15. Armitage P. *Statistical Methods in Medical Research*. Oxford, Blackwell Scientific Publications, 1973.
16. Berlinger NT. Deficient immunity in head and neck cancer due to excessive monocyte production of prostaglandins. *Laryngoscope* 1984, **94**, 1407–1410.
17. Balch CM, Dougherty PA, Tilden AB. Excessive prostaglandin E2 production by suppressor monocyte in head and neck cancer patients. *Ann Surg* 1982, **196**, 645–650.
18. McCormic KJ, Panje WR. Indomethacin-induced augmentation of lymphoproliferative response in patients with head and neck cancer. *Cancer Immunol Immunother* 1986, **21**, 226–232.
19. Rolland PH, Martin PM, Jacquemier J, Rolland AM, Toga M. Prostaglandin in human breast cancer. Evidence suggesting that an elevated prostaglandin production is a marker of high metastatic potential for neoplastic cells. *J Natl Cancer Inst* 1980, **64**, 1061–1070.
20. Bishop H, Haynes J, Evans D, Elston C, Johnson J, Blamey RV. Radioimmunoassay (RIA) of prostaglandin E2 (PGE) in primary breast cancer and its relationship to histologic grade. *Clin Oncol* 1980, **6**, 380–381.
21. Jung TTK, Berlinger NT, Juhn K. Prostaglandins in squamous cell carcinoma of the head and neck: a preliminary study. *Laryngoscope* 1985, **95**, 307–312.
22. Johnson RT, Rabin BS, Wagner RL. Prostaglandin E2 of the upper aerodigestive tract. *Ann Otol Rhinol Laryngol* 1987, **96**, 213–216.
23. Fulton AM, Heppner GH. Relationship of prostaglandin E and natural killer sensitivity to metastatic potential in murine adenocarcinomas. *Cancer Res* 1985, **45**, 4779–4784.
24. Kloppel TM, Keenan TW, Freeman KJ, Moore DJ. Glycolipid-bound sialic acid in serum: Increased levels in mice and humans bearing mammary carcinomas. *Proc Natl Acad Sci USA* 1977, **74**, 3011–3013.

Eur J Cancer, Vol. 29A, No. 6, pp. 845–850, 1993.
Printed in Great Britain

0964–1947/93 $6.00 + 0.00

A Prognostic Score for Patients Resected for Gastric Cancer

E. Marubini, G. Bonfanti, F. Bozzetti, P. Boracchi, D. Amadori, S. Folli, O. Nanni and L. Gennari

This paper describes the construction, validation and use of a simple prognostic score suitable for predicting survival of patients undergoing a curative gastric resection. Using death from all causes as outcome, the prognostic significance of age, sex, tumour site, stage of disease (nodal status and wall invasion), surgical treatment and histological type was investigated in a set of 213 patients recruited in a multi-centre clinical trial. A Weibull multiple regression model was adopted to evaluate the joint effect of these variables on survival. From a full model, containing all the variables, a final parsimonious model was obtained by means of a backward selection procedure. The prognostic score is based on the final model, including four variables which are easily detected in every institution: age, wall invasion, site of tumour, and nodal status. Three groups of patients with different probabilities of surviving 5 years from surgery were identified: group I (survival probability $\geq$ 70%), group II (30%–69%) and group III (< 30%). The prognostic score, obtained from the multicentre trial patients, was tested on a set of 135 consecutive patients in an independent institution, confirming its reliability in predicting survival. The score system presented can supply a simple tool for classifying patients radically operated for gastric cancer into three well discriminated groups from the prognostic point of view.
Eur J Cancer, Vol. 29A, No. 6, pp. 845–850, 1993.

INTRODUCTION

THE KNOWLEDGE of prognostic factors in patients with gastric cancer has a pivotal importance in clinical practice: in the single patient it enables improved assessment of the benefit–risk ratio and in clinical research it enables one to select prognostically homogeneous groups of patients better to assess the effectiveness of different therapeutical strategies.

