Comparison of Two Diverse Populations, British Columbia, Canada, and Ardabil, Iran, Indicates Several Variables Associated with Gastric and Esophageal Cancer Survival

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Abstract

Background Geographic variation and temporal trends in the epidemiology of esophageal and gastric cancers vary according to both tumor morphology and organ subsite. This study compares 1-year survival of gastric and esophageal cancers between two distinct populations: British Columbia (BC), Canada, and Ardabil, Iran.

Methods Data for invasive primary esophageal and gastric cancer patients were obtained from the population-based cancer registries for BC and Ardabil. The relative survival rate was calculated using WHO Statistical Information System (WHOSIS) life-tables for each country. Chi-square and Fisher’s exact tests were used to compare survival differences between BC and Ardabil. T-tests, chi-square tests, and Fisher’s exact test were used to compare patient characteristics and tumor factors between the populations.

Results The overall 1-year age-standardized relative survivals for gastric cancer were 48% and 21% in BC and Ardabil, respectively ($p<0.01$). The overall 1-year age-standardized relative survival for esophageal cancer was 33% and 17% in BC and Ardabil, respectively ($p<0.05$). Overall and separately for each gender, age group, tumor...
location, and histology, there was greater 1-year survival of the gastric cancer patients in BC compared to Ardabil. For esophageal cancer, patients under age 65, patients with tumors in the middle or upper third of esophagus, and patients with squamous cell carcinoma had significantly better survival in BC than in Ardabil.

Conclusion Findings of this study point to differences in disease characteristics and patient factors, not solely differences in healthcare systems, as being responsible for the survival difference in these populations.

Keywords Esophageal cancer · Gastric cancer · Survival · Cancer registry

Abbreviations
ASR Age-standardized incidence rate
BC British Columbia
GI Gastrointestinal
ICD-O International Classification of Diseases for Oncology, Third Edition
NS Non-significant

Introduction

Geographic variation and temporal trends in the epidemiology of esophageal and gastric cancers vary according to tumor morphology and organ subsite [1]. Both diseases are among the deadliest forms of cancer. Gastric disease incidence and mortality have fallen dramatically over the past 70 years in western countries, but it is the fourth most commonly diagnosed cancer and the second most common cause of cancer-related death worldwide [2]. The majority of esophageal carcinoma patients in the world die within a year of diagnosis and only 8–20% are alive after 5 years [3]. Gastric and esophageal cancers are relatively infrequent in Canada, but common in Iran [4].

This study compares 1-year survival of gastric and esophageal cancers between the populations of British Columbia (BC), Canada, and Ardabil, Iran. We chose BC and Ardabil because both areas have high-quality population-based cancer registries. The BC Cancer Registry has been in existence since 1969 (www.bccancer.bc.ca/HPI/CancerStatistics, accessed November 4, 2009), and the Ardabil Cancer Registry is the first such registry in the Islamic Republic of Iran [5]. This study does not compare survival rates for different types of esophageal or gastric cancer within Ardabil or within BC.

Methods

Data for invasive primary esophageal and gastric cancer patients diagnosed in 2004 were obtained from the cancer registries for BC and Ardabil. For the BC registry, completeness of case ascertainment was 86.8% and completeness of other information was 99.8% [6]. For the Ardabil registry, overall completeness was 89% based on reports from pathology centers, identity information, demographic information and percentage of coded cancer cases [7]. Dates in the Ardabil registry were converted to equivalent values in the western calendar. For both registries, the topography and histology of cases were coded according to the International Classification of Diseases for Oncology, Third Edition (ICD-O) [8]. Similar methods were used for the collection and classification of breast cancer data from BC and Ardabil data in an earlier report [9]. Esophageal cancers were grouped into four anatomic subsites: upper third (ICD-O codes C15.0–C15.3), middle third (C15.4), lower third and overlapping lesions (C15.5), and unknown (C15.8 and C15.9). Gastric cancers were grouped into three anatomic subsites: proximal third (i.e., cardia) in the gastroesophageal junction or upper third of the stomach (C16.0 and C16.1), distal stomach or lower two thirds of the stomach (C16.2–C16.7), and unknown or unspecified/overlapping lesion (C16.8 and C16.9). Histological categories for esophageal cancers were squamous cell carcinoma (ICD-O codes 8050–8082), adenocarcinoma (8140–8573), and others (mainly 8000–8020). Gastric cancers were categorized as diffuse or intestinal according to the Lauren classification system [10]. Diffuse gastric tumors are defined by ICD-O histology codes 8142, 8145, and 8490 [11]; other gastric tumors are defined as intestinal.

