2004 among white men and women in all stage and age groups. The incidence of adenocarcinoma among white men increased 463%, from 1.01 per 100 000 person-years in 1975–1979 to 5.69 per 100 000 person-years (95% CI = 0.95 to 1.24) and 0.84 per 100 000 person-years (95% CI = 0.95 to 1.24) in 2000–2004. A similar rapid increase was also apparent among white women, with an increased incidence of 335% from 0.17 per 100 000 person-years in 1975 – 1979 to 0.74 per 100 000 person-years.

**Implications**
Because the increases in incidence are independent of stage and age group, they appear to be real and not an artifact of surveillance.

**Limitations**
Cases of adenocarcinoma may have been missed or misclassified. Data for the most recent years may have been underreported.

Pathological diagnoses were not reviewed centrally.

*From the Editors*

 carcinoma and adenocarcinoma continued to narrow because rates in 2004 were 1.13 per 100 000 person-years (95% CI = 0.95 to 1.34) and 0.84 per 100 000 person-years (95% CI = 0.68 to 1.02), respectively.

Stage-specific adenocarcinoma rates among men increased steadily over the entire time period, and the slopes were remarkably similar, regardless of whether the men were diagnosed with localized (from 0.20 per 100 000 person-years in 1975–1979 to 1.48 per 100 000 person-years in 2000–2004), regional (from 0.28 to 1.86 per 100 000 person-years), or distant-stage (from 0.31 to 1.81 per 100 000 person-years) disease. There was, however, some suggestion that the rate of increase may be slowing, especially for localized disease. A similar pattern was observed for women, although the rates were much lower for each stage (ranging from 0.06 or less per 100 000 person-years in 1975–1979 to 0.21–0.22 per 100 000 person-years in 2000–2004).

Over the three decades studied, the increases in adenocarcinoma occurred across all age groups. Among men, the greatest rates of increase (about 600%) and the highest rates were observed for the two oldest age groups, those aged 65 years or older. Rates also increased across all age groups among women, and the slopes appear remarkably parallel.

This study has several limitations. Cases of adenocarcinoma of the esophagus may have been missed or misclassified, but this is unlikely because quality control efforts regarding case finding, abstracting, and coding have been an integral part of the SEER program since its inception (1). Data for the most recent years may be underreported, and SEER has estimated delay-adjusted rates in many instances. Thus, the upward trends in adenocarcinoma may be even more pronounced than what we have reported. The pathological diagnoses were not reviewed centrally, but the microscopic distinction between adenocarcinoma and squamous cell carcinoma has been recognized for decades. Furthermore, declines in the histological type category

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**Table 1. Esophageal cancer incidence among whites in nine SEER registries, 1975–1979 to 2000–2004**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1975–1979</th>
<th>2000–2004</th>
<th>% change in rate†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>White males</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total esophagus</td>
<td>1928</td>
<td>3943</td>
<td>8.34 (8.08 to 8.60)</td>
</tr>
<tr>
<td>Squamous cell</td>
<td>1303</td>
<td>889</td>
<td>1.90 (1.77 to 2.03)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>344</td>
<td>2706</td>
<td>5.69 (5.47 to 5.91)</td>
</tr>
<tr>
<td>Other and NOS</td>
<td>281</td>
<td>348</td>
<td>0.76 (0.68 to 0.84)</td>
</tr>
<tr>
<td><strong>Adenocarcinoma by stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>65</td>
<td>692</td>
<td>1.48 (1.37 to 1.60)</td>
</tr>
<tr>
<td>Regional</td>
<td>101</td>
<td>892</td>
<td>1.86 (1.74 to 1.99)</td>
</tr>
<tr>
<td>Distant</td>
<td>111</td>
<td>884</td>
<td>1.81 (1.69 to 1.94)</td>
</tr>
<tr>
<td>Unstaged</td>
<td>67</td>
<td>238</td>
<td>0.53 (0.47 to 0.60)</td>
</tr>
<tr>
<td><strong>Adenocarcinoma by age, y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–44</td>
<td>16</td>
<td>78</td>
<td>0.50 (0.39 to 0.62)</td>
</tr>
<tr>
<td>45–54</td>
<td>67</td>
<td>386</td>
<td>5.05 (4.55 to 5.57)</td>
</tr>
<tr>
<td>55–64</td>
<td>115</td>
<td>684</td>
<td>14.11 (13.07 to 15.21)</td>
</tr>
<tr>
<td>65–74</td>
<td>88</td>
<td>774</td>
<td>26.27 (24.45 to 28.19)</td>
</tr>
<tr>
<td>≥75</td>
<td>58</td>
<td>784</td>
<td>31.33 (29.17 to 33.60)</td>
</tr>
<tr>
<td><strong>White females</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total esophagus</td>
<td>855</td>
<td>1227</td>
<td>2.00 (1.89 to 2.12)</td>
</tr>
<tr>
<td>Squamous cell</td>
<td>622</td>
<td>589</td>
<td>0.98 (0.90 to 1.06)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>73</td>
<td>454</td>
<td>0.74 (0.67 to 0.81)</td>
</tr>
<tr>
<td>Other and NOS</td>
<td>160</td>
<td>184</td>
<td>0.29 (0.25 to 0.33)</td>
</tr>
<tr>
<td><strong>Adenocarcinoma by stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>18</td>
<td>135</td>
<td>0.21 (0.18 to 0.25)</td>
</tr>
<tr>
<td>Regional</td>
<td>13</td>
<td>131</td>
<td>0.22 (0.18 to 0.26)</td>
</tr>
<tr>
<td>Distant</td>
<td>25</td>
<td>129</td>
<td>0.22 (0.18 to 0.26)</td>
</tr>
<tr>
<td>Unstaged</td>
<td>17</td>
<td>59</td>
<td>0.09 (0.07 to 0.11)</td>
</tr>
<tr>
<td><strong>Adenocarcinoma by age, y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–44</td>
<td>2</td>
<td>15</td>
<td>0.10 (0.06 to 0.16)</td>
</tr>
<tr>
<td>45–54</td>
<td>7</td>
<td>36</td>
<td>0.47 (0.33 to 0.65)</td>
</tr>
<tr>
<td>55–64</td>
<td>12</td>
<td>79</td>
<td>1.57 (1.24 to 1.95)</td>
</tr>
<tr>
<td>65–74</td>
<td>26</td>
<td>100</td>
<td>2.89 (2.35 to 3.51)</td>
</tr>
<tr>
<td>≥75</td>
<td>26</td>
<td>223</td>
<td>5.20 (4.53 to 5.94)</td>
</tr>
</tbody>
</table>

