

BRIEF ARTICLES

Incidence and survival of stomach cancer in a high-risk population of Chile

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associated with survival were later included in a Cox multivariate model.

RESULTS: Between 1998 and 2002, 529 primary gastric cancers occurred in Valdivia (crude incidence rate 29.2 per 100000 inhabitants). Most cases were male (69.0%), residents of urban areas (57.5%) and Hispanic (83.2%), with a low education level (84.5% < 8 school years). SC SIR was higher in men than women (40.8 and 14.8 respectively, $P < 0.001$), risk factors were low education RR 4.4 (95% CI: 2.9-6.8) and 1.6, (95% CI: 1.1-2.1) for women and men respectively and Mapuche ethnicity only significant for women (RR 2.2, 95% CI: 1.2-3.7). Of all cases, 76.4% were histologically confirmed, 11.5% had a death certificate only (DCO), 56.1% were TNM stage IV; 445 cases (84.1%) were eligible for survival analysis, all completed five years follow-up; 42 remained alive, 392 died of SC and 11 died from other causes. Specific 5-year survival, excluding cases with DCO, was 10.6% (95% CI: 7.7-13.5); 5-year relative survival rate was 12.3% (95% CI: 9.1-16.1), men 10.9% (95% CI: 7.4-15.2) and women 16.1% (95% CI: 9.5-24.5). Five-year specific survival was higher for patients aged < 55 years (17.3%), with intestinal type of cancer (14.6%), without metastasis (22.2%), tumor size < 4 cm (60.0%), without lymphatic invasion (77.1%), only involvement of the mucous membrane (100%). Statistically significant independent prognostic factors were: TNM staging, diffuse type, metastasis, supraclavicular adenopathy, palpable tumor, and hepatitis or ascites.

CONCLUSION: Social determinants are the main risk factors for SC, but not for survival. An advanced clinical stage at consultation is the main cause of poor SC survival.

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Key words: Survival analysis; Stomach neoplasms; Survival rate; Incidence; Risk factors; Gastrectomy

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Abstract

AIM: To study the incidence and survival rate of stomach cancer (SC) and its associated factors in a high risk population in Chile.

METHODS: The population-based cancer registry of Valdivia, included in the International Agency for Research on Cancer system, covers 356396 residents of Valdivia Province, Southern Chile. We studied all SC cases entered in this Registry during 1998-2002 (529 cases). Population data came from the Chilean census (2002). Standardized incidence rates per 100000 inhabitants (SIR) using the world population, cumulative risk of developing cancer before age 75, and rate ratios by sex, age, ethnicity and social factors were estimated. Relative survival (Ederer II method) and age-standardized estimates (Brenner method) were calculated. Specific survival rates (Kaplan-Meier) were measured at 3 and 5 years and survival curves were analyzed with the Logrank and Breslow tests. Survival was studied in relation to demographics, clinical presentation, laboratory results and medical management of the cases. Those variables significantly

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INTRODUCTION

In 2002, stomach cancer (SC) was the fourth most common cancer in the world, with 900 937 cases and 700 349 deaths. Two-thirds of these occurred in developing countries^[1]. The high risk zones encompass Asia, Eastern Europe, and the Andean region of South America, all of diverse geographical characteristics^[2]. Chile, a representative of the Andean Region, presents an SC average mortality rate per 100 000 in 1990-2005 of 25.1 for men and 13.2 for women^[1]. This high SC mortality has not changed in the last 20 years^[3]. The existence of a population-based Cancer Registry in Valdivia^[4] gave us the opportunity to measure SC incidence and survival in a middle developing country. The Cancer Registry of Valdivia was initiated in 1982 and encompasses the inhabitants of an area of 18 429 square kilometres in Southern Chile; the data are included in the International Agency for Research on Cancer (IARC) cancer reports in 5 continents^[4]. The aims of this study were to measure SC incidence and risk factors and to assess SC survival.

MATERIALS AND METHODS

Cancer registry of Valdivia

The cancer registry of Valdivia covers a population of 356 396 people, and encompasses a systematic review of records in private and public clinical centers, hospitals and laboratories, and death certificates to identify every cancer case or cancer death occurring among residents of the Valdivia area. To guarantee complete case-ascertainment, it includes various national databases of particular cancers, death certificates and hospital records to identify residents of Valdivia who may have been diagnosed in other regions. This allows near 100% case ascertainment verification in the catchment area.