Correspondence to F. Bozzetti.
F. Bozzetti, G. Bonfanti and L. Gennari are at the Oncologia Chirurgica "A", Istituto Nazionale dei Tumori, Via Venezian, 1, 20133, Milano; E. Marubini and P. Boracchi are at the Divisione di Statistica Medica e Biometria, Istituto Nazionale Tumori di Milano; D. Amadori is at the Dipartimento di Oncologia, Ospedale G.B. Morgagni—L. Pierantoni di Forli'; S. Folli is at the Divisione di Chirurgia Generale, Ospedale G.B. Morgagni—L. Pierantoni di Forli'; and O. Nanni is at the Istituto Oncologico Romagnolo, Forli', Italy.
Received 24th July 1992; accepted 26 Aug. 1992.

Most of the data regarding prognosis are obtained from analyses of putative prognostic factors in a univariate fashion. However, in the presence of many factors, especially when they are correlated, this method fails to detect the contributory role of the single variable to the prognosis. Therefore, the information attained has a limited value and much attention has recently been given to multivariate analyses.

We previously focused our interest [1] on various prognostic variables which have been widely investigated in the literature and are easily detected in all patients who undergo a curative gastric resection; their prognostic value is confirmed not only in univariate, but also in multivariate analyses. They include: age of patient [1, 2] depth of neoplastic invasion of the gastric wall [1–5], site in the stomach where the tumour is situated [6, 7] and nodal involvement [1, 2, 5, 8]. Moreover, we argued that it would be possible to define more precisely the survival experience of patients by considering these variables overall.

This paper describes the construction, testing and use of a score suitable for predicting the survival of patients undergoing a curative gastric resection. The score was attained by means of a multivariate statistical analysis performed on a set of patients accrued in a multicentre randomised clinical trial coordinated by the Istituto Nazionale dei Tumori of Milan [9] and tested on a set of consecutive patients treated in a different institution.

PATIENTS AND METHODS

Multicentre trial patients

Between March 1977 and June 1981, 213 patients with gastric cancer, eligible for curative resection, were randomised to receive either no further therapy after surgery, adjuvant combination chemotherapy, or adjuvant combination chemotherapy plus levamisole.

Details on surgical techniques, drug doses, sequences and treatment duration, as well as trial results in terms of survival were previously reported [9]. Trial results failed to show any significant difference between the three treatment groups and it was therefore deemed appropriate to perform all subsequent analyses without taking into consideration the relative treatments.

Table 1 presents the main characteristics of patients. Patients were classified by the TNM [10] classification system.

G.B. Morgagni—L. Pierantoni Hospital of Forlì (MPH) patients

This case series consists of 143 consecutive patients with gastric cancer who have been treated by gastric resection with curative intention between 1975 and 1984.

Statistical analysis

Survival times were measured from the date of surgery and death from all causes (excluding postoperative mortality) was taken as outcome. Firstly, a univariate analysis was carried out; survival curves were traced by the product limit method [11] and comparisons of survival curves were based on the log-rank test [12].

A Weibull multiple regression model [13] was later adopted to evaluate the joint effect of the clinical–pathological characteristics of patients measured at the time of surgery.

This model, suitable for censored data, allows one to consider several variables simultaneously and their effect on survival is investigated by the linear predictor:

$$g(x_j) = \beta_0 + \beta_1 x_{1j} + \ldots + \beta_p x_{pj}$$

where, for the jth patient ($j = 1,2,\ldots,n$), x_{ij} ($i=1,\ldots,p$) is the value assumed by each of the p variables and β_i is the pertinent regression coefficient. The prognostic variables were categorical; thus for each of them one or more dummies have been built as indicated in the appendix. In such a way: exp (β_i/k) where k means the scale parameter (see appendix), may be interpreted in terms of hazard of death from a given category relative to that of the reference category. Furthermore, it may be shown that the ratio of the estimate β_i to its standard error [SE(β_i), i.e. $z = \beta_i/\mathrm{SE}(\beta_i)$] is approximately distributed as a Gaussian standardised random variable. Therefore, this statistic is used to test the null hypothesis: H_0: $\beta_i = 0$.

From an initial full model, containing all factors listed in Table 1, a final parsimonious model was obtained by means of a backward selection procedure.

