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Original article

Subtotal versus total gastrectomy for T3 adenocarcinoma of the antrum

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Abstract

Background. **The role of subtotal or total gastrectomy in the treatment of advanced gastric cancer of the antrum with serosal invasion was investigated.**

Methods. **The investigation involved 117 patients with a cancer of the lower third of the stomach invading the serosa (pT3) who underwent R0 resection with at least D2 lymphadenectomy between 1988 and 1998 at three different Italian centers. The choice of surgical procedure (40 total gastrectomies and 77 subtotal gastrectomies) was based on the preference of the surgeon; none of the patients underwent splenectomy. The Cox regression model was used to evaluate the prognostic significance of the type of surgery (subtotal versus total gastrectomy), controlling for age, sex, histology, nodal involvement, and surgical center.**

Results. **The morbidity and mortality rates did not vary significantly according to the type of surgery. Patients undergoing subtotal gastrectomy presented a better disease-related survival than patients undergoing total gastrectomy ($P = 0.011$): the median survival times were, respectively, 38 months and 23 months, and the overall cumulative 5-year survival rates (95% confidence intervals [CI]) were, respectively, 36% (22%–50%) and 22% (11%–37%). On univariate analysis, the relative risk (RR) of disease-related death was 1.84 (1.14–2.97) after total gastrectomy, with respect to subtotal gastrectomy. This difference was blunted on multivariate analysis (RR, 1.66; 0.99–2.78): in the final model, only nodal metastasis was a significant prognostic factor, while type of surgery had a borderline significance ($P = 0.057$).**

Conclusion. **Survival after subtotal gastrectomy is not lower than that after total gastrectomy in patients with tumor of the antrum invading the serosa.**

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Introduction

The choice between total gastrectomy and subtotal gastrectomy for carcinoma of the lower third of the stomach remains a matter of debate among surgeons.

The argument for total gastrectomy is that it shows better locoregional tumor control, whereas the argument for subtotal gastrectomy includes lower postoperative morbidity and mortality with a better quality of life.

In the 1980s, two randomized trials, comparing the survival rates for total gastrectomy and subtotal gastrectomy for distal gastric carcinoma were carried out, and they reported a similar 5-year survival rate for the two procedures [1,2]. However, it should be pointed out that, in the above-mentioned studies: (a) early gastric cancer patients were also enrolled; (b) splenectomy was frequently associated with total gastrectomy; and (c) in both studies, a D2 lymphadenectomy was performed, but the number of excised nodes was not mentioned, and this number constitutes a kind of quality control for this surgical procedure. For these reasons, the results of these trials have not been fully applied to clinical practice, and in many European centers total gastrectomy is still the treatment of choice for advanced antral cancer, especially that of the diffuse type according to the Lauren classification [3–5].

To estimate the role of subtotal or total gastrectomy in the treatment of advanced gastric cancer of the antrum with serosal invasion (T3) a prospectively documented multicenter study was performed in patients who underwent potentially curative resection.

Patients

Between January 1988 and December 1998, 1147 patients with histologically proven primary gastric carcinoma underwent surgical treatment at three Italian centers: Verona and Forlì in northern Italy, and Siena in central Italy. Of these patients, 921 underwent potentially curative resection with complete macroscopic and microscopic removal of the tumor (Verona, $n = 236$; Forlì, $n = 409$; Siena, $n = 276$). Among these 921 patients, the present study recruited the 117 subjects (12.7%) who had an advanced cancer invading the serosa (pT3) located in the gastric antrum and who underwent at least D2 lymphadenectomy. The antrum was defined by the anatomic limits of the pylorus and a transverse line drawn at the junction of the vertical and horizontal segments of the lesser curvature.

The mean (±SD) age of the patients was 66.3 ± 11.9 years; the male-to-female ratio was 1.4:1 (69 men and 48 women). The patients were followed prospectively through the outpatient clinics, which they attended regularly at least once every 4 months. All information on demographic and clinical characteristics used in the present analysis was stored in a computerized database at the time of surgery.

Patients were staged according to the pathologic classification (pTNM) of the International Union Against Cancer 1997 [6], and the histological classification followed the criteria of Lauren.

