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Long-term prognosis of gastric cancer in a European country: a population-based study in Florence (Italy). 10-year survival of cases diagnosed in 1985–1987

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Abstract

This paper analysed, in a population-based series of 1976 gastric cancers diagnosed in Florence (Italy), from 1985 to 1987, the relationship between prognostic variables (demographic, clinical and pathological) and 10-year survival rates. Gastric cancer was mostly detected in elderly patients (mean age: 70.5 years) and at advanced stages (i.e. approximately 50% of the patients could not undergo radical surgery). Ten-year observed survival was 12.1% (95% confidence interval (CI): 10.6–13.6%) for the whole series and 20.8% (95% CI: 18.3–23.3%) for resected cases; relative survival was, respectively, 20.9% (95% CI: 18.4–23.4%) and 32.0% (95% CI: 28.1–35.9%). Ten-year relative survival was 86% for stage IA (95% CI: 73–99%) and 67% for stage IB (95% CI: 52–82%). Multivariate analysis showed a significantly better prognosis in females and a significantly worse prognosis in patients aged 65 years or more (reference: $\leqslant$59 years). In addition, an independent prognostic effect was observed for pT in the resected cases (reference: pT3; pT1: RR = 0.47, 95% CI: 0.34–0.64; pT2 = 0.71, 95% CI: 0.58–0.87; pT4: RR = 2.02, 95% CI: 1.49–2.75), pN (reference: pN0; pN1: RR = 2.13, 95% CI: 1.70–2.68; pN2–3: RR = 3.14, 95% CI: 2.42–4.07; pN+ no. nodes involved unspecified: RR = 4.26, 95% CI: 3.11–5.83) and surgical margin involvement (reference: not involved; involved: RR = 1.36, 95% CI: 1.08–1.72). In addition, the stage, after adjustment for age, gender and surgical margin involvement, showed a strong independent prognostic value (reference: stage II; IA: RR = 0.37, 95% CI: 0.25–0.57; IB: RR = 0.70, 95% CI: 0.50–0.98; IIIA: RR = 1.80, 95% CI: 1.40–2.33; IIIB: RR = 2.82, 95% CI: 2.14–3.72; IV: RR = 3.29, 95% CI: 2.36–4.59). In conclusion, on the basis of a large population-based series, our results confirm the prognostic effect on long-term gastric cancer survival of pathological and demographic variables. In addition, the study shows that Italy had a relatively good, long-term survival when diagnosis was performed at early stages. However, only a few cases were diagnosed at stages when cure by radical surgery is more likely (i.e. stage I accounted for approximately 20% of the resected cases and less than 10% of all incident cases).

Keywords: Gastric cancer; Survival; Population-based; Stage; Prognostic factors; Demographic variables

1. Introduction

Among Western countries, Florence and the neighbouring area of Romagna have relatively high incidence rates of gastric cancer in both sexes: age-adjusted rates (world population, period 1988–1991) were 36.3/100 000 in males and 15.9/100 000 in females [1]. Despite the recent decline in incidence [1,2] and mortality, gastric cancer is still the second most common cancer in males and the third most common cancer in females, thus remaining a major public health problem.

Substantial differences in gastric cancer prognosis between Western countries and Japan have already been reported. By the middle of the 1980s, in population-based series, 5-year relative survival ranged between 18 and 19% for pooled databases of European [3] or US Cancer Registries [4] and 47% for the Osaka Cancer Registry [5]. In the Japanese surgical series, 5-year overall survival rates were 50% or higher [6], 89% for early and 46% for advanced carcinomas, respectively

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[7]. A higher incidence of early gastric cancer, more aggressive surgical procedures and accurate pathological staging have been advocated to explain the better gastric cancer prognosis in Japanese patients [6,7]. Moreover, different criteria for the histological diagnosis of early gastric cancer adopted by Japanese and Western pathologists may also contribute to the difference in incidence and prognosis of gastric cancer [8]. The differences in survival rates between Japan and Western countries were largely reduced when patients undergoing similar surgical treatment [9], or showing similar prognostic characteristics were compared, and when a similar classification of tumour stage was used [10].

This study aimed to evaluate the 10-year survival in a population-based series of patients affected by invasive gastric cancer, diagnosed in Florence in the middle of the 1980s, considering the effects of demographic, clinical and pathological variables.