The quantity $g(x_j)$ has been used to compute a score suitable for classifying each patient in groups with different prognoses (see appendix for details).

Table 1. Main characteristics of patients in the two series

Variables	Patient series: Multicentre trial n	%	G.B. Morgagni L. Pierantoni Hospital n	%
Age (years)				
≤ 60	128	60.1	65	45.5
> 60	85	39.9	78	54.5
Sex				
Male	138		90	
Female	75	64.8	53	62.9
Wall invasion				
pT1	40	18.8	11	7.7
pT2	70	32.9	31	21.7
pT3–4	103	48.3	101	70.6
Tumour site				
Lower third	126	59.1	76	51.0
Other	73*	34.3	56	39.2
Upper third	14	6.6	14	9.8
Histological type				
Intestinal			118	82.5
Diffuse	132	62.0	15	10.5
Mixed	66	31.0		
Missing information	15	7.0	10	7.0
Surgical treatment				
Total gastrectomy	26	12.2	48	33.6
Subtotal gastrectomy	154	72.3	92	64.3
Other*	33	15.5	3	2.1
Nodal status				
N−	89	41.8	45	31.5
N+	124	58.2	90	62.9
Missing information			8	5.6
Total	213		143	

*Other includes: middle third 51%; middle + upper third 11%; middle + lower third 28%; the whole stomach 10%.

The multicentre trial case series was used as a training set to construct the score which was subsequently applied to the MPH set to evaluate its performance.

RESULTS

Table 1 shows the main characteristics of patients in the two series and it appears that the distributions of the examined variables differ for almost all the variables except sex. In particular, MPH patients were older, and had more frequent pT3–4 wall invasion compared to the multicentre trial patients.

Construction of the scoring procedure on training set

Univariate analysis. Survival curve of the whole case series is depicted in Fig. 1; the 5 year survival probability is estimated to be 0.51.

Patients aged 60 years or more tend to show a prognosis worse than that of younger patients though the log-rank test is not significant ($P=0.15$). Five year survival probabilities for two patient groups are 0.45 and 0.54, respectively (Fig. 2a). The survival experiences of males and females are very similar (Fig. 2b).

Wall invasion beyond the mucosa adversely affects prognosis:

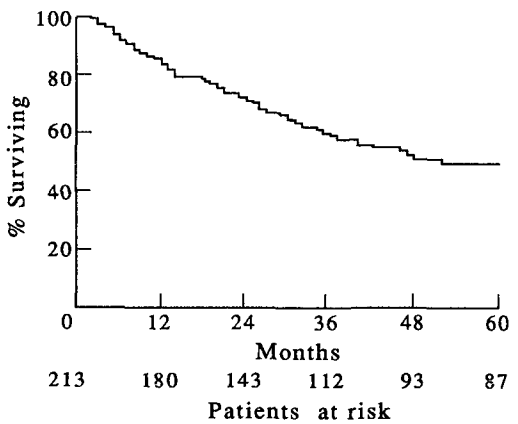

Fig. 1. Survival curve of the whole Multicentre Trial series (see text) (Kaplan and Meier estimate).

5 year survival probabilities of patients pT1, pT2 and pT3–4 are 0.84, 0.55 and 0.33, respectively [log-rank test = 26.14, 2 degrees of freedom (d.f), $P = 0.0001$] (Fig. 2c).

Patients with a tumour localised in the upper third have a lower survival probability than those with tumours on other sites (Fig. 2d) (log-rank test = 18.52, 2 d.f., $P = 0.0001$). Five year survival probability ranges from 0.14 for patients with upper third localisation to 0.59 for patients with lower third localisation.

Survival according to histological type is shown in Fig. 2e; survival curves are quite similar for the three groups of patients considered (log-rank test = 1.82, $P = 0.41$).

Patients with positive nodal status (N+) have poorer prognosis with respect to those with negative nodal status (N−) (Fig. 2f) (log-rank test = 21.74, $P = 0.0001$) and the 5 year survival probabilities of two groups of patients are 0.70 and 0.36, respectively.

