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Prognostic factors after curative resection for gastric cancer. A population-based study

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Abstract

The aim of this study was to document patterns of survival after resection for cure for gastric cancer in a well-defined population. A population-based series of 649 gastric cancers resected for cure between 1976 and 1995 in a 494 000 population, was used. Resection for cure was performed in 44.4% of the diagnosed cases. This proportion increased from 36.8% (1976–1979) to 45.0% (1992–1995) ($P=0.03$) whilst operative mortality decreased from 18.3 to 12.7% ($P=0.003$). The overall crude 5-year survival rate (excluding operative mortality) was 32.6% (95% confidence interval (CI) 28.7–36.5) and the corresponding relative survival rate was 40.9%. Prognosis did not improve during the study period. Stage at diagnosis was the most important prognostic factor, the 5-year relative survival rate being 81.2% (±5.9) in TNM stage IA, 76.9% (±8.0) in stage IB, 50.4% (±4.6) in stage II, 24.4% (±3.7) in stage IIIA, 5.6% (±3.2) in stage IIIB and 5.2% (± 2.2) in stage IV. Stage at diagnosis, age, subsite and macroscopic type of growth were independent prognostic factors, in a multivariate relative survival model. Earlier detection or development of an effective adjuvant therapy could contribute to improvement in prognosis.

Keywords: Gastric cancer; Resection for cure; Prognostic factors; Relative survival; Cancer registry

1. Introduction

Although declining in incidence, gastric cancer remains an important cancer problem [1]. In France, it ranks fifth amongst all cancers with an estimated 8700 new cases diagnosed per year [2]. Moreover, its prognosis is poor [3,4]. Surgical resection remains the primary treatment for gastric cancer. The influence of clinical and pathological factors on survival rates after potentially curative resection has been the subject of many investigations [5–11]. Most published data come from specialised surgical teams and, as such, their results cannot be used as a reference because of unavoidable selection bias (for example, concerning age, stage of diagnosis, health status, social status, place of residence). Community-based studies recording all diagnosed cases in a well-defined population have the advantage of not being affected by selection biases that affect the composition of clinical trials and hospital populations, so they represent the best way to identify prognostic factors. There are few published reports on the prognosis of all gastric carcinomas diagnosed in an unselected population [12–16]. The aim of our study was to document patterns of survival after resection for cure in a well-defined French population over a 20-year period.

2. Patients and methods

2.1. Patients

A population-based cancer registry, limited to digestive tract tumours, was set up in 1976 to cover the resident population of the Côte-d'Or area, Burgundy, France (494 000 residents according to the 1990 census). Information is routinely obtained from pathologists, medical specialists (gastroenterologists, surgeons, oncologists and radiotherapists), general practitioners as well as death certificates. No cases were registered from death certificates alone. However, these were used

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to trace missing cases. The quality and completeness of the registry is certified every 4 years by an audit of the 'Comité National des Registres'. The pathologists from the three laboratories of the area reviewed the slides concerning patients registered during the first 10 years of the study in order to standardise pathological reports.

Between 1976 and 1995, 1462 gastric carcinomas were diagnosed amongst Côte-d'Or residents, corresponding to a mean annual age-standardised incidence rate of 15.0 per 100 000 in males and 9.4 per 100 000 in females, according to the world population. Amongst them, 992 patients were operated upon. Of these, 800 patients underwent a resection, and 649 a resection with curative intent. In order to delineate the factors that interfere with long-term prognosis after curative surgery, the 88 patients who died in the postoperative phase were excluded from the survival analysis.

Resection was considered curative if all grossly visible tumour tissue was completely removed and the histological surgical margins were tumour-free (UICC R0 resection) [17]. Operative mortality was defined as death within 30 days of surgery [18]. One University Hospital including two surgical units, one Comprehensive Cancer Center with one surgical unit, four General Hospitals with eight surgeons, and four Private Hospitals with nine practicing surgeons were involved. Vital status of patients was ascertained from death certificates, registrars of the place of birth and place of residence, or from practitioners. In December 1998, vital status was available for 1433 patients (98.0%).

2.2. Studied variables

Patients were categorised into two age groups: under 70 years of age and 70 years of age and over. Place of residence was classified as Dijon city (the main town), other urban areas (towns of more than 2000 inhabitants) and rural areas. Subsite was coded according to the International Classification of Diseases, 10th revision (ICD-10) [19]: cardia (C 16.0), fundus (C 16.1), corpus (C 16.2), antrum and pylorus (distal third) (C 16.3 and C 16.4).