Cases

The subjects in the study were the 535 SC cases residents of Valdivia, identified in the Cancer Registry of Valdivia between the years 1998 and 2002. Of these, 6 cases were deemed non-eligible due to lack of information, leaving 529 subjects eligible for the study (98.9% of the total cases). In calculating the survival rate, 18 cases were excluded because they had a history of a previous cancer, apart from non-melanoma skin cancer; and 66 were excluded because the only information came from a death certificate or autopsy, leaving 445 cases (84.1%) to estimate SC survival. Deaths occurring within 30 d of a surgery with curative intention (3 cases) were considered deaths from other causes^[5]. Deaths from other causes were included, but censored.

Incidence and risk factors of stomach cancer

Standardized incidence rates, using the world population,

cumulative risk of developing cancer before the age of 75 and rate ratios were estimated according to the methodology proposed by the IARC^[6]. Population data were obtained from the National Institute of Statistics and the Chilean census of 2002^[7-9]. The risk of developing SC was estimated by sex, age, ethnicity (considering anyone with at least one Mapuche surname to be Mapuche, and the rest of the population to be Hispanic/European), education level (0-8 years and more than 8 years of education), urban or rural residency.

Survival analysis

Relative survival was calculated following the Ederer II method^[10] and age-standardized estimates were calculated using the approach proposed by Brenner *et al.*^[11]. Specific survival rates were measured at 3 and 5 years using the Kaplan-Maier method and survival curves for selected characteristics were compared using the Logrank and Breslow tests^[12]. Those variables significantly associated with survival were later included in a Cox multivariate model^[12]. Survival was studied in relation to demographics, clinical presentation, laboratory results and medical management of the cases. The characteristics of the tumor registered were: morphology according to the Lauren classification^[13], size measured at its largest diameter, location in the stomach (fundus, body or antrum or all the stomach) and invasion of the gastric wall. Stage of the tumor was based on TNM classification system^[14]. The intervals between the onset of symptoms, the diagnosis and definitive treatment were determined.

RESULTS

Incidence of gastric cancer

Between 1998 and 2002, 529 primary gastric cancers were detected amongst the residents of Valdivia (crude incidence rate 29.2 per 100 000 inhabitants). The majority of cases were men (69.0%), residents of urban areas (57.5%), had a low education level (84.5% had 8 or less years of schooling) and were predominantly of Hispanic origin (83.2%) (Table 1). Age of cases ranged from 27 to 94 years, being significantly lower in men than women with mean age of 66.8 years [95% confidence intervals (CI): 65.5-68.1] and 70.4 years (95% CI: 68.2-72.6), respectively. Relative risk (RR) of SC was higher among men, particularly at age 55-64 years. Mapuche ethnicity was a significant risk factor only for women (RR 2.2, 95% CI: 1.2-3.7), and low education status was a stronger risk factor for women than for men: RR 4.4, (95% CI: 2.9-6.8) and 1.6, (95% CI: 1.1-2.1), respectively; the highest differential of risk between men and women was found among cases with more than 8 years of education (RR = 7.5, $P < 0.001$) (Table 1).

Clinical characteristics of the cases

Weight loss and epigastric pain were the most common symptoms in patients at diagnosis, and both symptoms were significantly more common in males than females (Table 2). Signs considered to indicate poor prognosis:

Table 1 SIR of stomach cancer by selected characteristics, Valdivia, Chile, 1998-2002

Characteristic	Cases	Males: 365			Females: 164			Male vs female	
		%	SIR	95% CI	%	SIR	95% CI	RR	P-value
All	529	69	40.8	36.7-45.2	31	14.8	12.1-16.7	2.8	< 0.001
Age (yr)									
< 35	8	0.8	0.5	0.0-1.2	3.0	0.9	0.1-1.8	0.6	0.45
35-44	22	4.4	11.7	5.9-17.4	3.6	4.6	0.9-8.2	2.6	0.04
45-54	55	11.2	44.6	30.9-58.2	8.4	15.4	7.3-23.4	2.9	< 0.001
55-64	94	21.4	125.7	97.8-153.6	9.6	23.9	12.2-35.6	5.3	< 0.001
65-74	164	32.1	291.3	238.6-344.0	28.7	100.5	72.1-128.9	2.9	< 0.001
75-84	86	14.8	448.7	329.3-568.1	19.8	214.3	141.3-287.4	2.1	0.001
≥ 85	100	15.3	501.4	370.4-632.4	26.9	292.2	206.9-377.4	1.7	0.006
Ethnicity Mapuche	89	15	47.2	34.5-59.9	21.0	28.1 ^a	18.5-37.7	1.7	0.016
Hispanic/European	440	85	40.0	35.5-44.5	79.0	12.7 ^a	10.5-15.0	3.1	< 0.001
School years									
≤ 8	420	81	43.3 ^a	38.1-48.5	92.0	16.2 ^a	13.3-19.1	2.7	< 0.001
> 8	77	19	27.6 ^a	20.5-34.7	8.0	3.7 ^a	1.5-5.9	7.5	< 0.001
Residence rural	220	48	48.0 ^a	40.7-55.3	30.0	14.5	10.4-18.7	3.3	< 0.001
Urban	297	52	34.5 ^a	29.5-39.6	70.0	13.9	11.2-16.6	2.5	< 0.001