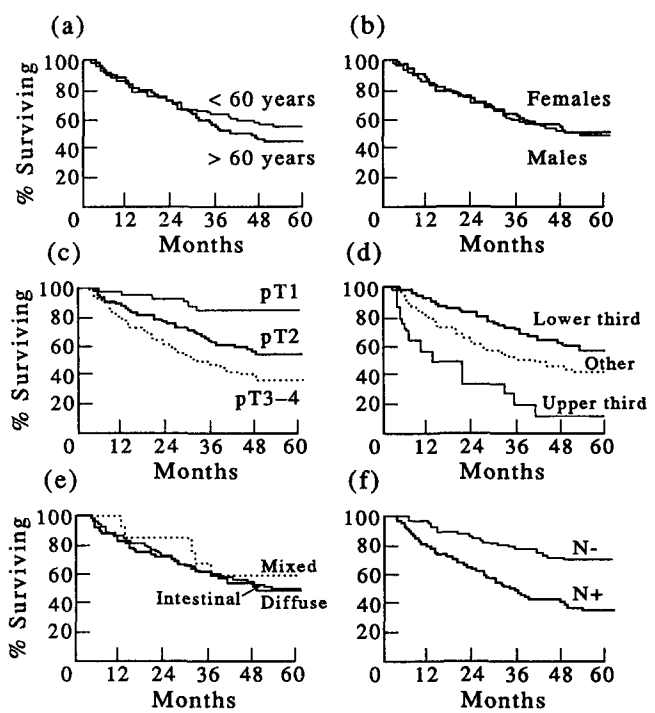

Fig. 2. Survival curves of subgroups of the Multicentre Trial series obtained by classifying patients according to the variables reported in Table 1 (Kaplan and Meier estimate).

Multiple regression analysis. As mentioned in the statistical methods section a Weibull regression model was utilised to investigate the joint effect of putative prognostic factors.

From the model containing all the variables, sex, histological type and kind of surgery were removed because the likelihood ratio test pertinent to each of these regressors had $P>0.10$. Table 2 reports the maximum likelihood estimate of the regression coefficient, its standard error and the pertinent Wald's statistic for each regressor in the final model.

The scoring procedure. The complete procedure utilised to construct the score useful for classifying patients in three groups with different prognoses is given in the appendix. The three groups include patients with predicted 5 year survival probability equal to or greater than 70% (group I), between 30% and 69% (group II) and less than 30% (group III). A patient can be classified in the pertinent group by means of the figures reported in Table 3, each of which represents the partial score associated with the corresponding category of the four variables retained in the final model. The total score for a given patient is obtained by adding his appropriate partial scores. If the total score is less or equal to 3.5 the patient is classified in group I, if it ranges between 3.6 and 7.0 the patient is classified in group II and if it is greater than 7 in group III.

Examples. The total score for a patient aged 45 years, wall invasion pT2, tumour localised in the lower third with negative nodes, is: 0 + 2.5 + 0 + 0 = 2.5: group I; consider a second patient aged 70 years, wall invasion pT1, tumour in "other" localisation with positive nodes, the total score is: 1 + 0 + 1 + 3 = 5: group II; a third patient aged 55 years, wall invasion pT4 and tumour localised in the upper third with positive nodes has a total score of: 0 + 3.5 + 4.5 + 3 = 11.0 and is classified in group III.

By this scoring procedure 30% of the patients of the multicentre trial (64) were classified in the risk group I, 41% (88) in the

Table 2. Maximum likelihood estimates of regression coefficients, their standard errors and pertinent Wald's statistics for the variables retained in the final model

Variables	β	SE (β)	z	P
Intercept	6.19	0.43		
Age (years)				
≤ 60	0.00			
> 60	−0.32	0.18	−1.78	.08
Wall invasion				
pT1	0.00			
pT2	−0.84	0.41	−2.05	.039
pT3–4	−1.14	0.40	−2.85	.004
Tumour site				
Lower third	0.00		−1.95	.05
Other	−0.37	0.19	−4.71	.0001
Upper third	−1.46	0.31		
Nodal status				
N−	0.00			
N+	−0.94	0.22	−4.27	.0001