2. Patients and methods

Between 1985 and 1987, 2240 new cases of GC (ICD-9, 151) were registered by the population-based Tuscany Cancer Registry (TCR) in Florence (1 185 000 inhabitants — 1991 Census). 264 cases (approximately 12%) were excluded for the following reasons: gastric cancer was identified by death certificate or detected at autopsy (8.5%), gastric cancer was diagnosed as a second primary cancer (1.2%), cases were wrongly coded as gastric cancer (0.8%), patients were unknown to the municipality of residence (1.2%).

For the 1976 cases included in the survival analysis, the life status at 31 December 1997 was assessed through a computerised linkage with the Mortality Registry of Tuscany (RMR). The RMR collects the death certificates for all causes of the individuals residing in this area who died in Tuscany or in other Italian regions. For unlinked cases, the Register Office of the municipality of residence was consulted. At the end of the follow-up period, 1719 subjects (87.0%) were deceased, 255 (12.9%) were still alive and only 2 (0.1%) could not be traced.

The index date for the calculation of survival was the date of incidence of the cases as recorded by the TCR (date of the first diagnosis of gastric cancer: i.e. the first hospital admission or the first pathology report for gastric cancer).

The observed and relative survival curves were obtained using the life-table method [11]. Relative survival was calculated by dividing the observed survival rate in cancer patients by that expected for a group of subjects in the general population similar to these patients in gender, age and period. Observed survival takes into account the overall mortality with no reference to the cause of death. Relative survival considers the differences among patients in the risk of dying from other causes and more accurately describes mortality attributable to the studied disease, without requiring information on the actual cause of death of each patient. Survival curves were compared using the likelihood ratio test.

The effect of clinical and pathological variables on observed survival was assessed by the Cox model [12]. The Cox model provides univariate and multivariate estimates of risk of dying (relative risk, RR) for subjects in a given category of a variable in comparison with subjects in the reference category, during the follow-up period. Moreover, a multivariate relative survival analysis was performed by the method described by Hakulinen [13], with the aim of including the effect of the mortality risk of the general population of the area on the prognostic value of gender and age. The significance of each variable was tested by the likelihood ratio test. The significance of each level of the variables was evaluated by the 95% confidence intervals (95% CI) of the RR.

The clinical and pathological parameters analysed for all patients were gender, age, site, histological type and grading. In addition, type of surgery, depth of invasion into the gastric wall, nodal status (the number of regional lymph nodes examined and the number of those invaded) and the status of surgical margins were analysed for the resected cases. The pTNM and the stage were coded according to the 1997 revised classification of malignant tumours [14]. Here, the spread to the regional lymph nodes (pN) was categorised on the basis of the number of nodes involved instead of their anatomical localisation, as was the case in the previous TNM editions. Furthermore, according to the more recent pTNM revision, the assessment of pN requires a number of 15 or more nodes to be examined. In our data-set (diagnosed in 1985–1987), the number of nodes examined was not specified in many cases. We applied the 1997 pTNM classification to the whole series of resected cases, with no reference to the number of nodes examined, but we performed analyses for cases with adequate pN staging (15 or more nodes examined) and for all resected cases (despite the number of nodes examined) separately.

The cancer site was divided into four groups: upper, medium and lower third, multiple sites or whole stomach involvement and unspecified site. The surgical treatment was classified into three groups: total, subtotal and unspecified gastrectomy. The histological type and grading were grouped on the basis of the following groups, according to the World Health Organization (WHO) classification: poorly differentiated carcinomas, moderately differentiated adenocarcinomas, well differentiated adenocarcinomas, mucinous adenocarcinomas and signet-ring adenocarcinomas.

Table 1
Florence, 1985–1987, gastric cancer patients stratified according to the information concerning pathological staging

Patients	Cases *n* (%)
All patients	1976 –
Patients with gastrectomy	1017 (51.5[a])
Depth of invasion specified	841 (82.7[b])
Nodal involvement specified	791 (77.8[b])
Number of nodes removed specified	385 (37.9)[b]
Adequate staging according to 1997 pTNM[c]	259 (25.5[b])

[a] Percentage of all patients.
[b] Percentage of patients with gastrectomy.
[c] Patients with depth of invasion specified, number of nodes involved specified and number of nodes removed $\geqslant 15$.