^aSignificant risk factors between characteristics groups; RR: Relative risk.

palpable epigastric mass, ascites or supraclavicular adenopathy, each were present in less than 15% of cases; only a palpable epigastric mass was significantly more common among females (Table 2). The main detection source was histology; only 11.5% of cases were identified by their death certificate only. The latter cases were significantly older: in those over 80, 45.5% and 15.1% were confirmed by death certificate only and histology, respectively ($P < 0.001$); there was also a higher proportion of women (22.6% versus 6.6%, $P < 0.001$) in this group.

In the majority of cases, the time interval between the beginning of symptoms and diagnosis was more than 3 mo. Early diagnoses were more frequent among men (Table 2). The main diagnostic procedures were gastric endoscopy and gastric biopsy (Table 2). At diagnosis only 5.5% of cases were in Stage I or II of the TNM classification; these earlier stages were more frequent among women (7.3%) than men (4.7%) (Table 2). The three most common histological types of SC both in men and women were: tubular adenocarcinoma (36%), undefined adenocarcinoma (20.2%) and signet ring cell carcinoma (18.7%) (Table 2). The fundus was the most frequent localization of the SC (29.9%) and the tumor location was not determined in a third of the cases. Information about tobacco or alcohol consumption was available for 65.4% and 63.9% of cases, respectively; tobacco use was declared by 51.4% of men and 29.1% of women ($P < 0.001$), and alcohol consumption was declared by 73.6% of men and 31.3% of women ($P < 0.001$) (Table 2).

Five years survival

Follow-up of the 445 cases included in the survival analysis was concluded on December 31st 2007, with 100% of the cases included in the 5-year analysis; only 42 cases remained alive, 392 cases had died of SC and 11 died from other causes. Specific survival at 5 years, including cases with a death certificate only, was

9.6% (95% CI: 6.9-12.3), excluding cases with a death certificate only, the survival was 10.6% (95% CI: 7.7-13.5); lower in men 9.8%, (95% CI: 6.5-13.1) than in women 12.9% (95% CI: 6.7-19.1). The 5-year relative survival rate, adjusted for the life expectancy of the population, was 12.3% (95% CI: 9.1-16.1), increasing the difference in survival of men 10.9% (95% CI: 7.4-15.2) and women 16.1% (95% CI: 9.5-24.5).

In univariate analysis, the significant factors for greater than 5 years survival were: younger age; Hispanic/European ethnicity; urban residency; lack of some clinical markers (supraclavicular adenopathy, palpable mass, ascites, or vomiting); gastrectomy; intestinal histological type; localized tumor (Figure 1A); size less than 4 cm, limited to the mucosa, without lymphatic invasion or metastasis; TNM stage 1 (Table 3). Tumors with proximal and distal localization had the same TNM distribution. However, tumors localized in the body had better 5-year survival than those localized to the fundus or in all the stomach, 23.0% vs 11.4% ($P = 0.049$) and 0% ($P < 0.001$), respectively; there was no statistical difference in survival between tumor location in the body and antrum (23.0% and 14.8%, $P = 0.16$, respectively).

The cumulative survival curve of Stage I SC was significantly higher than Stage III, Stage IV or unknown stage (Figure 1B), and was similar in men and women (Figure 1C and D).

Multivariate survival analysis

The multivariate models only included cases with sufficient clinical data (271 cases, 69%). All cases (445) had "unknown staging" more frequently than the cases included in the multivariate models (17.8% and 8.9% respectively, $P = 0.001$) while their 5-year survival was lower (10.6% vs 14.1% $P = 0.002$). Nevertheless, all cases were similar to those included in the multivariate analysis with regard to socio-demographics and to the variables associated with survival in the univariate analysis (listed in Table 3).