In BC, the vital status and date of death for cancer patients is routinely collected from government statistics. At least 1 year of follow-up information was available for each patient in BC. In Ardabil, information on a patient’s survival and date of death was obtained by interviewing cases or their families. Interviews were conducted by members of the Ardabil Cancer Registry whenever possible. The death registry in Ardabil was used to confirm this information and obtain data for patients who could not be interviewed. Based on this approach, 83.3% of Ardabil patients had completed 1-year follow-up information.

Survival time was defined as the time between cancer diagnosis and death. The relative survival rate [12] was calculated for various subgroups of each population using WHO Statistical Information System (WHOSIS) life-tables for each country [13]. Chi-square and Fisher’s exact tests were used to compare differences in 1-year survival proportions between BC and Ardabil. T tests, chi-square tests and Fisher’s exact test were used to compare patient characteristics and tumor factors between the populations. P values less than 0.05 were considered statistically significant. Other p values were denoted non-significant (NS).
Results

In 2004, 357 and 261 cases of gastric cancer were diagnosed in BC and Ardabil, respectively. Characteristics of the cases are summarized in Table 1. The mean ages of patients were 69.1 years in BC and 66.1 years in Ardabil ($p<0.01$). Women comprised about one third of gastric cancer patients in both BC and Ardabil (NS). Approximately 34.5% of gastric cancer cases (49% of cases with known topography) in BC and 41.8% (60% of cases with known topography) in Ardabil were diagnosed with proximal disease ($p<0.05$). Adenocarcinoma was the predominant histological type of gastric tumor, accounting for 87.4% and 79.7% of cases in BC and Ardabil, respectively ($p<0.01$). About 16.0% of gastric tumors in BC and 30.3% in Ardabil were the diffuse type ($p<0.05$).

In 2004, 232 and 124 cases of esophageal cancer were diagnosed in BC and Ardabil, respectively. Characteristics of cases are summarized in Table 2. The mean age of cases was 69.7 years in BC and 63.3 years in Ardabil ($p<0.01$). Women accounted for about one third of cases in BC and half of cases in Ardabil ($p<0.01$). Most tumors in BC cases were located in the lower third of the esophagus, while the lower and middle thirds of the esophagus had nearly equal incidence in Ardabil ($p<0.01$). Adenocarcinoma was the leading type of tumor in BC cases (50% of all cases), while only 10% of cases in Ardabil had this histology type ($p<0.01$).

Figures 1 and 2 show the overall 1-year age-standardized relative survival of gastric and esophageal cancers in BC and Ardabil. Details of the survival rates for gastric and esophageal cancer in BC and Ardabil are shown in Tables 3 and 4. Overall and separately for each gender, age group, tumor location, and histology, there was greater 1-year survival of gastric cancer patients in BC compared to Ardabil. Patients under age 65, patients with tumors in the middle or upper third of the esophagus, and patients with squamous cell carcinoma had significantly better esophageal cancer survival in BC than in Ardabil. Table 3 shows substantial differences for age and tumor location groups within gastric cancer patients in BC that are not seen in

Table 1 Gastric cancer patients in BC (Canada) and Ardabil (Iran)

|                | British Columbia | Ardabil |
|----------------|------------------|--------|
| Gender         |                  |        |
| Women          | 119 (33.3%)      | 75 (28.7%) |
| Men            | 238 (66.7%)      | 185 (70.9%) |
| Unknown        | 1 (0.4%)         |         |
| Age group      |                  |        |
| Less than 65   | 118 (33.1%)      | 108 (41.4%) |
| 65 or more     | 239 (66.9%)      | 153 (58.6%) |
| Location       |                  |        |
| Distal         | 127 (35.6%)      | 72 (27.6%) |
| Proximal       | 123 (34.5%)      | 109 (41.8%) |
| NOS/overlapping lesion | 107 (30.0%) | 80 (30.7%) |
| Lauren classificationa |     |        |
| Intestinal     | 262 (84.0%)      | 145 (69.7%) |
| Diffuse        | 50 (16.0%)       | 63 (30.3%) |

