GASTRIC CANCER IN NORTH SARDINIA, ITALY: AN EPIDEMIOLOGICAL REPORT

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ABSTRACT

\textbf{Aims:} The aim of this study was to describe the epidemiological characteristics and trends of gastric cancer in north Sardinia, Italy, in the period 1992-2010.

\textbf{Materials and methods.} Data were obtained from the cancer registry of the province of Sassari, which makes part of a wider registry web coordinated by the Italian Association for Tumor Registries.

\textbf{Results.} The overall number of gastric cancer cases registered was 1227. The male-to-female ratio was 1.7:1 and the mean age 69 years for males and 71 years for females. The standardized incidence rates were 15.6/100,000 and 7.3/100,000 and the standardized mortality rates 11.7/100,000 and 5.8/100,000 for males and females respectively.

\textbf{Conclusions.} Low and stable trends in incidence and mortality of gastric cancer in both sexes were evidenced in North Sardinia, in the period under investigation. Nevertheless, the relative survival at 5 years from diagnosis was relatively low. This suggests that there must be an enhancement of surveillance policies, and that the diagnosis and treatment methods adopted in the area must improve.

\textbf{Key words:} Gastric cancer, adenocarcinoma, screening, helicobacter pylori, Sardinia, Italy.

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Aims

Gastric cancer is the fifth most incident malignancy in the World, with approximately one million new cases estimated in 2012\textsuperscript{1,2}. Furthermore, it is the third leading cause of death in both sexes worldwide, with more than 700,000 deaths estimated in 2012, representing the 8.8% of the global cancer mortality\textsuperscript{1,2}. It has been extensively reported that the most relevant risk factors implied in the pathogenesis of stomach cancer are preservation of foods, dietary habits, helicobacter pylori eradication, socioeconomic - hygienic conditions, and tobacco smoking\textsuperscript{3,4}. The efforts and improvements registered in recent times in reducing the impact of these factors were consistent in both developed and developing countries throughout the globe, and led to a steady reduction of the incidence of gastric cancers in these countries; nevertheless, high or increasing incidence rates are still registered in vast areas, especially in Asia and South America\textsuperscript{1,2}. The aim of this population-based study was to analyze and describe the epidemiological characteristics and trends of gastric cancer in north Sardinia, Italy, in the period 1992-2010.

Materials and methods

The epidemiological data presented in this article were obtained from the “Registry of the tumors of the Province of Sassari”. This registry was created in 1992 by the local health agency for the epidemiological surveillance of cancer in the province. In 1999 it became part of a wider web of cancer registries, coordinated today by the Italian Association for Tumor Registries (Associazione
Italian Registri Tumori, AIRTUM). The association coordinates 34 registries in the country, collects and publishes data, and collaborates with international organizations in the field.

Every registry collects data on tumoral diseases affecting inhabitants in the territory of jurisdiction through the local hospitals and health care services, as with other registries (e.g., death registries). Demographic, clinical, pathological and prognostic data are collected for each case of cancer and are registered in a digital database. This database was the data source for the present population-based report, as well as for numerous periodic reports published in the past (5-9).

The demographic characteristics of the patients affected by gastric cancer were collected. Crude incidence and mortality rates per 100,000 inhabitants per year were calculated, as were standardized rates adjusted for European age-population standards (ASR). Furthermore, time trends of incidence and mortality rates were studied. The mean age at disease onset and at death, as well as changes in histology trends were evaluated. Additionally, the cumulative risk of developing the disease and of dying between zero and 74 years of age was estimated. A comparison between incidence and mortality in the province of Sassari and those in other Italian provinces was performed. Finally, relative 5-year survival was calculated by the Ederer II method.

Results

The overall number of cases of gastric cancer registered in the period 1992-2010 was 1227. Diagnosis was obtained by histological or cytological reports in 1105 cases (90%) and using other information sources (clinical reports, radiological referrals, death certifications, etc) in 122 cases (10%). Among the 1227 individuals registered, 768 were males and 459 females, with a male-to-female ratio of 1.7:1. The mean age was 69 years for males and 71 years for females. The cumulative risk of developing the disease was 1.2% for males and 0.5% for females.

As regards the anatomical distribution of the tumors 109 (8.9%) were sited in the cardia, 49 (4%) in the fundus, 202 (16.5%) in the body, 344 (28%) in the antrum, 50 (4.1%) in the pylorus, 126 (10.3%) in the small curvature, and 16 (1.3%) in the great curvature, while in 115 (9.4%) cases the lesions involved more than one gastric compartment; in 216 (17.6%) cases the anatomical localization was not known. Among the tumors that had histological or cytological diagnosis, 47.3% were non otherwise specified (NOS) adenocarcinomas, 31.9% were signet cell adenocarcinomas, 13.3% were other adenocarcinomas, and 7.5% were other than adenocarcinoma cancers. No relevant modifications in the trends of the principal histotypes were observed in the years under investigation. The histological grade was known in 75% of the adenocarcinomas observed: 4.7% were grade I, 40.9% were grade II, and 54.4% were grade III. Table 1 summarizes the TNM pathological stage of the adenocarcinomas observed in the cohort, according to the 7th edition of the AJCC cancer staging manual (10).