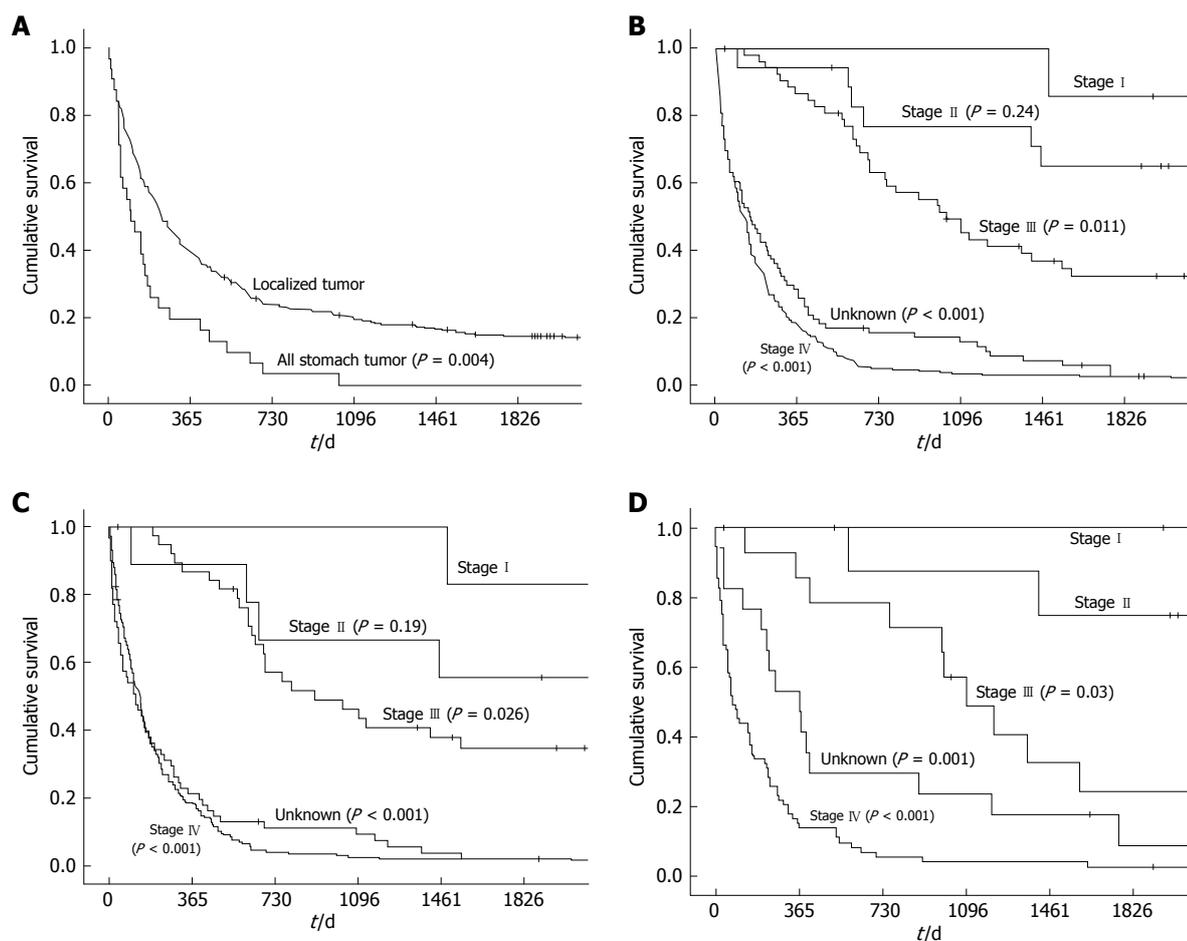


Figure 1 Stomach cancer-specific survival in Valdivia 1998-2005. A: Tumor location; B: TNM stage classification; C: Men by TNM; D: Women by TNM.

In the multivariate analysis, only 6 variables maintained their statistical significance as independent prognostic factors (Table 4). TNM staging was the strongest prognostic variable, the risk of dying in the following year was 23 times higher with stage IV compared with stage I. Other factors of poor prognosis were: diffuse type, presence of metastasis, supraclavicular adenopathy, a palpable tumor and hepatitis or ascites (Table 4).