Surgical procedures were divided into distal gastrectomy, proximal oesophago-gastrectomy (PEG), total gastrectomy and extended total gastrectomy (ETG). PEG was defined as a proximal gastrectomy including the lower portion of the oesophagus, performed by a combined abdominal and right thoracic approach. ETG was defined as a total gastrectomy extended to the spleen, and/or to the pancreatic tail, to distal oesophagus. Tumours were classified according to size: 30 mm or less, 31–70 mm, and greater than 70 mm. The gross morphological appearance was classified according to Borrmann's classification [20]. All tumours were staged according to the fifth edition of the TNM classification (1997) [17].

2.3. Statistical analysis

Time trends were established for 4-year periods, leading to five study periods. Crude survival rates were calculated using the Kaplan–Meier method. Survival curves were compared using the logrank test. Relative survival rates were also calculated, these being defined as the ratio of crude survival rates and expected survival rates derived from local population life tables. Survival curves were compared using the maximum likelihood ratio test. The standard error of crude and relative survival rates was calculated. Multivariate analysis was performed using a relative survival model with proportional hazard applied to the net mortality by interval [21]. This model makes it possible to calculate relative risks which are adjusted for competing causes of death. The multivariate model was filled using a backward procedure. The significance of covariates was tested by the likelihood ratio test. The computations were performed using BMDP statistical software (1L program) [22] and Hedelin software [23].

3. Results

3.1. Resection for cure and operative mortality

Resection for cure was performed in 649 patients (44.4% of all gastric cancer patients). It was conducted more frequently in patients less than 70 years of age (303/552: 54.9%) than in older patients (346/910: 38.0%) ($P < 0.001$) and more frequently in distal cancers (267/489: 54.6%, 267/649: 41.1%) and in cancers of the corpus (141/273: 51.6%, 141/649: 21.7%) than in cancers of the fundus or cardia (161/450: 35.8%, 161/649: 24.8%) or in cancers located in more than one site (80/250: 32.0%, 80/649: 12.3%) ($P < 0.001$). Over the study period, the proportion of patients in whom potentially curative resection was possible increased from 36.8% in 1976–1979 to 45.0% in 1992–1995 ($P = 0.03$) (Table 1). The mean number of examined nodes remained stable over the study period, being 8.1 ± 0.6 and 8.8 ± 0.6 (NS) at the beginning and end of the study, respectively. The proportion of cases with at least 15 examined nodes was 16.5% and 20.6% (NS), respectively.

The overall operative mortality was 13.6%. It was lower in patients under 70 years of age (7.6%) than in older patients (18.8%) ($P < 0.0001$). It was higher during the first two 4-year periods than during the last three 4-year periods, respectively, 20.6% and 9.1% ($P < 0.001$) (Table 1).

3.2. Univariate survival analysis

The overall crude survival rate, excluding postoperative death, was 70.4% (95% confidence interval

(CI): 66.7–74.12) at 1 year, 43.1% (95% CI: 40.0–47.2) at 3 years, 32.6% (95% CI: 28.7–36.5) at 5 years. The corresponding relative survival rates were 75.4, 49.0 and 40.9%. Tables 2 and 3 list patients' characteristics in relation to the 5-year crude and relative survival rates. Sex, place of residence, and period of diagnosis were not significant prognosis factors. However, age at diagnosis was a significant prognostic factor. Patients younger than 70 years of age survived longer than older patients ($\geqslant 70$ years of age) ($P < 0.0001$), even when comparing relative survival rates. Patients with a previous history of gastric ulceration had a better survival than the other patients. Prognosis was also better after partial gastrectomy than after total gastrectomy (Table 2). The site of the primary gastric growth had an important bearing on survival. Cancers located in the corpus (middle third) had the best survival rates followed by cancers of the antrum, cancers of the fundus or cardia and cancers located in more than one site. Cancers 30 mm or less in diameter also had a better prognosis than larger cancers

Table 1
Incidence of resection for cure and operative mortality

	Period of diagnosis					Total	*P* value
	1976–1979 *n* (%)	1980–1983 *n* (%)	1984–1987 *n* (%)	1988–1991 *n* (%)	1992–1995 *n* (%)	*n* (%)	
Number of cases *n* (%)	326 (22.3)	299 (20.5)	307 (21.0)	268 (18.3)	262 (17.9)	1462 (100)	
Resection for cure	120 (36.8)	132 (44.1)	142 (46.3)	137 (51.1)	118 (45.0)	649 (44.4)	0.03
Operative mortality	22 (18.3)	30 (22.7)	13 (9.2)	8 (5.8)	15 (12.7)	88 (13.6)	0.003

$P \leqslant 0.05$ taken as level of significance (chi-square test).