Table 3. Partial scores for categories of prognostic factors and classification of patients in three risk groups

Variables	Partial score	Variables	Partial score
Age (years)		Tumour site	
≤ 60	0	Lower third	0
> 60	1	Other	1
		Upper third	4.5
Wall invasion			
pT1	0	Nodal status	
pT2	2.5	N−	0
pT3–4	3.5	N+	3

Risk groups	Total score
I: 5 year survival probability ≥ 70%	≤ 3.5
II: 5 year survival probability 30%–69%	3.6–7
III: 5 year survival probability < 30%	> 7

Total score = Age score + wall invasion score + tumour site score + nodal status score.

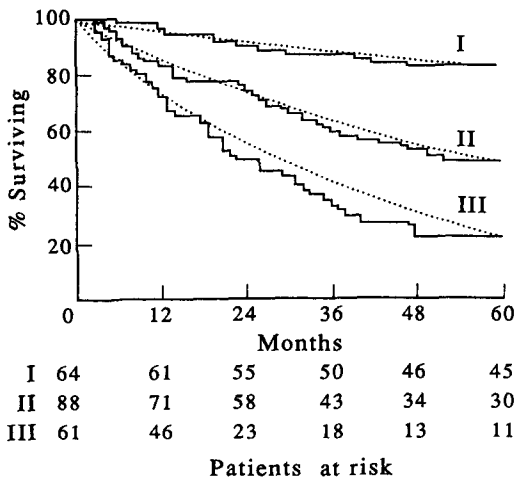

Fig. 3. Survival experience of the three groups of patients identified by the prognostic score of Table 3 in the Multicentre Trial series (training set). Surviving probabilities estimated by the Weibull model (dotted lines) and by the Kaplan–Meier method (continuous line).

risk group II and 29% (61) in the risk group III. The patients of the three risk groups have a different survival experience as is shown by Fig. 3 and their 5 year survival probability is, on average, equal to or greater than 70% (82%), between 30% and 69% (47%) and less than 30% (21%), respectively. Furthermore, Fig. 3 shows good agreement between survival curves estimated by the Weibull model and those estimated by the Kaplan–Meier technique.

The distribution of the four prognostic factors in the three risk groups is given in Table 4; only 2 patients with nodal status N+ and no patient with upper third localisation belong to group I and only 3 patients with nodal status N− and upper third localisation belong to group III.

Validation of the scoring procedure on the testing set

The model building exercise searched through different possible combinations of variables and has given the best possible agreement of the chosen model with the observed data. However, goodness of fit of a model does not necessarily reflect the degree of agreement one might obtain from future applications of the equation. Demonstration or confirmation that the equation is sound and effective for the purpose for which it was intended requires assessing the effectiveness of the fitted equation against an independent set of data and is essential if confidence in the model is to be expected.

For this reason, the scoring procedure given in Table 3, was applied to the MPH series.

Of the 135 patients with complete information on prognostic factors, 15% (20) are classified in the risk group I, 41% (55) in risk group II and 44% (60) in the risk group III.

Kaplan–Meier survival curves for the three risk groups of the MPH series are shown in Fig. 4. It is evident that the three groups have different survival experience during the follow-up period and their 5 year survival probability is, as expected, equal to or greater than 70% (90%), between 30% and 69% (54%) and less than 30% (23%) for groups I, II and III, respectively.

Table 5 is the counterpart of Table 4 for this series of patients and the patterns of classification in the three risk groups appear very similar in the two tables.