3. Results

Among the 1976 gastric cancer cases included in this study (mean age: 70.5 years, standard deviation (S.D.): 11.0 years), 62.3% were diagnosed at endoscopy and 72.5% had a histologically confirmed diagnosis. 51.5% had a total or subtotal gastrectomy, 9.5% had a laparotomy or palliative surgery and 39.0% did not receive any surgical treatment. The mean age was 67.8 years (S.D. = 11.1) for the resected cases, 68.2 years (S.D. = 10.5) for those with by-pass or explorative surgery and 74.7 years (S.D. = 9.7) for those not operated upon (*t*-test: $P < 0.001$). The number of lymph nodes examined was specified in 37.9% of the resected patients, (mean: 18.8, S.D.: 7.2; range: 10–60 nodes). Pathological information allowing tumour staging according to the 1997 pTNM rules was available in only 25.5% of the resected cases (Table 1).

The percentage of resected cancers progressively decreased with age, whereas it was similar among males and females ($P < 0.001$ and $P = 0.336$, respectively; Table 2).

In the whole series, both observed and relative survival rates were significantly higher in females ($P = 0.002$ and $P < 0.001$, respectively) and decreased progressively in the subsequent age groups ($P < 0.001$). In comparison to the reference categories, a multivariate relative survival analyses (model: gender, age, spread of disease, surgical treatment) displayed a significantly better prognosis in females (RR: 0.83, 95% CI: 0.74–0.93; reference: males) and a significantly worse prognosis in patients aged 65 years or more (60–64 years = RR: 1.14, 95% CI: 0.92–1.40; 65–69 years = RR: 1.26, 95% CI: 1.03–1.54; 70–74 years = RR: 1.21, 95% CI: 1.00–1.45; 75–79 years = RR: 1.25, 95% CI: 1.04–1.51; $\geqslant 80$ years = RR: 1.46, 95% CI: 1.20–1.77; reference: $\leqslant 59$ years). The differences in the 10-year observed and relative survival rates by gender ($P = 0.001$ and $P = 0.03$, respectively) and age-groups ($P < 0.001$) persisted among the resected cases.

The observed survival was lower at 10 years than at 5 years, especially for the resected cases (5-year survival was, respectively, 17.7% (95% CI: 16.0–19.4%), and 29.7%, 95% CI: 26.8–32.6%). The differences between 5 and 10 years were largely reduced when comparing the relative survival rates ((5-year survival was, respectively, 22.7% (95% CI: 20.5–24.9%), and 35.9% (95% CI: 32.4–39.4%, respectively). Operative mortality (death during surgery or within 30 days) was 8.0 (81/1017).

Fig. 1 shows the 10-year stage-specific relative survival curves ($P < 0.001$) for all of the resected patients: survival was 86% (95% CI: 73–99%) for stage IA disease, 67% (95% CI: 52–82%) for stage IB, 46% (95% CI: 33–58%) for stage II, 19% (95% CI: 12–26%) for stage IIIA, 5% for stage IIIB and for stage IV (95% CI: 0–9% and 0–12%, respectively). In general, the pattern

Table 2
Florence 1985–1987, patients stratified for gender and age-groups[a]

	No. cases *n* (%)	Resected cases (%)	10-year survival (%)			
			All cases		Resected cases	
			Observed survival (95% CI)	Relative survival (95% CI)	Observed survival (95% CI)	Relative survival (95% CI)
All patients	1976 (100.0)	51.5	12.1 (10.6–13.6)	20.9 (18.4–23.4)	20.8 (18.3–23.3)	32.0 (28.1–35.9)
Gender						
Males	1171 (59.3)	50.6	10.3 (8.5–12.1)	18.1 (15.0–21.2)	17.9 (16.8–23.0)	28.4 (23.4–33.4)
Females	805 (40.7)	52.8	14.6 (12.1–17.1)	24.7 (20.5–28.9)	24.9 (20.7–29.1)	36.7 (30.5–42.9)
Age groups (years)						
$\leqslant 59$	316 (16.0)	69.9	29.8 (20.9–38.6)	32.3 (22.7–41.8)	40.0 (33.4–46.6)	43.2 (36.1–50.3)
60–64	221 (11.2)	60.2	17.9 (12.5–23.3)	22.0 (15.3–28.6)	27.1 (19.4–34.8)	32.9 (23.5–42.3)
65–69	246 (13.3)	57.6	12.6 (8.1–17.1)	17.1 (11.0–23.2)	19.9 (13.4–26.4)	26.5 (17.8–35.2)
70–74	383 (19.4)	54.0	9.8 (6.3–13.3)	16.3 (10.4–22.2)	15.8 (10.7–20.9)	26.0 (17.6–34.4)
75–79	379 (19.2)	47.8	6.5 (3.6–9.4)	15.4 (8.8–22.0)	10.5 (5.9–15.1)	24.4 (13.5–35.0)
$\geqslant 80$	413 (20.9)	29.8	1.7 (0.1–3.3)	9.4 (0.7–18.1)	4.7 (1.1–8.3)	20.1 (2.5–37.7)

95% confidence intervals (95% CI) in parenthesis.
[a] Total number of cases and percentage of resected cases. 10-year observed and relative survival for all cases and for resected cases.