Table 2
5-year crude and relative survival rates after curative resection of gastric cancer according to sex, age at diagnosis, period of diagnosis, place of residence, previous history of gastric ulceration and type of gastric resection ($n = 561$)

	Number of cases	Crude survival rate (%)		Relative survival rate (%)	
	n (%)	5-year (SEM)	*P*[a] value	5-year (SEM)	*P*[a] value
Sex					
Female	196 (34.9)	31.4 (3.4)		46.0 (4.4)	
Male	365 (65.1)	32.3 (2.5)		39.5 (2.9)	
			0.83		0.19
Age at diagnosis (years)					
< 70	280 (49.9)	43.7 (3.0)		46.8 (3.1)	
$\geqslant 70$	281 (50.1)	21.2 (2.5)		33.7 (3.5)	
			< 0.0001		0.005
Period of diagnosis					
1976–1979	98 (17.5)	37.7 (4.9)		45.1 (5.3)	
1980–1983	102 (18.2)	36.2 (4.8)		43.7 (5.4)	
1984–1987	129 (23.0)	27.8 (4.0)		33.3 (4.5)	
1988–1991	129 (23.0)	29.6 (4.1)		41.5 (4.9)	
1992–1995	103 (18.3)	26.9 (5.8)		46.6 (5.9)	
			0.24		0.31
Place of residence					
Dijon city	305 (54.4)	31.6 (2.8)		42.5 (3.3)	
Other urban areas	157 (28.0)	37.9 (3.9)		45.7 (4.5)	
Rural areas	99 (17.6)	25.7 (4.5)		32.0 (5.0)	
			0.07		0.15
Previous history of gastric ulceration					
Yes	72 (12.8)	43.3 (5.9)		57.6 (6.6)	
No	489 (87.2)	31.0 (2.2)		39.0 (2.6)	
			0.04		0.007
Type of gastric resection					
Distal gastrectomy	350 (62.4)	35.2 (2.6)		47.0 (3.2)	
Proximal-oesophago-gastrectomy	42 (7.5)	30.1 (7.3)		41.5 (8.0)	
Total gastrectomy	104 (18.5)	26.7 (4.4)		33.2 (5.0)	
Extended total gastrectomy	60 (10.7)	17.5 (5.6)		26.1 (5.7)	
Unknown	5 (0.9)				
			0.1		0.006

[a] Chi-square test, $P \leqslant 0.05$ taken as level of significance.
SEM, standard error of the mean.

Table 3
5-year crude and relative survival rates after curative resection of gastric cancer according to location and size of tumour, macroscopic growth and stage at diagnosis

	Number of cases	Crude survival rate (%)		Relative survival rate (%)	
	n (%)	5-year (SEM)	*PP*[a] value	5-year (SEM)	*P*[a] value
Location of tumour					
Distal third	244 (43.5)	34.5 (3.1)		45.6 (3.7)	
Fundus and cardia	130 (23.2)	23.4 (3.8)		29.2 (4.3)	
Corpus	126 (22.5)	45.4 (4.5)		57.8 (5.0)	
More than one site	57 (10.2)	13.5 (4.7)		17.5 (4.8)	
Unknown	4 (0.7)				
			< 0.0001		< 0.0001
Size of tumour (mm)					
30	169 (30.1)	44.4 (4.0)		63.0 (4.5)	
31–70	250 (44.6)	28.9 (2.9)		36.6 (3.4)	
> 70	119 (21.2)	23.1 (4.0)		25.6 (4.3)	
Unknown	23 (4.1)	20.8 (9.3)		22.2 (8.6)	
			< 0.0001		< 0.0001
Borrmann classification					
Fungating I	45 (8.0)	43.8 (7.9)		65.0 (8.8)	
Ulcero fungating II	130 (23.2)	40.4 (4.3)		48.4 (4.9)	
Ulcero infiltrating III	308 (54.9)	28.9 (2.7)		39.3 (3.2)	
Infiltrative IV	59 (10.5)	18.1 (5.1)		22.0 (5.4)	
Unknown	19 (3.4)				
			0.001		< 0.001
TNM stage					
Stage IA	73 (13.0)	69.3 (5.6)		81.2 (5.9)	
Stage IB	53 (9.4)	52.9 (7.1)		76.9 (8.0)	
Stage II	160 (28.5)	38.1 (3.9)		50.4 (4.6)	
Stage IIIA	164 (29.2)	19.5 (3.2)		24.4 (3.7)	
Stage IIIB	34 (6.1)	2.5 (1.3)		5.6 (3.2)	
Stage IV	68 (12.1)	8.6 (3.4)		5.2 (2.2)	
Unknown	9 (1.6)				
			< 0.0001		< 0.0001