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1: 19%</td>
<td>N0: 44%</td>
</tr>
<tr>
<td>T2: 38%</td>
<td>N1: 32%</td>
</tr>
<tr>
<td>T3: 31%</td>
<td>N2: 12%</td>
</tr>
<tr>
<td>T4: 8%</td>
<td>N3: 8%</td>
</tr>
<tr>
<td>Tx: 4%</td>
<td>N1: 4%</td>
</tr>
</tbody>
</table>

Table 1: Distribution of the TNM pathological stage among patients with gastric adenocarcinoma in North Sardinia, 1992-2010.

The crude incidence of gastric malignancies in the period under investigation was 18.7/100,000 for men and 10.8/100,000 for women. Standardized incidence rates were 15.6/100,000 for males and 7.3/100,000 for females. Table 2 shows the distribution of incidence in relation to age in percentages, while table 3 shows the distribution of incidence rates in relation to age. Peak incidence occurred in patients with more than 85 years of age, in both males and females.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>0-14</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>15-29</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>30-44</td>
<td>24 (3.3)</td>
</tr>
<tr>
<td>45-59</td>
<td>138 (18)</td>
</tr>
<tr>
<td>60-74</td>
<td>327 (42.5)</td>
</tr>
<tr>
<td>75+</td>
<td>276 (35.9)</td>
</tr>
</tbody>
</table>

Table 2: Age-class incidence distribution of gastric cancer in North Sardinia, 1992-2010.
The trend of incidence rates in the period under investigation is depicted in Figure 1; no significant variations were observed. Analysis of the trend of mean age at disease onset, for the same period of time, did not reveal any relevant changes. Table 4 shows the comparison of the incidence and mortality in the province of Sassari with those in other Italian provinces.

There were 990 deaths in the period under investigation (591 males and 399 females). Crude overall mortality was 14.4/100,000 for males and 9.4/100,000 for females, while standardized mortality rates were 11.7/100,000 and 5.8/100,000 respectively. The mean age at death was 72 years in males and 75 years in females. The cumulative risk of death was 0.79% for males and 0.37% for females. Table 3 shows the age-class distribution of mortality rates. There was a relevant increase in mortality rates after the seventh decade of life. Figure 1 shows the time trend of mortality between 1992 and 2010: a substantially stable trend in both sexes was registered. Finally, relative survival at 5 years from diagnosis was 27.1% (29.7% for males and 23.6% for females).

**Table 3**: Age-class incidence and mortality rates of gastric cancer in North Sardinia, 1992-2010.

The trend of incidence rates in the period under investigation is depicted in Figure 1; no significant variations were observed. Analysis of the trend of mean age at disease onset, for the same period of time, did not reveal any relevant changes. Table 4 shows the comparison of the incidence and mortality in the province of Sassari with those in other Italian provinces.

**Table 4**: Comparison with incidence and mortality rates of other Italian provinces, 1992-2010.

Discussion

Gastric cancer is the fifth most frequent neoplastic disease in the world with approximately one million cases estimated in 2012\(^1\). World population age-standardized incidence calculated the same year was 12.1/100,000, ranging from less than 2/100,000 in Micronesia to more than 24/100,000 in Eastern Asia\(^1\). The higher incidence rates were registered in Japan, China, Mongolia and in the Republic of Korea, where the cancer of the stomach is traditionally very common\(^1,2\).
Eastern Asia cases account for half the world total cases. Gastric cancer is also the third leading cause of death in both sexes worldwide, with more than 700,000 deaths estimated in 2012\(^{(1)}\).

The incidence of gastric cancer is significantly higher in developing areas worldwide in comparison with developed countries; more than 70% of cases occur in developing countries\(^{(1-2)}\). In Europe more than 160,000 cases of gastric cancer have been estimated in 2012, with a standardized incidence rate of 14/100,000 for men and 6.8/100,000 for women, and approximately 126,000 deaths, with standardized mortality rates of 10.5/100,000 and 5.1/100,000 for males and females respectively\(^{(1)}\). The highest figures were observed in eastern European countries (Belarus, Russia, Ukraine, Latvia) and in developing areas in South Europe (Albania, FYR Macedonia)\(^{(1,2)}\).

In Italy approximately 13,000 new cases and 10,000 deaths for gastric cancer have been estimated in 2013\(^{(3,4)}\). Large part of the gastric cancer cases and deaths observed in Italy involve individuals with more than 70 years of age. Different incidence figures have been observed throughout the country: 22.6/100,000 in northern, 23.6/100,000 in central and 15.4/100,000 in southern regions for males, while the corresponding figures for females were 11.4/100,000, 12.2/100,000, and 7.3/100,000\(^{(1)}\). Standardized incidence rates in the province of Sassari weresimilar to those estimated by AIRTUM for southern Italian regions. Comparisons of the incidence rates with those of other Italian provinces place our province as that with the lowest incidence rates, followed by other southern provinces (Salerno and Ragusa) (Table 4).