NOS not otherwise specified

a Adenocarcinomas only

Table 2 Esophageal cancer patients in BC (Canada) and Ardabil (Iran)

|                | British Columbia | Ardabil |
|----------------|------------------|--------|
| Gender         |                  |        |
| Women          | 64 (27.6%)       | 61 (49.2%) |
| Men            | 168 (72.4%)      | 62 (50.0%) |
| Unknown        | 1 (0.8%)         |         |
| Age group      |                  |        |
| Less than 65   | 76 (32.8%)       | 67 (54.0%) |
| 65 or more     | 156 (67.2%)      | 57 (46.0%) |
| Tumor location |                  |        |
| Upper third    | 23 (9.9%)        | 6 (4.8%) |
| Middle third   | 40 (17.2%)       | 35 (28.2%) |
| Lower third    | 112 (48.3%)      | 38 (30.6%) |
| NOS/overlapping lesion | 57 (24.6%) | 45 (36.3%) |
| Tumor histology|                  |        |
| Squamous cell carcinoma | 88 (37.9%) | 89 (71.8%) |
| Adenocarcinoma | 116 (50.0%)      | 13 (10.5%) |
| Other          | 28 (12.1%)       | 22 (17.7%) |

NOS not otherwise specified

Fig. 1 Overall 1-year age-standardized survival rates for gastric cancer cases in Ardabil (Iran) and British Columbia (Canada). Bars are ± standard error
Ardabil. In contrast, esophageal cancer patients in Ardabil had substantial survival differences for age and tumor location groups that were not meaning in BC (Table 4).

**Discussion**

Based on available registry and follow-up information, this study compares 1-year survival of gastric and esophageal cancer in two populations. Results indicate major differences and some interesting similarities between the populations. In general, overall 1-year relative survival was better in BC than Ardabil. There were significant differences between the populations in gastric cancer survival according to patient gender, age, tumor location, and tumor histology. For esophageal cancer, patients under age 65, patients with tumors in the middle or upper third of the esophagus, and patients with squamous cell carcinoma had significantly better survival in BC than in Ardabil. Survival differences between the populations might be based on other tumor-related factors, other patient characteristics, cancer control measures, and treatment factors.

Stage at diagnosis is likely the main tumor-related factor affecting a patient’s prognosis, and stage at diagnosis determines the course of a patient’s treatment [14]. Unfortunately, we could not include stage in our analysis because both cancer registries provided only limited information about it. Cell histology is another tumor-related factor that might affect patient survival [14]. In this study, the Lauren classification (based on tumor histology) did not have prognostic significance for 1-year survival of gastric cancer patients in either population. Several clinical studies report better survival for adenocarcinoma of esophagus [15–17], but we did not observe this. In both BC and Ardabil, tumor histology did not have a substantial influence on the survival of esophageal cancer patients. In Ardabil, tumors in the middle third of the esophagus were associated with worse survival than tumors located in the lower third. In Ardabil, the low number of cases with a tumor in the esophagus’ upper third makes it difficult to derive any meaningful conclusion concerning this group. This result is consistent with a recent report from Turkey [18]. However, results from BC and other North American studies [1, 3] indicate that survival of patients with cancers in the upper, middle, and lower third of the esophagus are similar.

Ethnicity has been suggested to be a possible prognosis factor for cancer in upper GI tract [19, 20]. BC has an ethnically diverse population. The 2006 census reported that only 52% of people living in BC at that time had a single ethnic origin [21]. In contrast, the population of Ardabil is homogeneous, with 95% being of Azeri ethnic background, which is of Aryan Caucasoid ancestry [5]. Family history also has been shown to be a prognostic factor in gastric and esophageal cancer. Gastric cancer patients with a family history of this tumor have unique clinicopathologic characteristics [22]. Poor survival among young patients from Ardabil could be explained by the presence of a higher proportion of familial cases of the disease. This is consistent with reports from other high-incidence areas [23]. Also, the high incidence of diffuse gastric cancer in the ethnically homogeneous Ardabil