[a] Chi-square test, $P \leqslant 0.05$ taken as the level of significance.
SEM, standard error of the mean.

(Table 3). Prognosis was also related to macroscopic features: the highest survival rates were reported for the fungating type and the lowest for the infiltrative type. The extent of tumour spread was a major prognostic factor (Fig. 1). Relative survival in patients with a cancer limited to the submucosa (stage IA), was only slightly lower than that of a population with a similar age and sex distribution. Prognosis worsened with advancement of cancer stage. The prognosis was particularly poor when lymph nodes were involved.

3.3. Multivariate survival analysis

When a relative survival model including the variables significant in the univariate analysis and the sex was fitted, the variables sex, period of diagnosis, previous history of gastric ulceration, type of surgical resection and size were not statistically associated with relative survival (data not shown). Stage at diagnosis ($P < 0.00001$), age ($P = 0.003$), location of the tumour ($P = 0.01$) and gross morphological appearance ($P = 0.0005$) were independent prognostic factors (Table 4). The main prognostic factor was stage at diagnosis. The relative risk (RR) of death was 5 times higher in stage IIIA (RR (95% CI); 5.77 (2.57–12.94)) and at least 10 times higher in stage IIIB (10.88: 3.79–31.25) or IV (11.78: 4.81–28.86) when compared with stage IA. Prognosis was worse in the infiltrative type compared with other gross appearances, in cancers of the fundus or cardia and in cancers located in more than one site compared with more distal cancers, independent of cancer stage.

4. Discussion

This study has the advantage of including all cases of gastric cancer resected for cure in a well-defined French population over a 20-year period. Information on clinical and morphological features and treatment were available for nearly all cases and survival data were also exhaustive with complete follow-up in 98% of recorded cases. Thus, this study was carried out without the referral bias, which often occurs in hospital-based series.

The proportion of gastric cancers resected for cure increased slightly over the study period. The main change was observed when comparing the first 4-year