DISCUSSION

We confirmed that Chile, in particular southern Chile, where Valdivia is located, has one of the highest risks of stomach cancer reported, particularly among men (SIR 40.8 per 100 000 inhabitants). This population has many factors that have been associated with SC such as poverty, a high rural population (32%), poor sanitary conditions in 43% of houses^[15], high prevalence of smokers (37.4%), high alcohol consumption (alcohol dependence in the Chilean population varies from 7.2% to 14.1% among low and high socioeconomic groups and from 5.0% to 17.6% among females and males respectively)^[16]; low daily consumption of fruits and vegetables (32.1%)^[17]; and high prevalence of *Helicobacter pylori* (*H pylori*) infection, especially among young people^[18].

We could not demonstrate an independent effect of race in the incidence of SC among men; but, for women,

Mapuche ancestry was a significant risk factor (RR: 2.2, 95% CI: 1.2-3.7). Similarly low schooling was a stronger risk factor among women (RR: 4.4 and 1.6 for women and men, respectively) and the highest male/female ratio of 7.5 occurred among people with greater schooling, suggesting that behavioral or environmental factors preferentially protect women of Hispanic origin and with more years of education. In the 2003 National Health Survey of Chile, more educated women had significantly better nutritional indicators than men of high or low educational level and women of low educational level, with body mass index of 25.0 *vs* 27.8, 26.1 and 28.0, respectively^[19]. This better nutritional status is associated with a higher intake of fruits and vegetables among these women, a protective factor for gastric cancer^[20]. Also, the 2006 Quality of Life National Survey showed that women added salt to the meals before eating less frequently than men (8.5% and 10.9%, respectively)^[17]. In the population, as well as in our series, smoking and alcohol consumption were less frequent in women than men. Interaction of smoking and drinking has been demonstrated to play a role in SC^[21]. Plus, in Chile, *H pylori* infection was also 10% lower among women than men^[18]. These environmental factors may interact with susceptibility factors, such as alcohol dehydrogenase polymorphisms^[22-24], to explain the predominance among men and also the higher frequency of this cancer in the

Table 2 Clinical characteristics of the stomach cancer cases entered in the population-based cancer registry of Valdivia 1998-2002 (n = 529)

Characteristic	Cases	Total (%)	Males (%)	Females (%)	P-value sex diff.
Sign and symptoms at diagnosis					
Weight loss	294	55.6	61.1	43.3	< 0.001
Epigastric pain	285	53.9	57.0	47.0	0.03
Gastrointestinal bleeding	108	20.4	21.4	18.3	0.42
Vomiting	106	20.0	20.8	18.3	0.50
Abdominal distension	83	15.7	14.8	17.7	0.40
Palpable epigastric mass	56	14.7	12.9	19.2	0.016
Ascites	51	13.4	13.3	13.5	0.97
Supraclavicular adenopathy	31	8.5	9.7	5.1	0.16
Main detection source					
Histological studies ¹	404	76.4	81.3	65.2	< 0.001
Radiological diagnosis	25	4.7	4.9	4.3	0.74
Clinical or autopsy	39	7.3	7.2	7.9	0.75
Only death certificate	61	11.5	6.6	22.6	< 0.001
Duration of symptoms ²					
< 3 mo	126	32.9	35.9	24.2	0.033
3 to 6 mo	98	25.6	25.4	26.3	0.86
> 6 mo	159	41.5	38.7	49.5	0.06
Main diagnostic workout					
Gastric endoscopy	412	79.4	84.6	67.7	< 0.001
Gastric biopsy	401	75.8	80.8	64.6	< 0.001
Ecography	191	36.1	37.8	32.3	0.22
Computed tomography	114	21.6	22.7	18.9	< 0.001
Staging TNM					
Stage I	9	1.7	2.2	0.6	0.19
Stage II	20	3.8	2.5	6.7	0.02
Stage III	53	10.0	10.4	9.1	0.65
Stage IV	297	56.1	58.6	50.6	0.09
Not determined	150	28.4	26.3	32.9	0.12
Histological type					
Tubular adenocarcinoma	148	36.0	35.2	38.3	0.56
Tubulopapillary adenocarcinoma	35	8.5	7.6	11.2	0.25
Papillary adenocarcinoma	11	2.7	2.0	4.7	0.14
Mucinous adenocarcinoma	11	2.7	2.3	3.7	0.43
Undefined adenocarcinoma	83	20.2	22.4	14.0	0.06
Signet ring cell carcinoma	77	18.7	18.1	20.6	0.57
Non Hodgkin lymphoma	6	1.5	1.6	0.9	0.60
Neuroendocrine carcinoma	4	1.0	0.7	1.9	0.27
Other carcinoma	36	8.8	9.5	6.5	0.35
Tumor location					
Body	57	10.8	11.5	9.1	0.42
Fundus	158	29.9	33.7	21.3	0.004
Antrum	122	23.1	21.9	25.6	0.35
All stomach	33	6.2	6.8	4.9	0.39
Unknown	159	30.1	26.0	39.0	0.003
Habits					
Tobacco use	346	44.8	51.4	29.1	< 0.001
Alcohol use	338	61.2	73.6	31.3	< 0.001

¹Includes 3 cases diagnosed based on a biopsy of metastasis; ²Time between first symptoms and diagnosis.

