

• GASTRIC CANCER •

Adenocarcinoma of gastric cardia in the elderly: Surgical problems and prognostic factors

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CONCLUSION: As the age of the general population increases, more elderly patients with gastric cardia cancer will be candidates for surgical resection. Age alone should not preclude surgical treatment in elderly patients with gastric cardia cancer and a tumor resection can be carried out safely. Certainly, we should take care in defining the surgical treatment in elderly patients, particularly as regarding the surgical approach; although the surgical approach does not influence the survival rate, the transhiatal way still remains the best one due, to the lower incidence of respiratory morbidity and thoracic pain.

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Key words: Gastric cardia carcinoma; Esophagogastric junction carcinoma; Elderly; Surgery

Abstract

AIM: To analyze retrospectively, our results about patients who underwent surgical treatment for adenocarcinoma of the cardia in relation to age, in order to evaluate surgical problems and prognostic factors.

METHODS: From January 1987 to March 2003, 140 patients with adenocarcinoma of the cardia underwent resection in the authors' institution. They were divided into three groups with regard to age. Patients <70 and > 60 year old (31) were excluded; we also excluded 18 out of 109 patients with poor general status or systemic metastases. So, we compared 51 elderly (≥ 70 year old) and 58 younger patients (≤ 60 year old). The treatment was esophagectomy for type I tumors, and extended gastrectomy and distal esophagectomy for type II and III lesions.

RESULTS: Laparotomy was carried out in 91 patients (83.4%), 38 in the elderly (74.5%) and 53 in younger patients (91.3%, $P < 0.05$). Primary resection was performed in 81 cases (89%) without significant differences between the two groups. Postoperative death was higher in the elderly (12.1%) than the other group (4.1%, $P < 0.05$), while morbidity was similar in both groups. A curative resection (R0) was performed in 59 patients (72.8%), 69.6% in the elderly and 75% in the younger group ($P > 0.05$). The overall 3- and 5-year survival rates were 26.7% and 17.8% respectively for the elderly and 40.7% and 35.1% respectively for younger patients ($P = 0.1544$). Survival rates were significantly associated with R0 resection, pathological node-positive category and tumor differentiation in both groups.

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INTRODUCTION

In the Western world, we observe a lower incidence of gastric and esophageal cancer in contrast with the annual increase in the adenocarcinoma of the esophagogastric junction (EGJ) equal to 5-10%^[1-10]. Both for gastric adenocarcinoma and cardia cancer, we notice an increasing number of elderly patients^[11-14]. Anyway, with regard to clinicopathological features of the adenocarcinoma of the EGJ in the elderly and its surgical problems in relation to age, few data have been published in the international literature. Adenocarcinoma of the EGJ has been defined as a tumor whose center is within 5 cm proximal and distal of the anatomical cardia, and today this tumor is considered as a separate neoplasm because of its distinctive prognostic and pathological features^[4-6]. However, the surgical treatment of the cardia is still controversial, mainly regarding the extent of gastric and esophageal resection, the lymphadenectomy, the surgical approach and the importance of adjuvant chemotherapy^[4,5,15-17]. These themes are very important in order to define the treatment of old patients, especially for the increasing number of over 70 year old suffering from this neoplasm as well as from other comorbidities peculiar to old age.

The aim of this study is to analyze retrospectively, our results about patients who underwent surgical treatment for adenocarcinoma of the EGJ in relation to age, in order to

evaluate surgical problems and prognostic factors, in particular in patients over 70 year old.

MATERIALS AND METHODS

Between January 1987 and February 2003, in our Institute, we observed 140 patients with adenocarcinoma of the EGJ. They were divided retrospectively into three groups with regard to age: (1) Group A: age ≥ 70 years old; (2) Group B: age ≤ 60 years old; (3) Group C: age < 70 - and > 60 -years old.

The 31 patients of group C were excluded in order to characterize better the other two groups. Group A consists of 51 patients (44 male, 7 female), and group B 58 patients (50 male, 8 female, Table 1). A retrospective study was done on these two groups of patients.