DISCUSSION

The assessment of prognosis in the single patient apparently cured of a cancer has always represented a challenge for the

Table 4. Distribution of prognostic factors in the three risk groups. Training set (Multicentre Trial)

		Nodal status																	
		N−									N+								
		Lower third			Other			Upper third			Lower third			Other			Upper third		
Group	Age (years)	pT1	pT2	pT3–4	pT1	pT2	pT3–4	pT1	pT2	pT3–4	pT1	pT2	pT3–4	pT1	pT2	pT3–4	pT1	pT2	pT3–4
I	≤ 60	17	9	6	5	5					2								
(64 patients)	> 60	7	12		1														
II	≤ 60						4	1	2			17	25	2	8				
(88 patients)	> 60			7		2	8				3	7		2					
III	≤ 60									2						18		2	3
(61 patients)	> 60									1			14		5	13		1	2

Table 5. Distribution of prognostic factors in the three risk groups. Training set (M P H trial)

Group	Age (years)	Nodal status: N− Lower third pT1	pT2	pT3–4	N− Other pT1	pT2	pT3–4	N− Upper third pT1	pT2	pT3–4	N+ Lower third pT1	pT2	pT3–4	N+ Other pT1	pT2	pT3–4	N+ Upper third pT1	pT2	pT3–4
I	≤ 60		3	6		4					3								
(20 patients)	> 60	2	1		1														
II	≤ 60						4		1			3	16	2	3				
(55 patients)	> 60			9		5	6					6							
III	≤ 60									1						12			4
(60 patients)	> 60									2			18			17		1	5

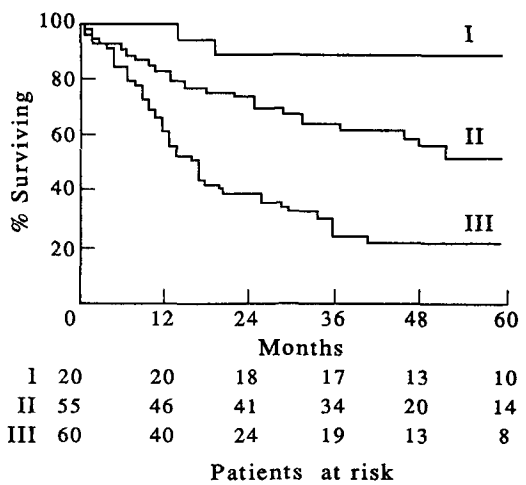

Fig. 4. Survival curves for the three groups of patients identified by the prognostic score of Table 3 in the MPH series (testing set) (Kaplan–Meier estimates).

oncologist especially when clinical or pathological prognostic factors are conflicting. Furthermore, a proper prognostic assessment is the mandatory requirement for stratifying patients to adjuvant postoperative treatments or for comparing homogeneous groups of patients in retrospective studies. Several studies have investigated the prognosis of patients with gastric cancer and have identified some prognostic variables which are patient-related [1, 3, 4, 6, 14, 15] or clinico-pathological [1, 5–8, 15, 16]. Nevertheless, to our knowledge, no analysis tried to assemble in a prognostic score the joint effect of a set of variables in order to obtain a more comprehensive prognosis of gastric cancer patients with curative resection. Consequently, most of the approaches usually adopted to estimate prognosis by results of univariate or multivariate analyses are questionable.

Tables 4 and 5 report in fact that sometimes N+ patients (who are reported to have a notoriously poor prognosis) can appear in the most favourable group (5 year survival ≥ 70%) if N+ is associated with other favourable variables. In contrast some N− patients can be included in group III, if other adverse variables are present such as high location of the tumour and deep penetration in the gastric wall.

The scoring system we present takes into account four prognostic variables: age, invasion of the gastric wall, localisation of tumour, and nodal status, the pertinent role of each of which has been evaluated by a multiple regression analysis of a homogeneous series of patients prospectively included in a multicentre randomised trial (training set of patients). The validation of the score, which relies on variables which are easily evaluated in any institution, has been tested on a second series of patients (testing set) confirming its reliability in predicting survival (see Fig. 4).

A clear advantage of this score, besides its simplicity, is that it enables a classification of the patients into three groups which are clinically well differentiated from the prognostic point of view: in fact, results of surgery in risk group I are quite satisfying and it is unlikely that an adjuvant therapy could be demonstrated to improve the prognosis. In any case, any adjuvant treatment could be proposed only if toxicity is minimal and patients compliance is high. In contrast, patients in risk group III have such a poor prognosis that further treatments are urgently needed to improve the outcome and a higher degree of toxicity or iatrogenic risk appear to be acceptable. Risk group II patients represent an intermediate category in which any further decision can be more accurately tailored to the individual patient.