Lymph node dissection was classified according to the Japanese Gastric Cancer Association (JGCA) rules: D_2 lymphadenectomy (resection of nodes of groups 1 and 2) and D_3 lymphadenectomy (resection extended to the nodes of group 3) [7]. Of the 117 patients, only 1 (0.9%) had fewer than 15 nodes examined and, strictly speaking, he could not be staged according to the new TNM classification. However, as he had 8 positive nodes out of 13 examined, he was classified as pN2.

The choice of surgical procedure (total or subtotal gastrectomy) was based on the preference of the surgeon. None of the patients underwent splenectomy, which is not indicated for cancer located in the lower third of the stomach [8,9].

Statistical analysis

Differences in baseline characteristics between patients undergoing subtotal or total gastrectomy were evaluated for continuous variables by *t*-test when normally distributed, by Mann-Whitney test otherwise, for nominal variables by χ^2 test or Fisher exact test, and for ordinal variables by χ^2 test for trend.

Survival data included postoperative mortality, while deaths from causes other than gastric cancer were considered as censored observations at the time of death. None of the patients was lost to follow-up.

The probability of survival was calculated according to the Kaplan-Meier method [10], and different survival curves were compared through the log-rank test. The Cox regression model was used to evaluate the prognostic significance (likelihood ratio test) of the type of surgery (subtotal versus total gastrectomy), controlling for age, sex, histological type (intestinal versus diffuse), nodal involvement, and surgical center [11]. The relative risk for the continuous variable (age) was calculated on the basis of an increase in the values of 1 SD. The assumption of proportional hazards over time was checked by a graphic method and it was found to be reasonable for all the prognostic factors considered.

Results

Three patients died within the first 30 postoperative days (operative mortality, 2.6%) and 17 patients developed general and surgical complications in the postoperative period (morbidity, 14.5%). The morbidity and mortality rates did not vary significantly according to the type of surgery (Table 1).

The median follow-up for surviving patients was 39.7 months (range, 14.5–105.6 months).

Table 1. Postoperative morbidity and mortality according to the extent of surgery

	Subtotal gastrectomy	Total gastrectomy	*P* value
Mortality	1/77 (1.3%)	2/40 (5%)	0.269
Complications			
Intraabdominal abscess	1	1	
Anastomotic leakage	1	1	
Duodenal stump leakage	1	—	
Pancreatic fistula	2	1	
Necrotizing pancreatitis	1	—	
Hemorrhage	1	—	
Cardiopulmonary	4	3	
Total rate	11/77 (14.3%)	6/40 (15.0%)	0.917

Table 2. Main demographic and baseline clinical characteristics of the 117 patients under study subdivided according to the type of surgery

Variables	Subtotal gastrectomy; $n = 77$ (%)	Total gastrectomy; $n = 40$ (%)	P value
Sex			
Male	46 (59.7)	23 (57.5)	0.81
Female	31 (40.3)	17 (42.5)	
Age (years; mean ± SD)	68.1 ± 11.3	62.9 ± 12.4	0.025
Size (mm; mean ± SD)	56.1 ± 24.1	61.1 ± 29.3	0.326
Histology			
Intestinal	47 (61.0)	21 (52.5)	
Diffuse	30 (39.0)	19 (47.5)	0.37
Nodal involvement			
N0	18 (23.4)	4 (10.0)	
N1	28 (36.4)	15 (37.5)	0.086
N2	16 (20.8)	9 (22.5)	
N3	10 (13.0)	8 (20.0)	
M1 lym	5 (6.5)	4 (10.0)	
Number of Dissected nodes (mean ± SD)	31.2 ± 12.5	35.5 ± 15.3	0.11
Number of positive nodes (mean ± SD)	7.5 (8.1)	11.3 (11.0)	0.034
Center			
Siena	26 (33.8)	7 (17.5)	
Forlì	40 (51.9)	17 (42.5)	0.005
Verona	11 (14.3)	16 (40.0)	

The characteristics of the study population and the details of the numbers of dissected and metastatic nodes for each type of surgical procedure are listed in Table 2. The overall number of excised lymph nodes amounted to 3824, yielding a mean ±SD of 32.7 ± 13.6 lymph nodes per patient (median, 30; interquartile range, 23–40.5). The mean number of metastatic lymph nodes amounted to 8.8 ± 9.4 per patient (median, 6; interquartile range, 1–14), corresponding to 26.9% of all excised lymph nodes. The type of surgery had no influence on the mean number of dissected nodes; nevertheless, the mean number of positive nodes was significantly higher in patients undergoing total gastrectomy (11.3 ± 11.0; median, 6.5; interquartile range, 4–18.5) than in patients undergoing subtotal gastrectomy (mean, 7.5 ± 8.1; median, 6; interquartile range, 1–10; $P = 0.034$). This difference was blunted when expressed as pN tiers (χ^2 for trend; $P = 0.086$). Moreover, patients undergoing total gastrectomy (62.9 years) were younger than the other patients (68.1 years). Total gastrectomy was the procedure of choice in Verona (59% versus 41%), while in Forlì and Siena subtotal gastrectomy was usually applied (respectively, 79% and 70% versus 21% and 30%). The two groups were well matched for the other variables considered (sex and histology).