The surgical risk has been evaluated preoperatively with ASA score^[18]. Eighteen out of 109 patients were excluded, 10 for poor general status with ASA score >3 (nine in group A, one in group B) and 8 for systemic metastases on preoperative staging (four in group A, four in group B). So, a total of 91 patients with gastric cardia cancer underwent laparotomy and only 81 underwent surgical resection. The surgical procedure was considered curative (R0), if gross tumor tissue including the metastatic lymph nodes were removed completely and the microscopic examination revealed no cancer cells at both proximal and distal margins. The procedure was considered palliative (R1), if microscopic disease was left behind. Resection specimens were assessed by an experienced pathologist. Staging is reported according to the most recent version of the UICC/AJCC guidelines for esophageal cancer (type I tumors) or gastric cancer (type II and III tumors)^[19,20].

A particular effort has been made to identify areas with intestinal metaplasia in the distal esophagus and in the region of the cardia in all resection specimens. The retrospectively collected data included demographic parameters, histomorphologic tumor characteristics, the presence of associated intestinal metaplasia in the distal esophagus (Barrett's esophagus), the type of resection, post-operative 30-d death rate, morbidity, the depth of tumor invasion (pT), the pN category, the presence of residual disease on intraoperative assessment and histopathologic analysis of the removed specimen.

Surgical approach

The choice of surgical approach was based on the tumor type and on the goal of achieving a complete macroscopic and microscopic tumor resection, both in elderly and younger patients. Regardless of the surgical approach, we have recently believed in the transhiatal approach according to Pinotti's technique as a more valid alternative than the transthoracic approach. In general, a radical transmediastinal or transthoracic en bloc esophagectomy with resection of the proximal stomach has been the procedure of choice in 14 patients with type I tumors (seven in group A, seven in group B). Radical transmediastinal esophagectomy and resection of the proximal stomach was performed by a laparotomy and wide exposure of the lower posterior mediastinum by anterior splitting of the diaphragmatic hiatus and a left

cervical incision. Extended esophagectomy was associated with proximal gastric resection in nine patients and with total gastrectomy in 5 cases. An extended total gastrectomy with transhiatal resection of the distal esophagus according to Pinotti's technique was performed in 42 patients with type III tumors. In 25 patients with type II tumors, an attempt was usually made to achieve a complete tumor resection by means of an extended gastrectomy with transhiatal resection of the distal esophagus according to Pinotti's technique. Lymphadenectomy comprised an en bloc removal of all lymphatic tissue in the lower posterior mediastinum, along the cardia, proximal two-thirds of the lesser curvature, and the fundus, and along the common hepatic and splenic artery toward the celiac axis. A transthoracic en bloc esophagectomy with resection of the proximal stomach was performed using a right posterolateral thoracotomy and laparotomy and included an extended en bloc mediastinal lymphadenectomy and an abdominal lymphadenectomy (two-field lymphadenectomy), as described above. The reconstruction after transmediastinal or transthoracic esophagectomy was performed with a narrow gastric tube or colon interposition and a cervical or high intrathoracic anastomosis. The extended total gastrectomy has always included a wide splitting of the diaphragmatic hiatus, transhiatal resection of the distal esophagus, and en bloc lymphadenectomy of the lower posterior mediastinum, in addition to a formal D2 lymphadenectomy (i.e., lymph node stations 1-11 of the Japanese classification)^[21]. A mediastinal Roux-en-Y end-to-side esophago-jejunostomy performed with a circular stapler, was the reconstruction procedure of choice, after extended total gastrectomy and distal esophagectomy.

Statistical analysis

The survival status of our patients was ascertained between January and February 2003 and the follow-up was completed.

Data are shown as prevalence or mean \pm SD. Continuous data were compared by the Mann-Whitney test, ordinal data by the χ^2 -test. Survival rate was analyzed by the Kaplan-Meier method and log-rank test. Prognostic factors were assessed by means of Cox regression analyses. $P < 0.05$ was considered significant.