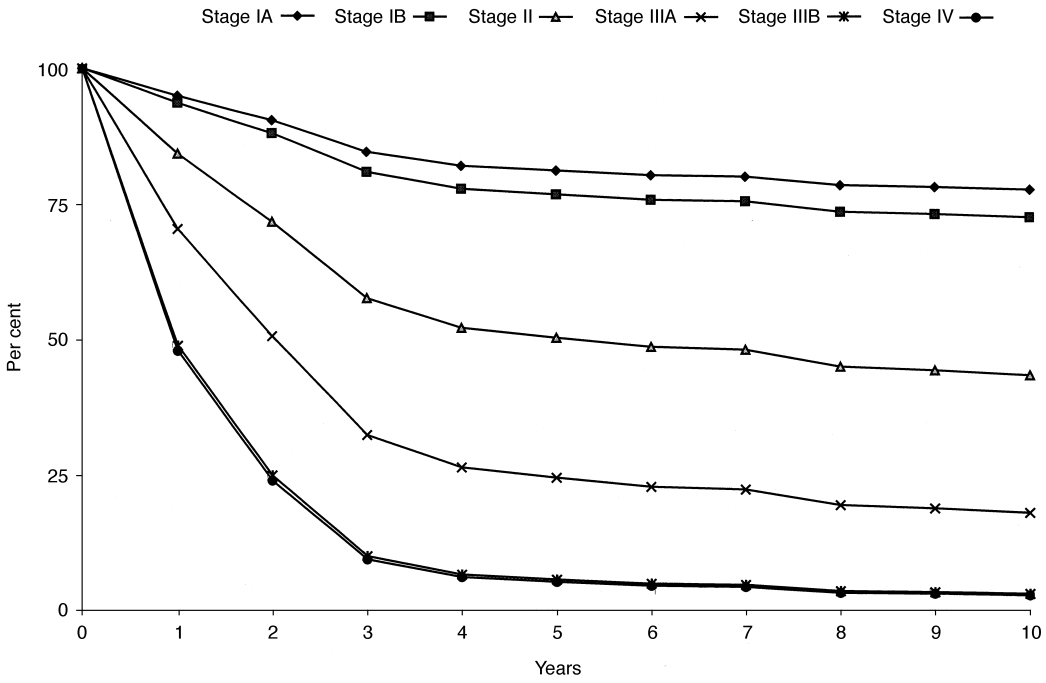

Fig. 1. Relative survival curves according to stage at diagnosis after curative resection for gastric cancer (TNM classification).

study period with the second one. Then the proportion of cases resected for cure levelled out. Similar trends have been reported in the scarce population-based reports [3,4,12,13]. Previous studies have already stressed that the development of endoscopy was associated with minor progress in gastric cancer care [24]. This can be explained by the fact that when symptoms occur, the cancer has often already spread. The only striking trend in the management of gastric cancer lies in the reduction of operative mortality, when comparing the first two 4-year periods with the last three. This trend may be attributable to improved surgical techniques, but it is likely to be due mainly to improvements in perioperative management and in postoperative resuscitation.

Table 4
Multivariate analysis of relative survival for gastric cancer

Variables	Relative risk (95% confidence interval)	P^a value
TNM stage		
Stage IA	1	
Stage IB	1.41 (0.55–3.65)	
Stage II	3.14 (1.55–6.37)	
Stage IIIA	5.77 (2.57–12.94)	
Stage IIIB	10.88 (3.79–31.25)	
Stage IV	11.78 (4.81–28.86)	
		<0.00001
Age group		
<70	1	
$\geqslant 70$	1.48 (1.15–1.91)	
		0.003
Location of the tumour		
Distal third	1	
Corpus	0.92 (0.64–1.32)	
Fundus or cardia	1.40 (1.02–1.91)	
More than one site	1.77 (1.18–2.67)	
		0.01
Borrmann's classification		
Fungating I	1	
Ulcero fungating II	0.70 (0.42–1.18)	
Ulcero infiltrating III	1.18 (0.73–1.91)	
Infiltrative IV	1.68 (1.05–2.86)	0.0005

[a] Likelihood ratio test, $P \leqslant 0.05$ taken as level of significance.

In hospital series, which often emanate from specialised surgical centres, data on the prognosis of gastric cancer are more favourable [5–11,25–27]. After curative surgery, the 5-year crude survival rate ranges from 47% to 54% [11,28,29], whereas in population-based series it ranges from 22 to 45% [3,4,12,13]. So far there are few population-based survival figures. They require more effort than cancer incidence statistics. In addition to identifying the patients, detailed information on the cancer characteristics is required, as well as a complete yearly follow-up. Most of the time, only overall survival rates are available [14–16]. The only detailed population-based statistics that can be compared with our series come from the West Midlands, UK [12], from The Netherlands [13] and from French Brittany [3,4]. The stability of the mean number of examined nodes and the low proportion of cases with at least 15 examined nodes suggest that most patients in this population had a D1 resection and, therefore, surgical practice did not change over time.

The main purpose of this study was to identify clinical or pathological characteristics easily available in a population-based series that influence the prognosis of