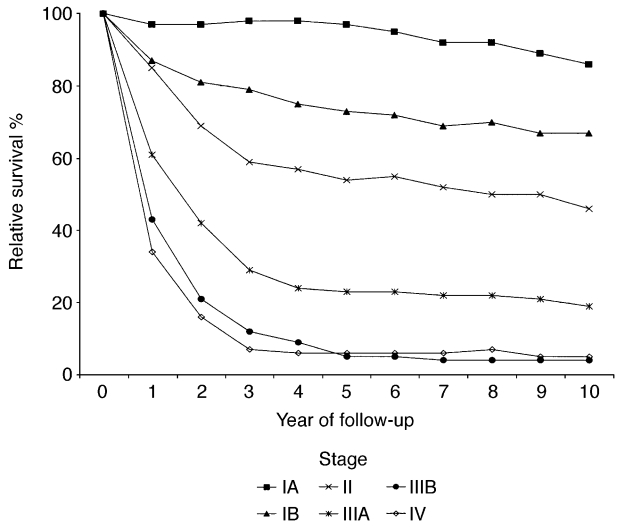

Fig. 1. Florence 1985–1987, gastric cancer: relative survival according to 1997 pTNM stage (all resected patients regardless of the number of lymph nodes removed).

of survival curves was similar among cases with 15 or more nodes removed (data not shown).

Early gastric cancer (EGC, carcinomas confined to the gastric mucosa and submucosa, without taking into account the nodal metastases) amounted to 11.2%, 78% of them (89/114) were node-negative. Ten-year relative survival was 88% (95% CI: 69–100%).

An independent prognostic effect on 10-year survival has been proved for pT and pN (Table 3) and for the stage (Table 4). The prognostic value was more evident in cases with adequate pN staging (according to the 1997 pTNM rules), but a strong impact was also observed when applying the 1997 pTNM classification to the whole series of resected cases. Cases with a number of nodes examined unspecified or inadequate for 1997 pTNM rules were older than cases with 15 or more nodes examined (mean age: 68.9 and 64.4 years, respectively; $P<0.001$) and showed a lower 10-year relative survival (34.1 and 31.1%, respectively; $P< 0.05$). Stratifying by pN, 10-year relative survival of cases with a number of nodes examined unspecified or inadequate was similar for pN0 (68.1%, 95% CI: 57.5–78.7%) and lower for pN1 (19.7%, 95% CI:12.1–27.3%) and pN2–3 categories (2.5%, 95% CI: 0.0–7.5%).

The multivariate analysis showed a worse prognosis for cases with histologically confirmed involvement of surgical margins, whereas type of surgery and histological type did not show independent prognostic effects (Table 5). Upper third cases showed the worse prognosis, but this was not significant.

4. Discussion

In the unselected series analysed in this study, gastric cancer was a disease of elderly patients (mean age: 70.5 years) and mostly detected at advanced stages (approximately 50% had surgical resection; 20% of resected cases were stage IA or IB and approximately 11% EGC). Ten-year relative survival was 21% for the whole series and 32% for patients undergoing surgical treatment (86% for stage IA, 67% for stage IB, 46% for stage II, 19% for stage IIIA and 5% for stages IIIB and IV).

The results of this study confirmed that in Western countries, gastric cancer is a fatal disease, often diagnosed at an advanced stage. In the EUROCARE study,

Table 3
Florence, 1985–1987, resected patients stratified according to the number of lymph nodes removed: prognostic value of depth of invasion and nodal involvement[a]