RESULTS

Regarding demographic data, both groups showed a preponderance of the male sex (Group A: M/F 4.8:1; Group B: M/F 6.2:1), but the male to female ratio was higher in the younger group than in the older group ($P < 0.05$). Median age was 75.4 ± 3.1 ; (range 70-84) for over 70 year old patients and 53.7 ± 5.6 ; (range 32-60) in the other group (Table 1). The most common comorbidities in both groups were diabetes mellitus, coronary artery disease, hypertension and chronic obstructive pulmonary disease. Patients were divided into three types of tumor according to Siewert's classification (Figure 1). Laparotomy was carried out in 91 patients (83.4%), 38 in group A (74.5%) and 53 in group B (91.3%) ($P < 0.05$). Primary resection was performed in 81 cases (89%), 33 in group A (86.8%) and 48 in group B (90.5%) (Table 1). There were no differences between the two groups regarding tumor stage.

Table 1 Demographic and surgical data in 109 patients with adenocarcinoma of the EGJ

	Group A (51) ¹	Group B (58) ¹	P	Total (109)
Median age (±SD)	75.4±3.1	53.7±5.6	P<0.05	62.6±13.8
Sex ratio (M/F)	4.8/1	6.2/1	P<0.05	5.5/1
Operability (%)	38 (74.5)	53 (91.3)	P<0.05	91 (83.4)
Primary resection (%)	33 (86.8)	48 (90.5)	NS	81 (89)
Postoperative death (%)	4 (12.1)	2 (4.1)	P<0.05	6 (7.4)
Morbidity (%)	16 (48.4)	16 (33.3)	NS	32 (39.5)
Mean hospital stay (±SD)	19.3±7.1 d	18.1±6.3 d	NS	19±6.9 d

¹Group A: ≥70 years old; group B: ≤60 years old.

In type I tumor, we observed a prevalence (71.4%) of associated intestinal metaplasia in the distal esophagus (Barrett's esophagus) of elderly patients; rarely it was noticed in type II (10% *vs* 13.3%; *P*>0.05) or in type III (11.7% *vs* 3.8%; *P*>0.05, Table 2). In types II and III, there was a prevalence of grading G2 (*P*<0.05) compared to type I, independent of the age.

A curative resection (R0) was performed in 59 patients (72.8%), 69.6% in group A and 75% in group B respectively (Table 2). Three out of 59 patients treated with resection of the distal esophagus had tumor infiltration of resection margins. Fifty patients (61.7%) had positive lymph nodes, 20 in group A (60.6%) and 30 (62.5%) in group B, respectively (Table 3). Analysis of the pattern of lymphatic spread showed a most important metastatic involvement of lower posterior mediastinum and paracardial stations for type I and abdominal lymph node stations for types II and III, without significant differences between the two groups (A *vs* B: *P*>0.05). A greater percentage of positive lymph nodes was noticed in elderly patients (25% *vs* 17.6%), but it was statistically insignificant.

Postoperative death was 12.1% (4/33) in elderly patients and 4.1% (2/48) in the other group (*P*<0.05), without any correlation with sex, type of tumor, extent of resection and stage. Regardless of morbidity, there are no significant differences between the two groups. The most frequent complications were respiratory insufficiency and anastomotic leakage. The mean hospital stay (SD) was 19.3±7.1 d for group A and 18.1±6.3 d for group B (*P*>0.05, Table 1).

The overall 3- and 5-year survival rates were 26.7% and 17.8% respectively for group A and 40.7% and 35.1% respectively for group B (*P* = 0.1544, Figure 2). The worst results were observed for type I in both groups (Figures 3A and B). We noticed a difference in survival rate for types I and II between group A and B, but not significantly. As regards the type III survival rates were similar in both groups (Figures 4A-C).

Analysis of prognostic factors showed significant differences in both groups regarding: (1) tumor resection (R0 *vs* R1-2, *P*<0.05); (2) lymph node involvement (N0 *vs* N+, *P*<0.05); (3) pT categories (*P*<0.05);

Statistical analysis showed that elderly patients had lower

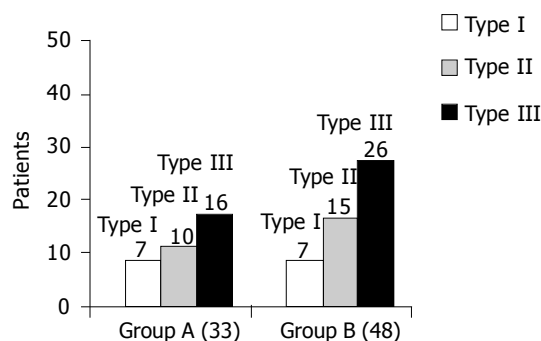


Figure 1 Subdivision of the 81 patients with adenocarcinoma of the EGJ, according to Siewert' Classification. Group A: ≥70 years old; group B: ≤60 years old. Type I A *vs* Type I B *P*>0.05; Type II A *vs* Type II B *P*>0.05; Type III A *vs* Type III B *P*>0.05.