patients with gastric cancer after resection for cure so as to predict outcome and to help define patients who may benefit from adjuvant therapy. All studies, population-based as well as hospital-based, indicate that the anatomical extent of gastric cancer is the main prognostic factor. In our study, little difference in prognosis between cases TNM stage IA and TNM stage IB is observed and these two groups can be considered together. In contrast, survival rates decrease sharply when the serosa is involved. The extent of lymph node involvement also plays a major role in prognosis [6,8]. Our study also confirmed these observations. The multivariate analysis suggests that if the anatomical extent of the cancer is the most important prognostic factor, age, growth appearance and location of the cancer have an independent influence on prognosis. The increased degree of comorbidity in the elderly can explain the worse prognosis in patients 70 years of age and above. The effect of age was more pronounced when considering crude survival rates than when using relative survival rates. This is due to the fact that crude survival models do not take into account the natural increase in mortality with advancing age. Relative survival models adjust for this natural mortality and thus provide mortality due to the disease itself. These types of models seem most appropriate for describing outcomes in population-based statistics. This study also indicates that there is a relationship between the site of the cancer and prognosis. Cancers of the upper part of the stomach are associated with a poorer survival compared with those of the middle or lower part of the stomach. Several other studies report an independent prognostic impact for this variable [11,13,30,31]. Cancer of the upper part of the stomach may have a more aggressive natural history. Furthermore, the model highlights the worse prognosis of patients with Borrmann type IV compared with other macroscopic types of growth. Similar results were reported in a population-based study in French Brittany [4]. This is probably because peritoneal diffusion of infiltrative tumours is faster than in other tumours, as has been suggested in a Japanese series of patients [32].

No improvement in the survival rates for gastric cancer after curative surgery has been achieved over the two decades of the study. This is not surprising as surgical techniques used in this paper were uniform throughout the time period studied and adjuvant therapeutic strategies have not been proved to be of significant benefit. Furthermore, we have shown in a previous study the absence of improvement in the stage observed at diagnosis [33]. The slight increase in prognosis seen in the overall statistics [14,33] can be attributed mainly to decreases in operative mortality and, to a lesser degree, to the moderate increases in the resection rate that have occurred with time.

Gastric cancer remains an important management problem even after resection for cure, because cases with a good prognosis still represent a too small proportion of the total number of gastric cancers. However, although surgery was standardised in our population-based study significant changes in surgery have occurred in recent years which might result in a better prognosis amongst these patients [8,28,29]. Nevertheless, in the short term, improvement can be achieved through earlier detection and/or the development of an effective adjuvant treatment. Thus, patients with recent upper gastrointestinal symptoms should be investigated rapidly and involved in trials evaluating adjuvant therapy after surgery for cure.

References

1. Parkin DM, Muir C, Whelan SH, Gao YT, Ferlay J, Powell J. *Cancer incidence in five continents*, Vol. VII. Lyon, IARC Scientific Publications No. 143, 1997.
2. Faivre J, Grosclaude P, Launoy G, *et al*. Les cancers digestifs en France. Distribution géographique et estimation de l'incidence nationale. *Gastroenterol Clin Biol* 1997, **21**, 174–180.
3. Arsene D, Chomontowski J, Pottier D, Rougereau A, Launoy G, Gignoux M. Epidémiologie et pronostic des carcinomes gastriques dans le département du Calvados: étude sur 10 ans. *Gastroenterol Clin Biol* 1995, **19**, 797–803.
4. Lepage M, Cauvin JM, Le Dréau G, *et al*. Prise en charge thérapeutique et survie de l'adénocarcinome gastrique dans le département du Finistère entre 1984 et 1989. *Gastroenterol Clin Biol* 1995, **9**, 804–810.
5. Msika S, Chastang C, Houry S, Lacaine F, Huguier M. Lymph node involvement as the only prognostic factor in curative resected gastric carcinoma: a multivariate analysis. *World J Surg* 1989, **13**, 118–123.
6. Hautefeuille P, Valleur P, Castaing D, *et al*. Influence de l'extension ganglionnaire sur la survie après résection des cancers gastriques infiltrants. *Gastroenterol Clin Biol* 1982, **6**, 849–856.
7. Elias D, Lasser P, Bognel C, *et al*. Adénocarcinomes gastriques réséqués curativement. Analyse multifactorielle des facteurs pronostiques. *Gastroenterol Clin Biol* 1988, **12**, 729–735.
8. Siewert JR, Bottcher K, Stein HJ, *et al*. Relevant prognostic factors in gastric cancer. Ten-year results of the German Gastric Cancer Study. *Ann Surg* 1998, **228**, 449–461.
9. Stipa S, Di Giorgio A, Ferri M, Botti C. Results of curative gastrectomy for carcinoma. *J Am Coll Surg* 1994, **179**, 567–572.
10. Maruyama K, Okabayashi K, Kinoshita T. Progress in gastric cancer surgery in Japan and its limits of radicality. *World J Surg* 1987, **11**, 418–425.
11. Meyer Ch, Lozac'h P, Schaffer P, Hedelin G, Sartori V. Enquête de l'Association Française de Chirurgie. In *Le cancer de l'estomac. Rapport du 100ème congrès de chirurgie Français*. Paris, France, Editions Arnette, 1998.
12. Allum WH, Powell DJ, McConkey CC, Fielding JWL. Gastric cancer: a 25-year review. *Br J Surg* 1989, **76**, 535–540.
13. Pinheiro PS, van der Heijden LH, Coebergh JW. Unchanged survival of gastric cancer in the southeastern Netherlands since 1982: result of differential trends in incidence according to Laureen type and subsite. *Int J Cancer* 1999, **84**, 28–32.
14. Faivre J, Forman D, Esteve J, Gatta G, the EUROCARE Working Group. Survival of patients with oesophagal and gastric cancers in Europe. *Eur J Cancer* 1998, **34**, 2167–2175.
15. Gafa L, Amendola P, Dardanoni G, Dardanoni L. Survival of patients with cancer of the stomach, colon and rectum, lung and breast in Ragusa, Sicily. *Tumori* 1991, **28**, 7–11.