As shown in Fig. 1, patients undergoing subtotal gastrectomy presented a better disease-related survival than patients undergoing total gastrectomy (log-rank test; $P = 0.011$): the median survival times were, respectively, 38 months and 23 months, and the overall cumulative 5-year survival rates (95% confidence intervals [CI]) were, respectively, 36% (22%–50%) and 22% (11%–37%).

According to the Cox model, patients undergoing total gastrectomy presented a worse prognosis than the other patients: on univariate analysis the relative risk (RR) of disease-related death was 1.84 (1.14–2.97) after total gastrectomy, with respect to subtotal gastrectomy ($P = 0.015$). This difference persisted after controlling for sex, age, histology, and center (RR = 1.84; 1.11–3.03; $P = 0.020$), and was blunted after also controlling for nodal metastasis (RR = 1.66, 0.99–2.78); in the final model, only nodal metastasis was a significant prognostic factor, while type of surgery had a borderline significance ($P = 0.057$; Table 3).

In order to reduce baseline differences between the two groups of patients, we focused on node-positive patients with fewer than 28 positive nodes ($n = 91$). In this way, the two groups also became rather comparable with respect to the number of positive nodes (9.4 ± 7.6 in the subtotal gastrectomy group and 10.3 ± 7.8 in the total gastrectomy group; $P = 0.605$). The results of survival analysis were somewhat blunted: total gastrectomy was associated with a higher risk of disease-related death (RR = 1.53; 95% CI, 0.90–2.60), although the difference was not significant ($P = 0.122$).

Discussion

The main results of the present study were: (1) in the present series comprising patients with advanced cancer

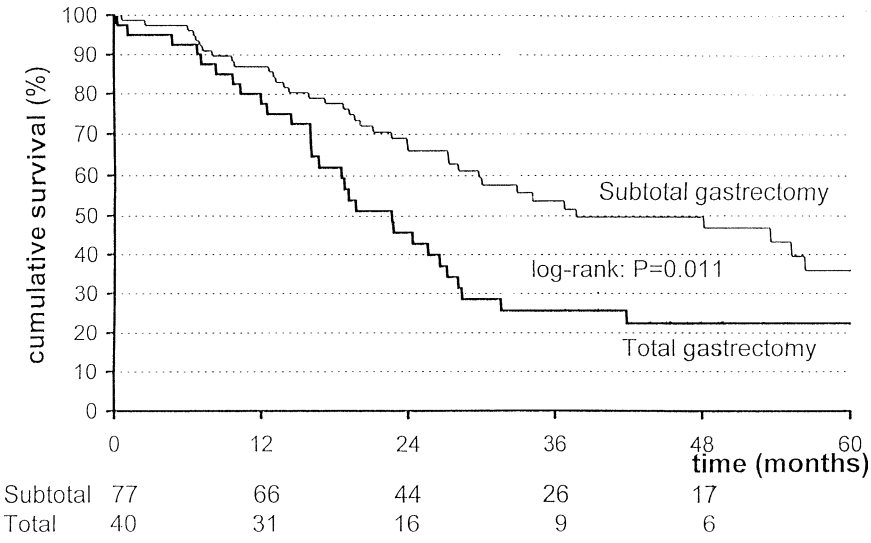

Fig. 1. Survival distribution of patients according to type of surgery; Kaplan-Meier plot

Table 3. Relative risks (95% confidence intervals in parentheses) of death from gastric cancer in the 117 patients who underwent R0 resection