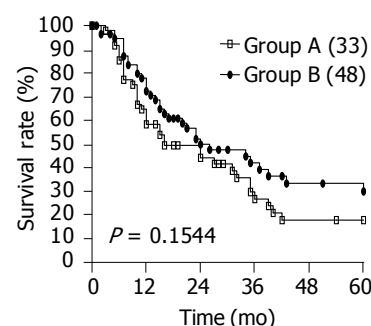


Figure 2 The 5-year survival rates of 113 patients with adenocarcinoma of the EGJ. The younger patients showed a better survival rate than the elderly (*P* = 0.1544). Group A: ≥70 years old; group B: ≤60 years old. Kaplan-Meier and log-rank test.

Table 2 Histopathologic data in 81 patients that underwent surgical resection for adenocarcinoma of the EGJ

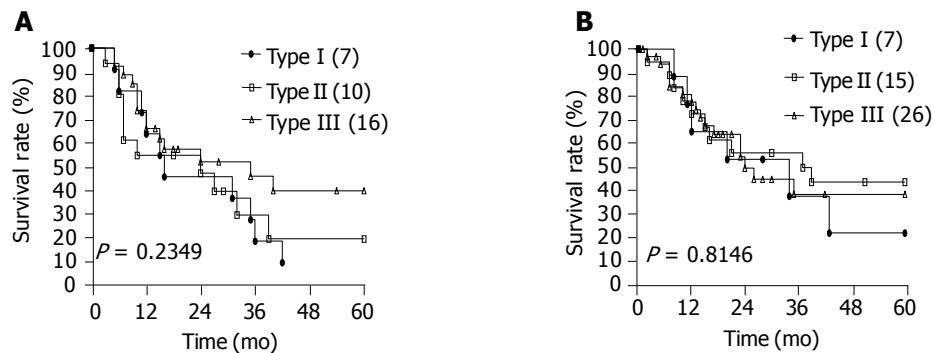
	Group A (33, %) ¹	Group B (48, %) ¹	P
Intestinal metaplasia	71.4	71.4	NS
Curative resection (R0)	69.6	75	NS
Tumor involvement of resection margin	3	4.1	NS
Lymph nodes involvement (N+)	60.6	62.5	NS

¹Group A: ≥70-years old; group B: ≤60-years old.

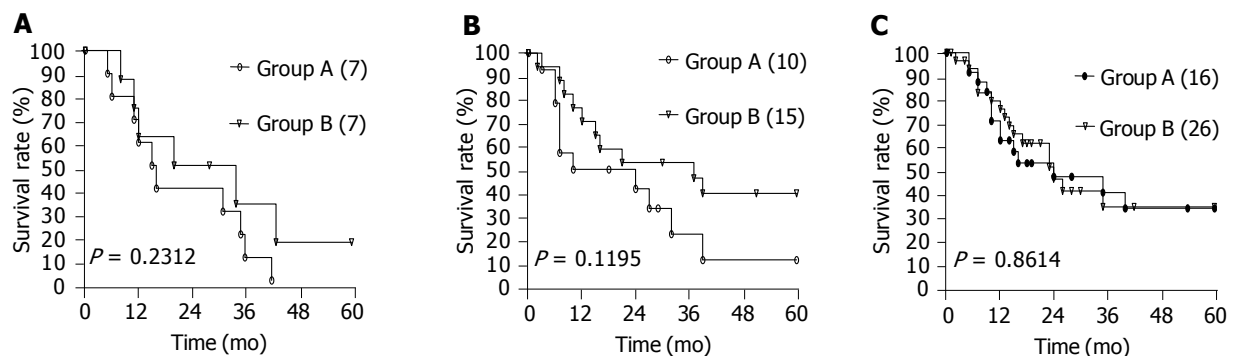
Table 3 Histopathologic data regarding pN category in 81 patients that underwent surgical resection for adenocarcinoma of the EGJ

pNcategory	Group A (33) ¹	Group B (48) ¹	P
Patients N0	13 (39.3) ²	18 (37.5) ²	NS
Patients N+	20 (60.6) ²	30 (62.5) ²	NS
Assessed lymph nodes	436	511	NS
Positive lymph nodes	109 (25) ²	90 (17.6) ²	NS