	⩾15 lymph nodes removed (total *n* 259)			All resected cases (total *n* 1017)		
	Cases (%)	10 years (95% CI)	Adjusted RR[b] (95% CI)	Cases (%)	10 years (95% CI)	Adjusted RR[c] (95% CI)
Depth of invasion						
pT1	30 (11.6)	88.3 (68.8–100.0)	0.33 (0.15–0.73)	114 (11.2)	77.6 (65.3–89.8)	0.47 (0.34–0.64)
pT2	58 (22.4)	49.2 (32.0–66.4)	0.74 (0.51–1.08)	231 (22.7)	41.5 (32.6–50.4)	0.71 (0.58–0.87)
pT3[d]	157 (60.6)	19.3 (11.5–27.1)	1.00 –	447 (44.0)	18.2 (13.5–22.9)	1.00 –
pT4	14 (5.4)	0.0 –	2.40 (1.35–4.26)	49 (4.8)	6.5 (0.0–15.4)	2.02 (1.49–2.75)
pTx	–	– –	– –	176 (17.3)	26.8 (17.5–36.0)	1.13 (0.86–1.47)
Nodal involvement						
pN0[c]	73 (28.2)	70.9 (55.0–86.8)	1.00 –	264 (26.0)	68.9 (60.0–77.8)	1.00 –
pN1	89 (34.4)	32.2 (19.9–44.5)	1.66 (1.07–2.59)	283 (27.8)	24.1 (17.5–30.7)	2.13 (1.70–2.68)
pN2-3	97 (37.4)	7.4 (1.0–13.8)	3.60 (2.30–5.63)	161 (15.8)	5.6 (1.1–10.1)	3.14 (2.42–4.07)
pN+, no. unspecified	–	– –	– –	83 (8.2)	14.3 (4.7–23.9)	4.26 (3.11–5.83)
pNx	259	– –	– –	226 (22.2)	20.6 (13.0–28.2)	2.45 (1.85–3.26)

[a] Ten-year relative survival rates (10 years). Multivariate relative risk of death (adjusted RR) provided by the Cox model, based on 10-year observed survival. 95% confidence intervals (95% CI) in parentheses.

[b] Model: gender, age, type of surgery, pT and pN (variables with an independent prognostic value).

[c] Model: gender, age, involvement of surgical margins, pT and pN (variables with an independent prognostic value).

[d] Reference category.

Table 4
Florence, 1985–1987, resected patients stratified according to the number of lymph nodes removed: prognostic value of stage[a,d]

	⩾15 lymph nodes removed (total no. 259)			All resected cases (total no. 1017)		
	Cases (%)	10 years (95%CI)	Adjusted RR[b] (95%CI)	Cases (%)	10 years (95%CI)	Adjusted RR[c] (95%CI)
Stage						
IA	26 (10.1)	94.1 (73.9–100.0)	0.25 (0.10–0.62)	89 (8.7)	86.1 (72.9–99.3)	0.37 (0.25–0.57)
IB	27 (10.4)	68.8 (43.3–94.3)	0.68 (0.35–1.32)	95 (9.3)	66.6 (51.6–81.9)	0.70 (0.50–0.98)
II[3]	42 (16.2)	45.0 (24.3–65.7)	1.00 –	131 (12.9)	45.6 (33.1–58.1)	1.00 –
IIIA	72 (27.8)	26.8 (19.3–39.7)	1.52 (0.97–2.39)	199 (19.6)	19.2 (12.0–31.2)	1.80 (1.40–2.33)
IIIB	76 (29.3)	5.7 (0.0–12.2)	3.38 (2.16–5.29)	135 (13.3)	4.5 (0.1–8.9)	2.82 (2.14–3.72)
IV	16 (6.2)	0.0 –	5.38 (2.82-10.03)	61 (6.0)	4.9 (0.0–11.7)	3.29 (2.36–4.59)
Unspecified	–	– –	– –	307 (30.2)	22.5 (15.9–29.1)	2.07 (1.60–2.68)

[a] Ten-year relative survival rates (10 years). Multivariate relative risk of death (Adjusted RR) provided by the Cox model, based on 10-year observed survival. 95% confidence intervals (95% CI) in parentheses.
[b] Model: gender, age, type of surgery and stage (variables with an independent prognostic value).
[c] Model: gender, age, involvement of surgical margins and stage (variables with an independent prognostic value).
[d] Reference category.

the European weighed relative survival was 21% at 5 years [15]. In most European countries, there was a slight improvement in prognosis between 1978 and 1989 [15]. Important differences were observed among European countries [15]. Survival was better in Germany, Austria, France, Spain and Italy. In contrast, it was lower in Denmark, England, Scotland and Poland. Differences in quality of care (i.e. perioperative mortality) and in the stage at diagnosis can partly explain the intercountry survival differences. A population-based study carried out in France [16] showed that, in the period 1984–1987, only 46% of cases received curative surgery and approximately 13% of patients were diagnosed with tumour confined to the gastric wall. Five-year relative survival after curative resection, excluding operative mortality, was 47%, and prognosis did not improved between 1976 and 1995. A similar percentage of patients who underwent resection was reported in a population-based series provided by the Rotterdam Cancer Registry [17]. In a British hospital series [18], the