Unfortunately, the scoring is available and valid only if patients are resected for cure and nowadays there is no real possibility to know preoperatively the nodal status and the degree of tumoral penetration in the gastric wall, even though recent progress in image technology and especially endoscopic sonography [17] has proved to be highly accurate (81–85%) in defining preoperative nodal status and T levels in preliminary investigations.

1. Bozzetti F, Bonfanti G, Morabito A, *et al.* A multifactorial approach for the prognosis of patients with carcinoma of the stomach after curative resection. *Surg Gynecol Obstets* 1986, **162**, 229–231.
2. Baba H, Korenaga D, Okamura T, *et al.* Prognostic factors in gastric cancer with serosal invasion: univariate and multivariate analyses. *Arch Surg* 1989, **124**, 1061–1064.
3. Cunningham D, Hole D, Taggart DJ, *et al.* Evaluation of the prognostic factors in gastric cancer: the effect of chemotherapy on survival. *Br J Surg* 1987, **74**, 715–720.
4. Korenaga D, Okamura T, Saito A, *et al.* DNA ploidy is closely linked to tumour invasion, lymph node metastasis and prognosis in clinical gastric cancer. *Cancer* 1988, **62**, 309–313.
5. Serlin O, Keehn RJ, Higgins GA Jr, *et al.* Factors related to survival following resection for gastric carcinoma. Analysis of 903 cases. *Cancer* 1977, **40**, 1318–1329.
6. Curtis RE, Kennedy BJ, Myers MH, *et al.* Evaluation of AJC stomach cancer staging using the SEER population. *Seminars in Oncology* 1985, **12**, 21–31.

7. De Mello J, Struthers L, Turner R, *et al.* Multivariate analyses as aids to diagnosis and assessment of prognosis in gastrointestinal cancer. *Br J Surg* 1983, **48**, 341–348.
8. Shiu Man H, Perrotti BS, Brennan MF. Adenocarcinoma of the stomach: A multivariate analysis of clinical, pathologic and treatment factors. *Gastroenterology* 1989, **36**, 7–12.
9. The Italian Gastrointestinal Tumour Study Group. Adjuvant treatments following curative resection for gastric cancer. *Br J Surg* 1988, **75**, 1100–1104.
10. TNM. *Classification of Malignant Tumours*. International Union Against Cancer, 1987. Eds Hermanek and Sobin: 4th edition.
11. Kaplan EL, Meier P. Non parametric estimation from incomplete observations. *J Am Stat Assoc* 1958, **53**, 457–481.
12. Mantel N. Evaluation of survival data and two new rank order statistics arising in its considerations. *Cancer Chemother Rep* 1966, **50**, 163–170.
13. Lawless JS. *Statistical Models and Methods for Life-time Data*. JS Lawless ed. New York, John Wiley and Sons, 1982.
14. Soreide O, Lillestol J, Viste A, *et al.* Factors influencing survival in patients with cancer of the stomach. *Acta Chir Scand* 1982, **148**, 367–372.
15. Bedikian AY, Chen TT, Khankhanian N, *et al.* The natural history of gastric cancer and prognostic factors influencing survival. *J Clin Oncol* 1984, **2**, 305–310.
16. Lavin PT, Brukner HW, Plaxe SC, *et al.* Studies in prognostic factors relating to chemotherapy for advanced gastric cancer. *Cancer* 1982, **50**, 2016–2023.
17. Tio TL, Schouwink MH, Cikot RJLM, Tytgat GNJ. Preoperative TNM classification of gastric carcinoma by endosonography in comparison with the pathological TNM system: a prospective study of 72 cases. *Hepato-gastroenterology* 1989, **36**, 51–56.
18. SAS User's Guide; Statistics Lifereg Procedure (The). 1981. In: Release 6.03 Edition.

APPENDIX

The Weibull model incorporating covariates

Let T be the survival time and x_j the vector of covariates of the jth patient; if there are p covariates then x_j, is a $p+1$ column vector, the first element of which is taken as 1 to represent the intercept and the other elements are the values of the p covariates.