¹Group A: ≥ 70 years old; group B: ≤ 60 years old. ²Percentage in parenthesis.

**Figure 3** Survival curves according to Siewert's classification in the elderly (A) and in the younger group (B). In both groups the worst survival rate

regarding type I. Group A: ≥ 70 years old; group B: ≤ 60 years old. Kaplan-Meier and log-rank test.

**Figure 4** Survival curves according to Siewert's classification for type I (A), type II (B) and type III (C), respectively. There is a difference in survival rate

only for types I and II between groups A and B, but not of much significance. Group A: ≥ 70 years old; group B: ≤ 60 years old. Kaplan-Meier and log-rank test.

5-year survival rate both into R0 (21% *vs* 49.9%) and N0 (24.1% *vs* 70%) category ($P < 0.0001$) (Figures 5A and B). Differently, surgical approach and extent of esophago-gastric resection does not influence significantly the survival rates, both in the elderly and in the other group. The extent of esophago-gastric resection for type II tumor still remains a subject of controversy and debate. Regarding this type of tumor, we did not observe any significant improvement in patients that underwent total esophagectomy (Figure 6).

DISCUSSION

There are no major controversies in the surgical therapy of patients with esophageal and gastric cancer, but the management of patients with adenocarcinoma of the EGJ continues to be a matter of debate. Despite their rising incidence, there are marked discrepancies in the definition of such tumors, the selection of the surgical approach, and the outcome of surgical therapy^[4,6,7,15]. The classification

of Siewert, based purely on anatomical/topographic parameters, is needed for a valid comparison of data from various centers and assessment of different diagnostic and therapeutic approaches^[4-6].

Anyway, the evaluation of our surgical results in relation with age was very difficult because not much information was available in the international literature. By comparison of two groups of patients that underwent surgical resection for adenocarcinoma of the EGJ, we did not observe significant differences as regarding demographic data and survival rates. Younger patients showed a better but not a significant overall survival rate than the elderly people. In our study, this result is independent of the type of tumors, but the worst survival rate regarding type I, probably due to the inefficacious endoscopic screening in patients with EG chronic reflux disease. In elderly patients, we also observed that operability was significantly lower ($P < 0.05$) while post-operative death was higher ($P < 0.05$) than in the other group. Probably, both operability and primary

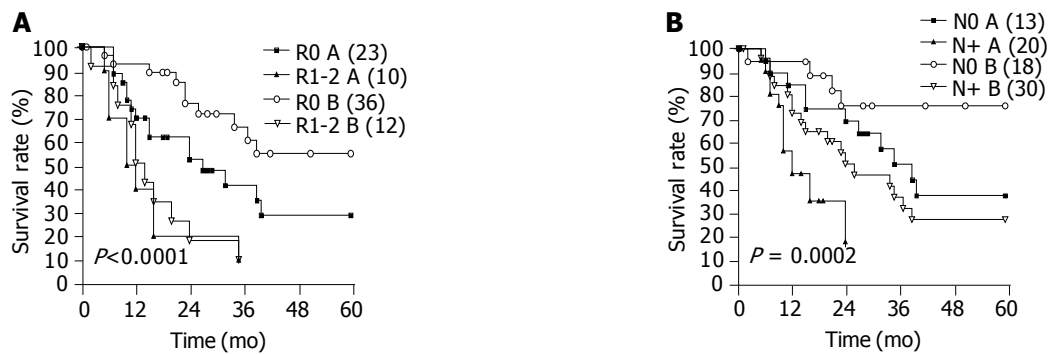


Figure 5 Overall 5-year survival rates of 81 patients with resected adenocarcinoma of the EGJ regarding type of resection (R0 vs R1-2) (A) and pN category (B). Elderly patients showed a lower 5-year survival rate than that of

younger patients, both for pN0 category and curative resection (R0). Group A: ≥ 70 years old; group B: ≤ 60 years old. Kaplan-Meier and log-rank test.