Table 5
Florence, 1985–1987, all resected patients. Prognostic value of some clinical and pathological variables.[a]

	Cases (%) (total no. 1017)	10 years (95% CI)	Adjusted RR[b] (95% CI)
Surgical margins			
Negative[c]	348 (34.2)	36.0 (29.3–42.7)	1.00 –
Positive	112 (11.0)	5.5 (0.1–10.9)	1.36 (1.08–1.72)
Unspecified	557 (54.8)	35.0 (29.4–40.6)	0.98 (0.81–1.19)
Type of surgery			
Total gastrectomy[c]	294 (28.9)	22.3 (16.2–28.4)	1.00 –
Subtotal gastrectomy	535 (52.6)	38.5 (32.6–44.4)	0.89 (0.76–1.05)
Unspecified gastrectomy	188 (18.5)	30.4 (21.5–39.3)	1.04 (0.85–1.28)
Site			
Upper third	138 (13.6)	17.5 (9.3–25.7)	1.23 (0.90–1.68)
Medium third[c]	75 (7.4)	26.3 (13.6–39.0)	1.00 –
Lower third	382 (37.5)	37.0 (30.3–43.7)	0.97 (0.74–1.28)
Multiple	111 (10.9)	25.1 (14.3–35.9)	0.97 (0.70–1.34)
Unspecified	311 (30.6)	36.8 (29.1–44.5)	0.93 (0.69–1.25)
Histological type[d]			
Poorly differentiated ADK[2]	441 (43.4)	27.0 (21.5–32.5)	1.00 –
Moderately differentiated ADK[c]	244 (24.0)	36.4 (27.6–45.2)	0.85 (0.71–1.02)
Well differentiated ADK	63 (6.2)	48.6 (30.6–66.6)	0.85 (0.61–1.19)
Mucinous ADK	57 (5.6)	24.6 (9.4–39.8)	1.06 (0.78–1.44)
Signet-ring ADK	115 (11.3)	33.3 (22.4–44.2)	0.96 (0.75–1.22)

[a] 10-year relative survival rates (10 years). Multivariate relative risk of death (Adjusted RR) provided by the Cox model, based on 10-year observed survival. 95% confidence intervals (95% CI) in parentheses.
[b] RRs adjusted for variables with an independent prognostic value (gender, age, involvement of surgical margins, pT and pN).
[c] Reference category.
[d] 97 (9.5%) cases with an unknown morphology were excluded.

proportion of gastric cancer cases diagnosed in 1985–1989 with stage I disease was 26%, while that of patients with potentially curative resection amounted to 53%. In The Netherlands, a relative increase in the incidence of histological subtypes and subsites with the worst prognosis have been suggested to be partly responsible for the lack of improvement in gastric cancer survival [19]. In a large US data set collected in the 1980s and at the beginning of 1990s from hospital cancer registries, 5-year disease-free survival of gastric cancer was 26% [20] and 5-year relative survival of gastric cancer was 20% [21]. For 42% of patients, cancer-directed surgery was not reported [21], and only 17% of patients had stage I disease [20,21].

Comparison of survival in different gastric cancer series is affected by some potential biases (i.e. criteria of case selection, staging system, surgical procedure). Nevertheless, in our population-based data set, gastric cancer with limited extension showed relative survival rates quite similar to those reported in the German Gastric Cancer Study (the 5-year observed survival in the latter study was 86, 72 and 47%, respectively, for stage IA, IB and II disease) [22] and in a British hospital series (i.e. 5-year corrected survival rates of 87 and 65% for Stage I and II disease, respectively [18]. In contrast, prognosis was very different for more advanced stage disease (III and IV). In a French population-based study, stage-specific survival rates were similar to those reported in our study [16]. Differences in patient recruitment criteria (hospital versus population-based series) and inclusion/exclusion of perioperative mortality could, at least partly, explain the worse prognosis for patients with more advanced stage disease.