Mapuche areas of southern Chile^[18].

In this population-based study only 10.6% of SC survived the 5-year period following the detection of SC. When cases detected by death certificate only were included, the 5-year survival dropped to 9.6% (95% CI: 6.9-12.3). Previous studies based on cases detected at the hospital, reported higher survival rates of 12% to 48.9%^[25-27], probably due to a selection bias created at hospital admission, when cases in the advanced stages of the disease who will not benefit from medical care are referred to palliative care units. The mean age of SC in our series was similar to that reported by European population-based cancer registries^[28,29], and was 10 years

greater than the mean age reported in hospital-based survival studies. The 5-year relative survival rate, adjusted for the life expectancy of the population, was 12.3%, half that reported in population registries in North America^[30] and Europe^[31], where the survival rates are between 20.1% and 25.6%. Main risk factors of this poor survival were either clinical (palpable tumor, ascites, hepatitis) or related to the tumor characteristics (stage, histological type, metastasis, nodes); there were no significant social determinants of survival. This underlines the relevance of the advanced stage at consultation of most cases. When a gastrectomy with the intention to cure was undertaken the 5-year specific

Table 3 Factors associated with SC survival. Valdivia 1998-2002. Kaplan-Meier (*n* = 445 cases). Univariate analyses

Variable	<i>n</i> (%)	3-yr survival		5-yr survival		<i>P</i> -value 5-yr survival
		%	95% CI	%	95% CI	
Sex						
Female	120 (27.0)	20.3	13.0-27.6	12.9	6.7-19.1	-
Male	325 (73.0)	13.4	9.7-17.1	9.8	6.5-13.1	0.56
Age (yr)						
< 55	81 (18.2)	21.0	12.1-29.9	17.3	9.1-25.5	0.037
55-79	300 (67.4)	15.5	11.3-19.7	9.9	6.4-13.4	0.006
> 80	64 (14.4)	6.3	0-12.8	4.2	0-9.7	-
Ethnic group						
Mapuche ¹	76 (17.1)	7.3	1.2-13.4	4.4	0-9.2	-
Hispanic	369 (82.9)	16.9	13.0-20.8	11.9	8.5-15.3	0.02
School years						
0 to 8	348 (83.6)	9.1	6.0-12.2	6.4	3.7-9.1	-
> 8	68 (16.4)	19.7	10.2-29.3	8.9	2.0-15.8	0.08
Home						
Urban	248 (57.1)	18.7	13.8-23.6	12.9	8.6-17.2	0.006
Rural	186 (42.9)	10.6	6.1-15.1	8.2	4.1-12.3	-
Sign and symptoms at diagnosis						
Supraclavicular adenopathy						
Yes	28 (8.0)	0	-	0	-	-
No	321 (92.0)	18.6	14.3-22.9	13.8	9.9-17.7	0.00018
Palpable mass						
Yes	52 (14.4)	8.7	1.0-16.4	6.2	0-13.1	-
No	310 (85.6)	17.8	13.5-22.1	13.0	9.2-16.8	0.00001
Ascitis						
Yes	47 (13.0)	0	-	0	-	-
No	315 (87.0)	18.9	14.5-23.3	13.8	9.9-17.0	0.000002
GI bleeding						
Yes	101 (22.7)	20.1	12.2-28.0	13.7	6.9-20.5	0.87
No	344 (77.3)	13.8	10.1-17.5	9.7	6.5-12.9	-
Vomiting						
Yes	100 (22.5)	10.3	4.3-16.3	6.2	1.4-11.0	-
No	345 (77.5)	16.8	12.8-20.8	11.9	8.4-15.4	0.046
Weight loss						
Yes	277 (62.2)	13.6	9.5-17.7	10.0	6.4-13.6	0.45
No	168 (37.8)	18.1	12.2-24.0	11.5	6.5-16.5	-
Abdominal distension						
Yes	78 (17.5)	11.5	4.4-18.6	7.7	1.8-13.6	0.13
No	367 (82.5)	16.1	12.3-19.9	11.2	7.9-14.5	-
Pain						
Yes	271 (60.9)	19.0	14.2-23.8	14.5	10.2-18.8	0.14
No	174 (39.1)	9.6	5.2-14.0	4.6	1.4-7.8	-
Months with symptoms						
< 3	117 (32.3)	14.9	8.3-21.5	9.3	3.9-14.7	-
3 to 6	95 (26.2)	17.6	9.9-25.3	14.2	7.1-21.3	0.32
> 6	150 (41.4)	16.6	10.5-22.7	13.7	8.1-19.4	0.30
Gastrectomy						
Yes	128 (28.8)	44.8	36.0-53.6	33.6	25.1-42.1	0.0000001
No	317 (71.2)	3.5	1.4-5.6	1.3	0-2.6	-
Surgical intention						
Curative	89 (42.4)	50.4	39.9-60.9	38.6	28.3-48.9	0.0000001
Palliative	121 (57.6)	14.4	5.8-23.0	10.4	2.6-18.2	-
Lauren class						
Intestinal	220 (59.1)	21.0	15.5-26.5	14.6	9.8-19.4	0.0000003
Diffuse	152 (40.9)	11.2	6.1-16.3	7.0	2.9-11.1	-
Tumor						
Localized	325 (91.0)	20.0	15.6-24.4	14.6	10.6-18.6	0.004
All stomach	32 (9.0)	0	-	0	-	-
Size						
< 4 cm	16 (12.8)	67.0	43.3-90.7	60.0	35.1-84.9	-
4 to 9.9 cm	71 (56.8)	48.3	36.3-60.3	35.5	23.9-47.1	0.161
> 10 cm	38 (30.4)	29.0	15.6-43.4	21.1	8.1-34.1	0.006
Depth						
Mucosa	9 (7.1)	100	-	100	-	-
Muscle/subserosa	7 (5.6)	85.7	59.8-100	71.4	37.9-100	0.14
Serosa	110 (87.3)	38.2	29.0-47.5	27.2	18.6-35.8	0.003