*SEER = Surveillance, Epidemiology, and End Results; CI = confidence interval (generated by the Tiwari method) are 95% for rates; NOS = not otherwise specified; — = statistic could not be calculated because the rate was based on fewer than 10 cases.
† Rates are per 100 000 person-years, age-adjusted to the 2000 US standard population.
Adenocarcinoma rates are rising rapidly and at a similar pace among both white men and women. This increase was not clear in earlier reports (3–6) because of the rarity of adenocarcinoma among women. Improving diagnosis or increasing exposures may be affecting both sexes. All rates by stage rose at similar paces; however, the rate of increase may be slowing, especially for localized disease, indicating that the overall increase in adenocarcinoma incidence is unlikely to reflect heightened surveillance and earlier diagnosis. The increases appeared across all age groups, and the slopes were remarkably similar to each other. The parallel upward trends by age groups make it difficult to determine whether the patterns are reflecting only period effects, as observed for prostate cancer and prostate-specific antigen screening (10), or whether birth cohort effects may play a role, as observed convincingly for lung cancer and cigarette smoking (11,12). An earlier analysis that developed multistage carcinogenesis models by use of 1973–2000 SEER data indicated that the adenocarcinoma temporal trends were driven more by period than birth cohort effects (13).

Our findings are consistent with a Dutch study (14) that reported a substantial increase in Barrett esophagus, the precursor lesion for adenocarcinoma, that was not explained by changes in endoscopic practice or histopathological criteria. Although the exact mechanism is unclear, Barrett esophagus may be related to the higher intraabdominal pressure and increased prevalence of gastroesophageal reflux disease in obese individuals. We previously presented (6) data showing rapid increases in reflux disease among US veterans, with rates of increase that were similar to those for adenocarcinoma. Also, increases in obesity by age and sex since the mid-1970s appear to parallel increases in adenocarcinoma (15), and recent data (16) indicate that increases in obesity, particularly abdominal obesity, may account for part of the upward trend in the incidence of adenocarcinoma (13,17). Another reason for the increasing frequency of Barrett esophagus–associated adenocarcinoma may be the decreasing frequency of infection with *Helicobacter pylori*, which is associated with gastric atrophy and reduction in gastric acid secretion (18,19). Our data indicate that the increase in adenocarcinoma is real.

Figure 1. Trends in age-adjusted (2000 US standard) esophageal cancer rates across six 5-year periods, from 1975–1979 through 2000–2004, among white individuals by sex. Data are from nine Surveillance, Epidemiology, and End Results Registries. For adenocarcinoma rates by age group, ages are shown in years. For 95% confidence intervals for the earliest and latest points plotted, see Table 1.
and a growing health problem for both white men and women.

References


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Notes

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Conflict of interest: The authors declare no conflict of interest.

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