![Fig. 2 Overall 1-year age-standardized survival rates for esophageal cancer cases in Ardabil (Iran) and British Columbia (Canada). Bars are ± standard error](image)

**Table 3** One-year relative survival for gastric cancer patients in BC (Canada) and Ardabil (Iran)

|                          | BC         | Ardabil    | p   |
|--------------------------|------------|------------|-----|
| Gender                   |            |            |     |
| Male                     | 0.48±0.07  | 0.18±0.09  | <0.01|
| Female                   | 0.46±0.09  | 0.26±0.08  | <0.01|
| Age                      |            |            |     |
| Less than 65             | 0.62±0.07  | 0.22±0.09  | <0.01|
| 65 or more               | 0.41±0.04  | 0.20±0.05  | <0.01|
| Tumor Location           |            |            |     |
| Distal                   | 0.61±0.07  | 0.23±0.06  | <0.01|
| Proximal                 | 0.45±0.08  | 0.19±0.06  | <0.01|
| Lauren Classification*   |            |            |     |
| Intestinal               | 0.48±0.07  | 0.18±0.04  | <0.01|
| Diffuse                  | 0.50±0.10  | 0.24±0.04  | <0.05|

Values are age-standardized rates ± standard error

* Adenocarcinomas only
population is consistent with some cases having inherited mutations in the E-cadherin gene that underlie hereditary diffuse gastric cancer [24].

Treatment is likely to be the greatest determinant of cancer patients’ survival, and province-wide treatment guidelines in BC result in nearly uniform treatment (http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gastrointestinal/default.htm). Patient characteristics include inherent and demographic characteristics such as age, sex, ethnicity, physical performance status, comorbidity, and immune status. These variables are usually unrelated to the presence of tumor but may have a profound impact on treatment choices [18]. The general treatment for esophageal and respectable gastric cancer was surgery. Some patients also received radiation and chemotherapy depending on the stage of disease [1]. In Ardabil, guidelines do not exist and treatment is not uniform. Based on previous reports, only 28% of patients with gastric and esophageal cancer in Ardabil received curative resectional surgery and about 25% of patients did not receive any treatment [25]. This study does not compare the distribution of patient/tumor characteristics within either the BC or Ardabil population, but it is obvious that the distributions are different. One of the interesting differences between BC and Ardabil is the survival pattern for proximal and distal gastric cancers. In BC, patients with proximal gastric tumors had poorer survival than patients with distal ones. In Ardabil, there was very little difference between survival for proximal and distal gastric cancers. In BC, only about one-third of tumors occurred in the middle and upper third of the esophagus. In Ardabil, more than half of tumors with known topology were located in this anatomic region. More men than women had gastric and esophageal cancers in BC; however, the incidence of esophageal cancer in Ardabil seemed independent of gender (i.e., the same in both sexes).

The strength of this study was the availability of population-based data with details of tumor histology and pathology. This study’s limitations include the lack of complete staging information, incomplete follow-up data, and the relatively large proportion of esophageal tumors with unspecified histology. Differences in the quality of registry data between two populations could also have influenced survival comparisons. As noted in the Report of National Cancer Registration in Iran [7], there are challenges in interpreting registry information regarding the health care system in Iran. There is vast, uncontrolled population movement in and out of Ardabil, an uncoordinated medical services system, and inconsistent referrals to different centers for diagnosis and treatment [7]. It is also possible that patients with better socioeconomic status are referred to better medical facilities in central cities.

Population-based survival studies cannot assess specific treatments but can quantify the effect of cancer control measures at the population level [26]. Neither BC nor Ardabil has a screening program for gastric and esophageal cancers. In BC, these cancers are infrequent and feasibility of screening is questionable. However, Ardabil has the highest rates of gastric and esophageal cancers in the world, and a screening program should be considered.

Conclusion

Gastric and esophageal cancers are heterogeneous diseases, but they share important features. They remain clinically asymptomatic until late in the disease process with consequent poor prognoses and high mortality rates. This study points to differences in disease characteristics and patient factors, not solely differences in healthcare systems, as being responsible for the survival difference in these populations. Even so, the outcomes of these cancers are poor for both populations, and improvements in diagnosis and management are urgently needed.

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