Lymphatic invasion stage						
0	21 (17.8)	94.9	85.1-100	77.1	57.3-96.9	-
I	36 (30.5)	55.4	39.1-71.7	40.2	23.8-56.6	0.008
II	33 (28.0)	38.3	21.5-55.1	25.3	10.1-40.5	0.0005
III	28 (23.7)	10.7	0-22.2	10.7	0-22.2	0.00001
Metastasis						
0	185 (47.0)	30.6	23.5-37.4	22.2	16.0-28.4	-
1	209 (53.0)	2.5	0.3-4.7	1.5	0-3.2	0.0000001
TNM						
I	9 (2.1)	100	-	85.7	59.8-100	-
II	18 (4.1)	77.3	57.7-96.9	65.4	42.9-87.9	0.24
III	53 (12.1)	49.2	35.5-62.9	32.2	19.1-45.3	0.011
IV	281 (64.0)	3.0	1.0-5.0	2.2	0.4-4.0	0.00003
Unknown	78 (17.8)	12.3	4.9-19.7	3.8	0-8.3	0.00007

¹Native American Indian residents of southern Chile.

Table 4 Multivariate analysis of prognostic factors of stomach cancer survival population-based registry of Valdivia (Kaplan-Meier)

	OR	95% CI	P-value
Staging TNM			
Stage I	1.0		
Stage II	2.77	0.3-23.8	0.35
Stage III	6.87	0.9-50.6	0.06
Stage IV	22.53	3.1-165.2	0.002
Unknown	23.35	3.1-173.6	0.002
Lauren classification			
Intestinal	1.0		
Diffuse	1.68	1.3-2.2	< 0.001
Metastasis			
No	1.0		
Yes	1.58	1.1-2.3	0.019
Supraclavicular adenopathy			
No	1.0		
Yes	1.69	1.0-2.8	0.037
Palpable tumor			
No	1.0		
Yes	2.04	1.4-3.1	0.001
Hepatitis or ascites			
No	1.0		
Yes	2.51	1.6-3.9	< 0.001