The higher incidence of cases with early stage disease, accounting for 40–60% of newly diagnosed tumours [23], due to an endoscopic screening policy, is one of the most important factors that have been proposed to explain the better gastric cancer prognosis in Japanese patients [6,7]. Screening programmes for asymptomatic patients were generally considered impractical or not justified in Western countries [18,23]. As a possible alternative, a policy of endoscopic monitoring of patients with dyspepsia, gastric ulcer, etc., has been suggested to be a practical way of diagnosing gastric cancer at an early stage [15,18].

With reference to the effect of clinico-pathological variables analysed in our study, multivariate analysis showed an independent prognostic value for surgical margins involvement, pT, pN and for stage. The role of pathological stage in gastric cancer prognosis is well established [24] and the 1997 pTNM classification of regional lymph node metastasis, based on the number of involved nodes, leads to an estimation of prognosis superior to the previous classification based on their localisation [22]. Our population-based study shows that the staging system based on the number of nodes involved had a strong prognostic value without taking into account the number of nodes examined. In our series diagnosed in 1985–1987, the main reason for the low percentage of resected cases that were adequately staged (25.5%) is that the number of nodes examined was rarely specified on the pathological report (before 1997, this information was not required in the pTNM rules). On the other hand, when specified, the number of examined nodes was $\geqslant 15$ in approximately 15 in 2/3 of cases (259/385), suggesting that, in our area, the TNM classification could be applicable for most patients.

The study did not detect an independent prognostic value for morphology, classified according to the WHO guidelines. This finding confirms the results of a recent French population-based study designed to assess the prognostic significance of four widely-used pathological classifications (WHO, Laurén, Ming and Goseki), suggesting an independent prognostic impact only for the Ming subtypes [25].

The study did not detect significant differences in survival by site; nevertheless the worse prognosis of the resected tumours that were located in the upper third is consistent with the results of previous studies, and explained by the more aggressive natural history of cancers in this part of stomach [16].

Differences in prognosis according to gender and age have been reported in previous studies [3,4,15,26]. Several hypotheses could explain these differences. Similar resection rates in both genders and a lower post-operative mortality in females, despite a higher median age, suggested that the excess of risk in males was related to underlying cardiovascular or pulmonary problems, reflecting the general shorter life expectancy in men [17]. However, some evidence suggests that, even if the stomach is not a target for sex hormones, receptors for these hormones may play a role in the prognosis of gastric cancer [27,28]. For the effect of age, clinico-pathological features of gastric cancer have been shown to differ between young and elderly patients and the survival rate after curative resection has also been reported to be lower in the elderly [29]. Furthermore, even if age alone was not a contraindication to surgery in gastric cancer patients, operative mortality is markedly increased and the resection rate decreased in the elderly [17], reflecting the increase in co-morbidities seen in these patients.

Ten-year survival was worse for patients aged 65 years or more and for males. The prognostic value of age and gender persisted after adjustment for stage and surgical treatment and considering the different effect of general mortality (as in the multivariate analysis based on relative survival). These results indirectly supported the hypothesis that the prognostic role of age and gender were, at least partly, related to the different aggressiveness of cancers and did not merely reflect differences in stage distribution or in life expectancy.

In conclusion, the independent prognostic value of pathological (staging parameters, surgical margins involvement) and demographic variables (age, gender) was confirmed. In addition, as in other Western countries, gastric cancer may have good, or relatively good, long-term survival when diagnosed at stages with a limited spread of the disease. However, only few cases are diagnosed at these early stages when cure by radical surgery is more likely.

