Mortality trend from cancer of the gastric cardia in the Netherlands, 1969–1994

RJF Laheij, H Straatman, ALM Verbeek and JBMJ Jansen

Background Time trends of cancer of the gastric cardia differ between populations and the reasons are not fully understood. The object of this study was to investigate the occurrence of cancer of the gastric cardia in descriptive relation to age at death, calendar period, birth cohort and gender in the Netherlands between 1969 and 1994.

Methods Data on the number of people with cancer of the gastric cardia as the underlying cause of death from 1969 to 1994 were obtained from annual publications by the National Causes of Death Registry of Statistics Netherlands. To estimate the separate effects of age, calendar period and birth cohort on the trend in mortality, a simultaneous analysis of these factors was performed using a log-linear Poisson model.

Results In 1969, the mortality rates from cancer of the gastric cardia for males and females per 100 000 people were 2.1 and 1.1; in 1994 the mortality rates were 1.5 and 0.7, respectively. Examination of the time trend suggested that mortality for cancer of the gastric cardia may reflect a period phenomenon, although a cohort effect may have also contributed to the observed time trend. Furthermore, more males than females died from cancer of the gastric cardia. The difference was most striking in the younger age categories.

Conclusion In this Dutch population, the age-period-cohort-gender analysis indicated that the mortality rates decreased after the period 1975–1979 which might be explained by a decrease in exposure to risk factor(s) or an increase in exposure to protective factor(s).

Keywords Cancer, gastric cardia, mortality, age-period-cohort analysis

Accepted 12 January 1999

Epidemiological studies have shown that worldwide, incidence and mortality rates for gastric cancer have decreased considerably during the past decades. However, studies that investigated time trends of stomach cancer by anatomical subsite found an increase in the incidence of cancer of the gastric cardia in contrast with cancer of the distal parts of the stomach. Increasing incidence and mortality rates for cancer of the gastric cardia have been found in studies from the USA and UK. Studies on populations in New Zealand, Switzerland and Norway did not report any changes in the occurrence of cancer of the gastric cardia. Time trends of cancer of the gastric cardia differ between populations and the reasons are not fully understood.

The object of this study was to investigate the trend of cancer of the gastric cardia in descriptive relation to age at death, calendar period, birth cohort and gender in the Netherlands between 1969 and 1994, based on mortality data. Coding complexities, in the routine mortality data sets, caused major problems in describing the time trend of cancer of the gastric cardia. It is unclear what proportion of cancers of the gastric cardia may have been coded as unknown, unspecified or lower third oesophageal. Unfortunately, national incidence data on cancer of the gastric cardia have only become available recently. However, the incidence rates were almost identical to those for gastric cancer mortality, because only a small proportion of the patients survived the disease.

Methods Data on the number of people with cancer of the gastric cardia as the underlying cause of death from 1969 to 1994 were obtained from annual publications by the National Causes of Death Registry of Statistics Netherlands. In this period, two revisions of the International Classification of Diseases were published (ICD 8 and 9). In the ICD, cancer of the gastric cardia was coded as 151.0.
Mortality rates per 100,000 people were calculated by gender, standardized to the European population and accumulated over 5 years. For statistical analysis, the numbers of deaths were grouped according to 5-year calendar periods of registration. The oldest age group that was used in the analysis was 85–89 years. Anyone younger than 35 years were ignored, because of the rarity of mortality from the disease at that age. From these data, 5-year birth cohorts were constructed by combining age groups and calendar periods.

To estimate the separate effects of age, calendar period and birth cohort on the trend in mortality, a simultaneous analysis of these factors was performed using a log-linear Poisson model. This model describes the mortality for a specific age-period-cohort combination, apart from random fluctuations, as a product of age at death, calendar period and birth cohort. As the mortality rates for females were very low, we added gender to the age-period-cohort model. Age, calendar period, birth cohort, gender and interaction terms between these factors were fitted so that their predicted rates were close to the observed rates in all strata. The maximum likelihood method was used to estimate these factors using the Genmod procedure from SAS software. For testing the goodness-of-fit of the models, the deviance was used while for testing the difference between models, the difference in the deviances with the degrees of freedom (d.f.) was used. The fundamental problem with interpreting parameter estimates from an age-period-cohort-gender and age × gender model is that there is no single solution. To overcome the non-identifiability property, we used the more simple age-period-gender and age × gender model to describe the time trend in mortality for cancer of the gastric cardia. We estimated cohort effects from the age-period-cohort-gender, and age × gender model based on the solution for period according to the more simple age-period-gender, and age × gender model. The nearest estimates for the age and period effects in both models occurred when the second and third cohort effects of the age-period-cohort-gender, and age × gender model were zero.