16. Lundegardh G, Adami H, Malker B. Gastric cancer survival in Sweden. Lack of improvement in 19 years. *Ann Surg* 1986, **204**, 546–551.
17. Sobin LH, Wittekind C. *TNM Classification of malignant tumours*. 5th edn. New York, John Wiley & Sons, 1997.
18. Kajitani T, Japanese Research Society for Gastric Cancer. The general rules for the gastric cancer study in surgery and pathology. *Jpn J Surg* 1981, **11**, 127–145.
19. World Health Organisation. *International classification of diseases for oncology*. 10th revision. Geneva, WHO, 1993.
20. Borrmann R. Geschwulste des mangens und duodenums. In Henke, Lubarsch, eds. *Hand-buch des speziellen pathologischen anatomie und histologie*. Berlin, Springer, 1926, 865.
21. Esteve J, Benhamou E, Crosdale M, Raymond L. The relative survival and the estimation of the net survival: elements for further discussion. *Stat Med* 1990, **9**, 529–538.
22. Dixon WJ, ed. *BMDP dynamic 7.0 manuals*. Los Angeles, University of California Press, 1992.
23. Hedelin G. *Relsurv a program for relative survival*. (version 2.0c) Strasbourg, Université Louis Pasteur, 1997.
24. Holdstock G, Bruce S. Endoscopy and gastric cancer. *Gut* 1981, **22**, 673–676.
25. Akoh JA, Sedwick DM, Macintyre IMC. Improving results in gastric cancer — an 11 year audit. *Br J Surg* 1991, **78**, 349–351.
26. Akoh JA, Macintyre IMC. Improving survival in gastric cancer: review of 5-year survival rates in English language publications from 1970. *Br J Surg* 1992, **79**, 293–299.
27. Sue-Ling HM, Johnston D, Martin IG, *et al*. Gastric cancer: a curable disease in Britain. *Br Med J* 1993, **307**, 591–596.
28. Bonenkamp JJ, Hermans J, Sasako M, *et al*. for the Dutch Gastric Cancer Group. Extended lymph-node dissection for gastric cancer. *N Engl J Med* 1999, **340**, 908–914.
29. Cuschieri A, Weeden S, Fielding J, *et al*. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group. *Br J Cancer* 1999, **79**, 1522–1530.
30. Hundahl SA, Menck HR, Mansour EG, Winchester DP. The National Cancer Data Base report on gastric carcinoma. *Cancer* 1997, **80**, 2333–2341.
31. Harrison LE, Karpeh MS, Brennan MF. Proximals gastric cancers resected via a transabdominal only approach: results and comparisons to distal adenocarcinoma of the stomach. *Ann Surg* 1997, **225**, 678–685.
32. Maehara Y, Moriguchi S, Orita H, *et al*. Lower survival rate for patients with carcinoma of the stomach of Borrmann type IV after gastric resection. *Surg Gynecol Obstet* 1992, **175**, 13–16.
33. Msika S, Tazi MA, Benhamiche AM, Couillault C, Harb M, Faivre J. Population-based study of diagnosis, treatment and prognosis of gastric cancer. *Br J Surg* 1997, **84**, 1474–1478.