survival was 38.6%, which is comparable to reports from Europe and North America in either population-based or hospital-based registries: 45% in Spain^[32], 46.1% in Japan^[33], 29.7% in Florence^[29] and 32.6% in Côte d'Or^[34]. We found that the stage of the disease was the main prognostic factor for survival as has been reported by others^[26,27,32,33]. Thus, in our population the high incidence of SC was aggravated by a very late diagnosis of the disease. 11.5% of cases were never recognized by the medical system and were discovered based on death certificates, while another 20% of cases were inoperable at their first medical consultation. Only 5.5% of cases were found in stages I or II at the moment of diagnosis, lower than what has been reported in other population-based cancer registries in places with no screening programs such as Florence (36.7% of cases in stages I or II)^[29] and Changle, China (30.9% in stages I or II)^[35]; in Florence, where methods are the same as those in our study, a higher 5-year relative survival was reported than in our series (22.7%, 95% CI: 20.5%-24.9% and 12.3%, 95% CI: 9.1-16.1, respectively). Most cases presenting at

earlier stages, stage I or II, were under age 54 in men and under age 68 in women, suggesting that in men the disease is initiated earlier or evolves faster (data not presented in the tables). Time elapsed between the onset of symptoms and medical attention, 8.4 mo, was twice as high as that reported in La Coruña, Spain^[32]. Most cases (55%), exceeded the current Chilean standard of less than 45 d between first consultation and diagnosis, and 44% of operated cases exceeded the 30 d interval between diagnosis and treatment. Thus late consultation and slow medical management contributed to the high mortality of SC in this series.

In our series, there were 0.7 proximal tumors for each distal tumor, half of that described in industrialized countries such as the USA 1.46^[36] or Canada 1.5^[37]. Distal cancers, the majority in our series, are mostly associated with *H pylori* and poverty, and have a somewhat better prognosis than proximal cancers, so that the biological characteristics of the tumor did not provide a plausible explanation for our poor survival rates.

Screening of SC based on endoscopy and radiography has been shown to reduce the mortality rate in Japan^[38] but not in Chile^[39,40]. In mid 2006, a nationwide screening program was initiated in Chile, offering endoscopic examination to patients over 40 years with dyspeptic symptoms. The usefulness of symptoms as selection criteria for endoscopy has recently been discussed by Maconi^[41] because symptoms of early stage SC are highly nonspecific while warning symptoms, such as a palpable abdominal mass, represent an advanced stage of the disease. Others are proposing a combination of serological tests to screen for gastric atrophy, *Helicobacter*^[42] plus alcohol dehydrogenase^[24], followed by gastroscopy of cases that screen positive. Such a strategy would allow screening of a broad population in a short time to be followed by more invasive techniques in a much smaller group, estimated as 12% in Chile^[42].

SC has a high incidence rate and a poor prognosis in the province of Valdivia. Main factors associated with poor survival were delays in obtaining medical care: time taken to seek medical care, time to be diagnosed and time to receive medical treatment; once medical care was obtained survival was comparable to other series. Current efforts to shorten these times with greater use of gastric endoscopy may improve this situation.

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COMMENTS

Background

Stomach cancer (SC) has been the main cancer killer in the Chilean population since the 1950s. Despite important socioeconomic development of the country and improvements in health indicators, SC mortality has not decreased. To date, there are no population-based studies of SC incidence and survival in Chile which would illuminate the causes behind the high SC mortality, particularly among men. The cancer registry of Valdivia is currently the only population-based cancer registry in Chile included in the International Agency for Research on Cancer reports and is one of 10 cancer registries in Latin America. This is the first report of SC survival in the Chilean population.

Research frontiers

There have been few studies of the real magnitude of the SC problem and the characteristics of the patients who survive or die from this cancer.

Innovations and breakthroughs

The most innovative product is the exact measurement of the incidence and survival of SC using the most up-to-date statistical methods which provide data which is easily comparable among populations.

Applications

This report represents a baseline of the SC situation in Valdivia and will permit evaluation of future interventions aimed to control SC. The methods presented here can be used to analyze any other cancer covered by a cancer registry.

Terminology

Incidence rate: calculated from the new occurrences of primary SC in the whole area divided by its population in the study period. Standardized incidence rate: the incidence rate adjusted by the age structure of a theoretical population, the world population, to permit direct comparisons between populations of diverse age structure. Specific survival rate: the number of cancer cases that are alive at the end of the study period divided by the person-time of cases over the period at risk of dying of SC. Relative survival rate: the specific survival rate adjusted by the life expectancy of the baseline population.

Peer review

This report presents invaluable data on SC incidence and SC survival in an area at high risk of SC in a middle developing country of Latin America. It provides information about the clinical presentation of SC cases, their socio-demographic characteristics and risk factors and prognostic factors of survival. The results indicate that a late stage at diagnoses is by far the principal explanatory factor of poor survival of SC in the area.

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