Results

The mortality rates from cancer of the gastric cardia have remained stable in males or at the most have slightly decreased in females (Figure 1). In 1969, the mortality rates from cancer of the gastric cardia for males and females per 100,000 people were 2.1 and 1.1; in 1994 the mortality rates were 1.5 and 0.7, respectively. Table 1 presents the age-specific mortality rates for males and females. The time trends for cancer of the gastric cardia shown in Figure 1 were investigated by fitting the data from Table 1 into an age-period-cohort-gender model. The deviance summaries of the age-period-cohort-gender models are presented in Table 2. The most simple model (model 4) that fitted the data was age-period-gender, with the interaction term age × gender model (deviance 99.9 by 84 d.f.). Model 5 was the only model that gave a better description of the data than model 4 (difference in deviance: 99.9–67.7 = 32.2, d.f. 13, P-value = 0.01).

The estimated effects due to the calendar period of mortality calculated by the age-period-gender and age × gender model (model 4) showed that mortality from cancer of the gastric cardia was not consistent over the period 1969–1994 (Figure 2).

Table 1  Age-specific mortality rate per 100,000 person-years (average number of deaths per year in the Netherlands) for males (M) and females (F) from 1970 to 1994

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>35–39</td>
<td>0.1 (2)</td>
<td>0.1 (2)</td>
<td>0.2 (4)</td>
<td>0.0 (1)</td>
<td>0.2 (6)</td>
</tr>
<tr>
<td>40–44</td>
<td>0.6 (12)</td>
<td>0.1 (1)</td>
<td>0.8 (15)</td>
<td>0.2 (3)</td>
<td>0.6 (13)</td>
</tr>
<tr>
<td>45–49</td>
<td>1.1 (20)</td>
<td>0.2 (4)</td>
<td>1.3 (24)</td>
<td>0.3 (4)</td>
<td>1.4 (28)</td>
</tr>
<tr>
<td>50–54</td>
<td>1.4 (23)</td>
<td>0.2 (4)</td>
<td>2.5 (44)</td>
<td>0.7 (14)</td>
<td>1.7 (31)</td>
</tr>
<tr>
<td>55–59</td>
<td>2.7 (41)</td>
<td>0.7 (12)</td>
<td>3.7 (60)</td>
<td>1.0 (17)</td>
<td>3.0 (52)</td>
</tr>
<tr>
<td>60–64</td>
<td>5.2 (70)</td>
<td>1.3 (20)</td>
<td>5.4 (75)</td>
<td>1.8 (28)</td>
<td>6.9 (102)</td>
</tr>
<tr>
<td>65–69</td>
<td>9.2 (103)</td>
<td>1.8 (24)</td>
<td>11.2 (132)</td>
<td>1.9 (27)</td>
<td>9.9 (121)</td>
</tr>
<tr>
<td>70–74</td>
<td>15.2 (126)</td>
<td>3.5 (38)</td>
<td>16.2 (146)</td>
<td>4.4 (54)</td>
<td>13.6 (130)</td>
</tr>
<tr>
<td>75–79</td>
<td>16.7 (93)</td>
<td>5.8 (45)</td>
<td>18.9 (112)</td>
<td>6.9 (62)</td>
<td>20.5 (133)</td>
</tr>
<tr>
<td>80–84</td>
<td>23.2 (74)</td>
<td>9.2 (41)</td>
<td>21.0 (71)</td>
<td>8.9 (49)</td>
<td>20.9 (76)</td>
</tr>
<tr>
<td>85–89</td>
<td>22.2 (30)</td>
<td>9.9 (19)</td>
<td>28.7 (43)</td>
<td>7.0 (17)</td>
<td>26.9 (44)</td>
</tr>
<tr>
<td>90–94</td>
<td>13.9 (5)</td>
<td>7.5 (4)</td>
<td>15.8 (7)</td>
<td>15.1 (11)</td>
<td>31.0 (16)</td>
</tr>
</tbody>
</table>
When we took the first period 1970–1974 as the baseline, the relative risk gradually declined to a relative risk of 0.84 in the period 1990–1994. The accompanying cohort effects of mortality calculated by the age-period-cohort-gender, and age × gender model (model 5) showed that mortality was stable over the cohorts born between 1885 and 1930. The effects for cohorts born between 1930 and 1955 fluctuated. The period and cohort effects were similar in males and females.

In both males and females, the risk of developing cancer of the gastric cardia continued to rise in most age groups (Figure 3). Comparison of age-specific mortality rates between males and females showed that more males died from cancer of the gastric cardia. However, gender ratios were not constant over age. In those aged 40–44 years, the male to female mortality ratio was 7; at the age of 90 years it decreased to 2.

Discussion

A worldwide decline in gastric cancer has been evident for many years. In the Netherlands mortality from gastric cancer has decreased steadily in both males and females from 1950 to 1994. The results of previous investigations have shown different time trends for anatomical subsites of the stomach, incidence rates for adenocarcinoma of the gastric cardia have increased. In contrast with the results of other studies, the mortality rates for cancer of the gastric cardia in the Netherlands have remained stable or decreased slightly between 1969 and 1994. Studies by Armstrong and Borman from New Zealand, Levi et al. from the Swiss Canton of Vaud and Hansen et al. from Norway revealed a similar time trend for cancer of the gastric cardia. The variability in incidence or mortality rates for cancer of the gastric cardia between geographical areas suggests different exposures to risk factors or differences in susceptibility.

