Prognosis of Gastric Carcinoma after Curative Surgery
A Population-Based Study Using Multivariate Crude and Relative Survival Analysis

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A population-based series of 246 gastric cancer patients operated for cure and who survived the postoperative phase was reviewed to determine prognostic factors after potentially curative treatment. The overall five-year observed survival rate was 34.8%, and the relative survival rate was 43.9%. Previous history of gastric ulceration, tumor location, tumor size, gross appearance, extension within the gastric wall, and number of proximal lymph nodes involved were significantly related to both crude and relative survival rates. Age was a significant prognostic factor when considering crude survival rates, but it had no influence on relative survival rates. Multivariate analysis of crude and relative survival gave similar results except for age. The covariates retained in the final model were, by decreasing importance, extension within the gastric wall, lymph node involvement, gross appearance and tumor location. Combining the two major prognostic criteria, tumor extension through the gastric wall and lymph node involvement, four prognostic categories could be determined with five-year corrected survival rates ranging from 92% in patients with a carcinoma limited to the gastric wall to 17% in patients with more than two positive nodes whatever the extension in the gastric wall. Gross appearance had no influence on prognosis for carcinomas limited to the gastric wall, but had a significant impact on prognosis of more extended carcinomas. From these data, a simple staging system requiring only routinely available pathological data was proposed. This classification could be helpful for planning multicenter clinical trials on this disease where progress in therapy is needed.

KEY WORDS: gastric carcinoma; prognosis; multivariate analysis; relative survival.

Primary therapy for gastric carcinoma is surgical resection. The influence of clinical and pathological factors on survival rates after potentially curative surgery for gastric carcinoma has been the subject of many investigations. Identifying prognostic factors in resected gastric carcinoma is necessary to predict the outcome of patients and to stratify populations entering clinical controlled trials. There are few published reports on prognosis of all gastric carcinoma diagnosed in an unselected population. Most reports are hospital-based and cannot be used as reference values because of possible selection bias (for example concerning age, stage of diagnosis, health status, social status, place of residence).
Recent studies have used the Cox multiple regression model of crude survival to establish the relative importance of several prognostic factors. This model does not take into account the natural increasing mortality with advancing age. Recently available multivariate models of relative survival may be of great interest. The goals of this study, which used the data from the population-based Cancer Registry of the Côte d’Or (France), were to document patterns of survival after potentially curative surgery of gastric carcinoma using crude and relative survival models and to propose a prognostic scale based on these findings.

MATERIALS AND METHODS

Patients
A population-based registry, including all digestive tract tumors, covers the resident population of the Côte d’Or area, France (480,000 residents according to the 1982 census) (1). A total of 753 gastric carcinomas were diagnosed among Côte d’Or residents in the 1976–1985 period, corresponding to age-standardized incidence rates of 13.7 per 100,000 in males and 5.3 per 100,000 in females. Of the 753 gastric carcinomas, 305 were resected for cure. Surgery was considered curative when the primary tumor was completely removed with tumor-free margins and no evidence of distant metastases. In order to delineate the factors that interfere with long-term prognosis after curative surgery (ie, mostly cancer recurrence), the 59 patients who died in the postoperative phase (death within 30 days after surgery), usually of causes unrelated to the cancer itself, were excluded from the analysis. The 448 patients who were not operated for cure had one-year and five-year survival rates of 15.6% and 0%, respectively.

All original histologic slides, except for 11 cases diagnosed outside the area, were double-checked by one university pathologist. The gross morphological appearance was classified according to Borrman’s classification (2). Microscopic features were defined according to the WHO classification (3). Tumor extension (unknown in two cases) was classified as limited to the mucosa and the submucosa, involvement of the muscularis propria, and involvement of the serosa. The number of involved lymph nodes was known in all cases.

Methods
Survival data were obtained from the patients’ medical files and death certificates. The living status of all patients was known at the end of follow-up, August 1988. Crude and relative survival were studied. Relative survival, which corrects for the mortality of a population similar in age and sex distribution except for having the studied disease, is considered the best approach to the notion of net mortality, ie, mortality strictly due to the disease. Indeed, it is usually unfeasible to record the exact causes of death for all cases in the absence of systematic autopsies, and net mortality tends to underestimate the mortality rate as the cancer may be indirectly responsible for some deaths such as pulmonary embolism. As it has been recommended for studying cancer mortality (4), the model chosen for this study is an additive relative survival model, considering that the mortality due to the cancer adds to the mortality due to other causes.

Univariate Analysis. Observed survival rates were computed by an actuarial method and univariate comparisons were performed using the log-rank test. Corrected survival rates were computed using the Hakulinen software (5), which also computes the loss in life expectancy for each studied category of patients. Relative survival curves were established for the same variables as for observed survival and were compared by the maximum likelihood ratio test. Baseline probability of survival and life expectancy of the French population was provided by sex and year of age for the studied period by the INSEE (National Institute for Statistics and Economic Sciences).

Multivariate Analysis. Multivariate analysis was performed on crude survival using the Cox model (6) and on relative survival using the model developed by Hakulinen and Tenkanen (7). The variables tested in both models were age, sex, and all variables significant at the 5% level in the univariate analysis. The proportionality of risks along the studied period, which is a prerequisite for both multiple regression models, was tested for each covariate using a graphical method. The model for crude survival and the model for relative survival were both built up by forward stepping; the significance of the covariates was tested by the change in the log likelihood for the Cox model and the change in the deviance in the Hakulinen model. The follow-up time was divided into one-year periods, and survival rates were computed for the first five years of follow-up.

The computations were performed using the 1L and 2L programs of the BMDP statistical software (8) and the Hakulinen software (5) implemented on the Microvax II (VMS system) at the registry of digestive cancers of Côte d’Or.

RESULTS

Univariate Analysis

Observed Survival Rates. Observed survival rates after surgery for cure for gastric carcinomas excluding postoperative mortality were 71.5% at one year, 42.3% at three years, and 34.8% at five years. There was no sex difference in prognosis (Table 1). Age was a significant prognostic factor: patients older than 70 had a lower survival curve than younger patients (P < 0.001). Patients living in urban areas survived longer than patients living in rural areas, and patients with a previous history of gastric ulceration had a better survival than the other patients (P < 0.05). Carcinomas located in the antrum and the body had similar survival rates; their survival curve was significantly better than the