Variables	Relative risk adjusted for all other variables	*P* value
Sex (women vs men)	0.82 (0.47–1.43)	0.48
Age (SD = 11.9 years)	1.21 (0.88–1.66)	0.24
Histology (diffuse vs intestinal)	0.61 (0.35–1.07)	0.084
Metastatic Nodes		
N1 vs N0	12.7 (1.7–95.4)	
N2 vs N0	31.7 (4.2–240.5)	<0.001
N3 vs N0	76.6 (9.8–599.6)	
M1lym vs N0	37.2 (4.4–313.4)	
Center		
Forlì vs Siena	0.71 (0.35–1.42)	
Verona vs Siena	1.45 (0.73–2.90)	0.115
Surgery		
TG vs SG	1.66 (0.99–2.78)	0.057

Relative risks and significance of differences (likelihood ratio test) were derived from the Cox regression model, controlling for all other variables. Calculation of the relative risk for age was based on an increase in the values of 1 SD
TG, total gastrectomy; SG, subtotal gastrectomy

of the antrum, survival after subtotal gastrectomy was higher than that after total gastrectomy; (2) however, as the study was not randomized, subtotal gastrectomy was preferentially performed in older patients and when the surgeon perceived that the disease was less aggressive, as suggested by the lower number of positive nodes but not of excised nodes; (3) when controlling for nodal involvement and other risk factors and when selecting only node-positive patients with fewer than 28 positive nodes, the survival advantage associated with subtotal gastrectomy was blunted but not completely abolished; (4) taking into account the limitation of the study design (lack of randomization), a careful conclusion could be that survival after subtotal gastrectomy is not lower than that after total gastrectomy in patients with tumor of the antrum invading the serosa.

This conclusion is in agreement with two other studies, performed in Italy and in France in the 1980s [1,2]. These studies, both randomized, found no difference in survival after total and subtotal gastrectomy.

However, in the two above-mentioned randomized trials, patients were enrolled in the 1980s when the surgical and staging procedures were rather different from the procedures nowadays.

First, in the Italian trial, splenectomy was "an optional procedure left to the preference of the surgeon" in order to allow the removal of lymph nodes along the distal splenic artery and splenic ilum and, hence, to

ameliorate the prognostic definition; splenectomy was performed in 23.7% of the patients after total gastrectomy and in 5.7% of the patients after subtotal gastrectomy. In the French study, some participating surgeons performed an elective splenectomy in patients with total gastrectomy. Nowadays, splenectomy is considered to be a procedure which has an adverse impact on surgical morbidity [12–14] and prognosis in gastric cancer patients [15,16]. Hence, splenectomy is no longer performed during surgery for cancer of the lower third of the stomach, unless the spleen is inadvertently injured during the surgical procedure [17,18].

Second, in the French study, according to the old TNM (1987), the number of positive nodes was not taken into account, while at present, the N staging is based on the number of nodes [6].

Third, the two studies did not distinguish among early, advanced, and very advanced cancer, when comparing survival after total or subtotal gastrectomy. A T1/T2 cancer was present in more than half of the patients (317/618) in the Italian study and in 42% of the patients in the French trial. It should be pointed out that, during the 1990s, the indications for total gastrectomy were progressively restricted to patients with advanced cancer of the antrum (pT3–pT4) and, consequently, the present study focused on this subgroup of patients, whereas the two above-mentioned clinical trials were also performed for early gastric cancer. Of note, the consensus among surgeons in the present trial was achieved rather independently of the findings in the two above-mentioned trials, which did not analyze the effect of subtotal and total gastrectomy separately according to stage.

In contrast, to the two studies noted above [1,2], the present observational study is in line with current surgical practice; with respect to surgical procedure, splenectomy was never performed; extended or superextended lymphadenectomy was always performed; at least 15 lymph nodes were retrieved; and cancers were staged according to the 1997 TNM classification. Moreover, the present series was rather homogeneous: only antral tumors with serosal invasion were considered.

Indeed, prognosis was more favorable after subtotal than after total gastrectomy ($P = 0.057$). However, the authors are not aware of any physiological or clinical reason why the risk of cancer relapse should be higher after total than after subtotal gastrectomy. Indeed, baseline differences between our two groups were minimized both by considering only patients with advanced antral tumor and by controlling for the most important known predictors (nodal involvement, histology) on multivariate survival analysis. However, it is possible that some unknown prognostic factors — other than T, N, histology, site, sex, and age — were not balanced between the two groups. For all these reasons, a careful conclusion could be that the prognosis after subtotal gastrectomy is not lower than that after total gastrectomy. Even though the surgical choice was not randomized, in the present study, these results could be useful in planning future randomized trials.

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