Considering the distribution of the disease in relation to age, less than 5% of the cases occurred in individuals <45 years, while more than 75% occurred after the sixth decade of life. Incidence rates increased with aging in both sexes, reaching peak values in individuals ≥80 years. This distribution pattern is similar to those reported in other western populations.

The time trends analysis showed a certain stability of incidence rates of gastric cancer in both sexes in north Sardinia. A global reduction of gastric cancer incidence has been registered in the last decades in the World. In 1975 stomach cancer was the leading neoplastic disease in terms of new cases\(^{(2)}\). In Italy, an annual incidence reduction of 3.4% in males and -3.6% in females has been recently estimated\(^{(1)}\).

These reductions in incidence are more likely to occur in higher incidence areas, rather than in regions with currently low incidence rates, like our province.

The events which led to this continuous reduction of gastric cancer incidence in developed countries are widely related to the removal of some important risk factors, and, in high incidence areas, to the adoption of organized screening and surveillance programs. Probably the most relevant factor, contributing to the reduction of stomach cancer incidence, has been the change in dietary habits in western countries, especially after refrigeration of foods had become available\(^{(4-6)}\). Higher consumption of fruits and vegetables, and the reduction of salty and starchy foods, seem to have played a protective role against gastric cancer.

In a recent report of Bertuccio et al. a dietary pattern rich in fruits and vegetables has been demonstrated to reduce by approximately 25% the risk for gastric cancer, as opposed to the so called “western” dietary patterns, which are rich in meat, high fat dairy foods, starchy foods and sweets, and rise by approximately 50% the risk for gastric cancer\(^{(13)}\). Dietary habits rich in healthy components, such as fruits and vegetables, are diffused in the south of Italy and in Sardinia, and this may explain the lower incidences of gastric cancer in the corresponding populations, in comparison to northern Italian populations.

The role of Helicobacter Pylori (HP) infection in the genesis of gastric cancer has been widely elucidated in the past. Screening for HP infection and eradication of positive cases has been demonstrated effective in interrupting the biological evolution of inflammatory changes of the mucosa, to premalignant lesions and finally to invasive cancer\(^{(14-16)}\). The same beneficial effects can be achieved by endoscopic surveillance of patients with other inflammatory benign conditions or with preneoplastic lesions occasionally discovered. Currently, organized screening strategies for gastric cancer are available in high incidence developed countries. In Japan a universal screening program exists for the general population, using fluoroscopy and upper digestive tract endoscopy. The role of screening programs in low incidence countries is still a matter of debate, as their cost-effectiveness in those areas is not yet clear\(^{(17)}\).

Endoscopic surveillance allows early detection of gastric cancer and offers the possibility to avoid surgery in patients with early gastric cancer (EGC).
Endoscopic mucosal resections (EMR) or endoscopic submucosal dissections (ESD) are indicated in cases of EGC of intestinal type, which involve the mucosa or the external layer of the submucosa (sm1), smaller than 3 cm in maximum diameter and without nodal or vascular invasion. In cases of diffuse type EGC, ECG larger than 3 cm, or ECG involving the deeper layers of the submucosa a surgical resection is recommended. Unfortunately, the detection of EGC in regions where screening programs are not available is sporadic and fortuitous, furthermore given the lack of specific clinical manifestations like dysphagia, weight loss, or abdominal pain. These manifestations, along with anorexia, anemia, nausea, vomit, palpable mass and signs of distant metastasis are common in more invasive stages.

Concerning mortality, 990 (591 males and 399 females) deaths occurred in the 18 years we studied. The standardized mortality rate in women was approximately the half of that in males. Considering the age-class mortality trend, a natural increase in relation to age was observed in both sexes, with peaks after the eighth decade of life (Table 3). Standardized mortality rates trends remained substantially stable in the years under investigation. Finally, relative survival at 5 years from diagnosis was 27.1% (29.7% in men and 23.6% in women). These figures were slightly inferior in comparison with those recently published for the entire country (34% for males and 36% for females).

Several factors impact in such a low survival in patients with gastric cancer such as lack of effective screening programs, non-specific clinical manifestations in early stages, delays in diagnosis, high percentage of advanced stages at diagnosis, ineffectiveness of current therapeutic strategies, and others. The relative 5 years survival was slightly better in men, as opposed to national estimates in which 5-years survival is slightly better in women. These figures suggest that diagnostic and therapeutic strategies must be enhanced to improve survival outcomes in north Sardinia.

Conclusions

Our data showed a low and stable trend in incidence and mortality rates of gastric cancer in both sexes in the last decades in north Sardinia. Conversely, lower survival rates were registered in the area in comparison to national estimates. These findings suggest that there must be an enhancement of surveillance policies, and that diagnosis and treatment methods must be improved.

### References


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