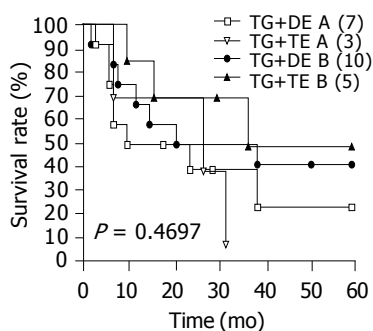


Figure 6 Survival rates of elderly and younger patients regarding the extent of esophagogastric resection for type II tumor: total gastrectomy with distal esophagectomy (TG+DE) vs total gastrectomy with total esophagectomy (TG+TE) ($P = 0.4697$). Both in the elderly and younger patients with type II tumor, total esophagectomy did not improve survival rates significantly. Group A: ≥ 70 years old; group B: ≤ 60 years old. Kaplan-Meier and log-rank test.

resection are lower in elderly patients due to their age-related comorbidity. Morbidity was higher but not significant in elderly patients^[11,22]. Unlike other authors^[11], R0 and N0 categories had significantly lower survival rates in the elderly group. It is very difficult to interpret these results, so further studies are needed. There were no differences between the two groups regarding other parameters. Moreover, in patients with type II tumor total esophagectomy did not improve survival rates^[4,5].

A radical surgery is also necessary in distal esophagectomy through a safety margin of 3 cm according to some authors or 10 cm according to others^[4,5,9,23-25]. In our experience, it is enough to have a safety distance of 5 cm from the upper margin of the tumor to ensure R0 resection. Therefore, the aim of the surgical treatment of the adenocarcinoma of the EGJ is to get a radical oncological resection, taking care of achieving R0 resection.

In conclusion, gastric cardia cancer is usually diagnosed in an advanced stage and is still associated with poor prognosis, particularly in elderly patients. As the age of the general population increases, more elderly patients with gastric cardia cancer will be candidates for surgical resection. In our study, as also observed by other authors for gastric cancer^[26], the overall survival data were similar in both groups. Survival rate is strongly linked to curative resection

(R0), lymph nodes involvement and stage of disease, which is advanced in more than half of patients. In our experience, unlike other authors, worst results regarding type I, is due to the inefficacious endoscopic screening in patients with EG chronic reflux disease which is correlated to intestinal metaplasia, independent of age. However, just like other authors^[3], we observed a high percentage of Barrett's esophagus in elderly patients over 70 years. So, endoscopic secondary prevention should be enhanced in patients with EG reflux disease and particularly in the elderly.

Other authors just observed that an oncologically correct surgical procedure can safely be prosecuted, because age alone should not preclude gastric resection in elderly patients suffering from gastric cancer^[26,27]. Regarding the adenocarcinoma of the EGJ, the extent of distal esophagectomy for type II tumor does not influence survival rates on the condition that it achieves a curative resection (R0). The role of lymphadenectomy continues to be a matter of debate. We agree with the necessity of extended lymphadenectomy by transthoracic^[28,29] approach but, its potential benefits may be nullified by an associated increase in post-operative morbidity, particularly in over 70-year-old patients. However, we believe that the transhiatal approach according to Pinotti's technique is a more valid alternative than the transthoracic approach, due to the lower incidence of respiratory morbidity and thoracic pain^[7,9,30-32]. According to some authors, in selected cases, it is also possible to perform a distal esophagectomy entirely by laparoscopy, without the need for any thoracic or cervical access^[33].

In conclusion, age alone should not preclude surgical treatment in elderly patients with gastric cardia cancer and a tumor resection can be carried out safely. Certainly, further studies are needed to confirm the peculiarities observed in elderly patients, just like lower operability and survival rates for type I-II tumors and R0-N0 categories, higher post-operative death and morbidity after thoracotomy. If these data should be confirmed, we should take care in defining the surgical treatment in elderly patients, particularly as regarding the surgical approach.

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