References

1. Parkin D, Whelan Y, Ferlay J, *et al. Cancer Incidence in Five Continents*, vol VII. Lyon, IARC, 1997.
2. Parkin D, Muir S, Whelan Y, *et al. Cancer Incidence in Five Continents*, vol VI. Lyon, IARC, 1992.
3. Berrino F, Sant M, Verdecchia A, Capocaccia R, Hakulinen T, Estève J. *Survival of Cancer Patients in Europe. The EUROCARE study*. Lyon, IARC, 1995.
4. Kosary CL, Ries LAG, Miller BA, Mankey BF, Harras A, Edwards BK. *SEER Cancer Statistics Review 1973–92*. NIH, Bethesda, 1995.
5. Osaka Cancer Registry. *Survival of Cancer Patients in Osaka, 1975–89*. Osaka, 1998.
6. Noguchi Y, Imada T, Matsumoto A, Coit D, Brennan M. Radical surgery for gastric cancer. A review of the Japanese experience. *Cancer* 1989, **64**, 2053–2062.
7. Nakamura K, Ueyama T, Yao T, *et al*. Pathology and prognosis of gastric carcinoma. Findings in 10,000 patient who underwent primary gastrectomy. *Cancer* 1992, **70**, 1030–1037.
8. Schlemper R, Itabashi M, Kato Y, *et al*. Differences in diagnostic criteria for gastric carcinoma between Japanese and Western pathologists. *Lancet* 1997, **349**, 1725–1729.
9. Jatzko G, Lisborg P, Denk H, Klimpfinger M, Stettner H. A 10-year experience with Japanese-type radical lymph node dissection for gastric cancer outside of Japan. *Cancer* 1995, **76**, 1302–1312.
10. Bollscweiler E, Boettcher K, Hoelscher A, *et al*. Is the prognosis for Japanese and German patients with gastric cancer really different? *Cancer* 1993, **71**, 2918–2925.
11. Hakulinen T, Abeywickrama KA. A computer program package for relative survival analysis. *Computer Programs in Biomedicine* 1985, **19**, 197–207.
12. Cox DR. Regression models and life tables. *J Stat Soc B* 1972, **34**, 187–220.
13. Hakulinen T, Tenkanen L. Regression analysis of relative survival rates. *Appl Stat* 1987, **36**, 309–317.
14. Sobin L, Wittekind C. *TNM Classification of Malignant Tumours (International Union Against Cancer)*, 5th edn. New York, John Wiley & Sons, 1997.
15. Faivre J, Forman D, Estève J, Gatta G, the EUROCARE Working Group. Survival of patients with oesophageal and gastric cancers in Europe. *Eur J Cancer* 1998, **34**, 2167–2175.
16. Msika S, Benhamiche A, Jouve SL, Rat P, Faivre J. Prognostic factor after curative resection for gastric cancer. A population-based study. *Eur J Cancer* 2000, **36**, 390–396.
17. Damhuis R, Tilanus H. The influence of age on resection rates and postoperative mortality in 2773 patients with gastric cancer. *Eur J Cancer* 1995, **31**, 928–931.
18. Sue-Ling H, Jonson D, Martin I, *et al*. Gastric cancer: a curable disease in Britain. *Br Med J* 1993, **307**, 591–596.
19. Pinheiro PS, van der Heijden ?, Coeberg JW. Unchanged survival of gastric cancer in southeastern Netherlands since 19882: results of differential trends in incidence according to Lauren type and subsite. *Int J Cancer* 1999, **84**, 28–32.
20. Wanebo H, Kennedy B, Steele G, Winchester D, Osten R. Cancer of the stomach: a patients' care study by the American College of Surgeons. *Ann Surg* 1993, **218**, 583–592.
21. Lawrence W, Menck H, Steele G, Winchester D. The National cancer data base report on gastric cancer. *Cancer* 1995, **75**, 1734–1744.
22. Roder D, Bottcher K, Busch R, Wittekind C, Hermanek P, Siewert R. Classification of regional lymph node metastasis from gastric carcinoma. *Cancer* 1998, **82**, 621–631.
23. Fuchs C, Mayer R. Gastric carcinoma. *New Engl J Med* 1995, **333**, 32–41.
24. Alexander H, Kelsen D, Tepper J. Cancer of the stomach. In: De Vita V, Hellman S, Rosenberg S, eds. *Cancer: Principles and Practice of Oncology,* 4th edn. Philadelphia, JB Lippicott, 1993, 818–848.
25. Roy P, Piard R, Dusserre-Guion L, Martin L, Michiels-Marzais D, Faivre J. Prognostic comparison of the pathological classifications of gastric cancer: a population-based study. *Histopathology* 1998, **33**, 304–310.
26. Maguire A, Porta M, Sanz-Anquela J, Ruano I, Malats N, Pinol J. Sex as a prognostic factor in gastric cancer. *Eur J Cancer* 1996, **32**, 1303–1309.
27. Harrison J, Jones J, Ellis I, Morris D. Oestrogen receptor D5 antibody is an independent negative prognostic factor in gastric cancer. *Br J Surg* 1991, **78**, 334–336.
28. Matsui M, Kojima O, Kawakami S, Uehara Y, Takahashi T. The prognosis of patients with gastric cancer possessing sex hormone receptors. *Surg Today* 1992, **22**, 421–425.
29. Maehara Y, Emi Y, Tomisaki S, Oshiro T, *et al*. Age-related characteristics of gastric carcinoma in young and elderly patients. *Cancer* 1996, **77**, 1774–1780.