In our series, the examination of the plot of ln $\{-\ln[S(t)]\}$ [where $S(t)$ is the Kaplan–Meier estimate of the survival curves] against ln time for each level of the factors studied suggested that the Weibull model might serve for a parametric modelling of the data.

For this model the cumulative survival probability of the jth patient at time t is:

$$S(t,x_j) = \exp(-r_j t^{1/k}) \tag{A1}$$

and the corresponding hazard function is:

$$h(t,x_j) = r_j(1/k)t^{(1/k)-1} \tag{A2}$$

where:

$$r_j = \exp\left[-1/k\,(\beta_0+\beta_1 x_{1j} + \ldots + \beta_p x_{pj})\right] \tag{A3}$$

and k is a parameter modelling the hazard function. If $k > 1$ (< 1) the hazard decreases (increases) in time and if $k = 1$ the hazard is constant and the Weibull model reduces to the exponential one. The maximum likelihood method has been used to estimate the parameters K and β by resorting to the LIFEREG procedure of SAS [19].

All the variables presented in Table 1 were categorical and the whole set was inserted in the initial linear predictor. A backward selection procedure was then adopted to get the more parsimonious model. To remove a variable the corresponding P value (likelihood ratio test) had to be greater than 10%. The variables inserted in the initial model were coded as follows: age (0 = $\leq$ 60 years; 1 = $>$ 60 years), sex (0 = males, 1 = females), wall invasion [(0,0) = pT1; (1,0) = pT2; (0,1) = pT3 − 4], localisation of tumour [(0,0) = lower third; (1,0) = other; (0,1) = upper third], histological type [(0,0) = mixed; (1,0) = intestinal; (0,1) = diffuse], nodal status (0=N−; 1=N+). It is to be remembered that for each variable the reference category is the one at better prognosis.

The regression coefficients pertinent to the variables retained in the final model are reported in Table 2.

The value of k is 0.88 and indicates an increasing death rate with time from surgery. Though this value differs from 1.0 at the significance level of 6.7% (one tailed test) it tends to indicate that the death rate cannot be considered constant.

Identifying risk groups

As previously mentioned, the quantity $x_j'\beta$ can be used as a prognostic score and, from a clinical point of view, it appears sensible to identify a limited number, say L, of risk groups for patients with similar prognosis.

To this end, one must select $(L-1)$ cut points in terms of survival probability $(S_1, S_2, \ldots, S_{L-1})$ at a given time t^*. After deleting j for the sake of simplicity, from A1 and A3 the following expression can be derived:

$$x'\beta = \ln(t) - k\ln\{-\ln[S(t,x)]\}. \tag{A5}$$

Since $x'\beta$ includes the intercept parameter β_0 for all patients, this value can be subtracted to find the cut points which define the risk groups.

Let c_l be the l-th cut point

$$c_l = \ln(t) - k\ln\{-\ln[S(t,x)]\} - \beta_0. \tag{A6}$$

Inserting t^* and $S_1, S_2, \ldots$ and S_{L-1} in this latter, one gets $L-1$ value $(c_1, c_2, \ldots, c_{L-1})$ which enables dividing the distribution of $x'\beta$ in L groups.

In the present context, the choice of t^* and of two values of $S(t)$ (S_1, S_2) has been made in terms of clinical considerations.

Namely, $t^* = 60$ months and $S_1 = 0.70$ and $S_2 = 0.30$ corresponding to $c_1 = -1.19$, $c_2 = -2.25$, respectively.

Finally, to obtain the easy-to-handle score given in Table 3 for the prognostic factors retained in the final model, the value of each regression coefficient and of the cut points was divided by the smallest regression coefficient and the results were rounded to the nearest integer, or to the nearest integer +0.5 (for instance: wall invasion pT3–4 score = $-1.14/-0.32 = 3.56$ 3.5; N+ score = $-0.94/-0.32 = 2.94 \simeq 3$; $c_1 = -1.19/-0.32 = 3.71 \simeq 3.5$; $c_2 = -2.25/-0.32 = 7.05 \simeq 7$).