Routine data sets were used to evaluate mortality from cancer of the gastric cardia. In almost every routine data set, and in particular mortality data sets, the largest category for any type of cancer will be coded under unknown or unspecified subsites for gastric cancer (ICD code 151.9). Therefore it is unclear what proportion of cancers of the gastric cardia may have been coded as unknown, unspecified or lower third oesophageal, but it may well have varied over time according to interest and rigour in coding. In addition there was often overlap between the registration of mortality from cancer of the gastric cardia and adenocarcinoma of the lower oesophagus. Some of the discrepancies between the results of this study and those of other studies may be due to such problems. However, we have three reasons for
believing that the differences between this study and the other studies were not caused by these problems. First, our mortality rates correspond with those reported in other populations (from 1.5 to 4.0). 2–7 Second, in view of the overlap between the registration of mortality from cancer of the gastric cardia and adenocarcinoma of the lower oesophagus, one would expect that one or the other would have shown an increase. However, there have been upward trends in mortality from oesophageal cancer in the Netherlands since 1979, both in males and females. 1 This reinforces the finding of a lack of increase in cancer of the gastric cardia, because there may have been a tendency to code such tumours as adenocarcinoma to the stomach. Third, one of our striking findings confirms a conclusion drawn by other authors based on another routine data set, the Netherlands Cancer Registry, who measured the incidence of cancer in the Netherlands. 14

So far, only one study has considered the effects of age at diagnosis, calendar period at diagnosis and birth cohort for gastric cancer by anatomical subsite. 4 The results suggested an increasing trend for adenocarcinoma of the gastric cardia which may reflect a cohort phenomenon, although a period effect may have also contributed. The trends in mortality from cancer of the gastric cardia found in this study could be explained by an age-period-gender and age × gender effect. Generally, period effects reflect influences on all age groups simultaneously, because of changes in classification, improved death certification, or improvement in survival rates. However, we observed that the classification of cancer of the gastric cardia did not change during the study period. If death certification has improved because of more accurate tumour localization methods (lower third of the oesophagus or gastric cardia) the mortality rates for cancer of the gastric cardia would have increased. However, this was not observed, so improved death certification probably did not cause the time trend. Unfortunately we were not able to verify the extent to which improved death certification contributed to a decrease in the mortality rates for cancer of the gastric cardia, because death certificates are not made available for research purposes. Another explanation for the time trend might be improvement in survival rates. In the Netherlands, the 5-year survival rates of patients with gastric cancer were low and did not change between 1955 and 1992. 15

As changes in classification, improved death certification, or improvement in survival rates were probably not the reason for the time trends observed in this study, there may have been a decrease in exposure to risk factors or an increase in exposure to protective factors. A possible protective factor is the use of gastric-acid inhibitors (H2 receptor antagonists or proton-pump inhibitors). H2 receptor antagonists were introduced on the Dutch market in 1978, while proton-pump inhibitors were introduced in 1988. However, this medication has also been available in most other countries and has not led to a decrease in mortality from cancer of the gastric cardia. Furthermore, several reports have suggested that gastric acid inhibitors may have increased the risk of gastric cancer. Another possible reason for the observed mortality rates might be the decrease in exposure to *Helicobacter pylori*. The organism plays an important role in the pathogenesis of not only persistent gastritis, but also peptic ulcers and gastric cancer. The decreasing prevalence of *H. pylori* infection in the Netherlands over the past few decades, because of antibiotic treatment, correspond with the period effects. However, *H. pylori* is chiefly located in the fundus and antrum.

Besides calendar period effect, gender was also visible in the time trend in mortality from cancer of the gastric cardia in the Netherlands. Cancer of the gastric cardia was more common in males than in females. Furthermore, there was divergence in the time trend for cancer of the gastric cardia between males and females. The interaction term age × gender indicated that the time trend varied because of the different age distributions between males and females. The mortality for gastric cancer and cancer of the gastric cardia was higher in the older age groups. However, there was an excess of male deaths from cancer of the gastric cardia particularly in the younger age categories. The high male to female ratio may indicate differences in exposure to risk/preventive factors between the sexes. This finding confirms the remarkable age-dependent sex differences reported by

![Figure 3: Estimates of the age effect on a logarithmic scale for cancer of the gastric cardia by gender](image-url)
Schouten and Kiemeney, although their results were based on another data set. However, it should be noted that cancer of the gastric cardia is very rare in young males and females.

In summary, the mortality rates for cancer of the gastric cardia in the Netherlands remained stable or decreased only slightly between 1969 and 1994. This time trend could be related to a period effect, a decrease in exposure to risk factors or an increase in exposure to protective factors in the entire Dutch population. A cohort effect may have also contributed to the time trend.

References


