Diseases of the Esophagus (2000) **13,** 32–38

DISEASES OF THE ESOPHAGUS

Original article

Recurrence and survival after resection of adenocarcinoma of the gastric cardia

L. P. S. Stassen,[1] F. T. Bosman,[2] P. D. Siersema,[3] W. C. J. Hop,[4] J. G. A. M. Blomjous,[1] H. W. Tilanus[1] representing the Rotterdam Esophageal Tumor Study Group

Departments of [1]Surgery, [2]Pathology, [3]Internal Medicine and [4]Epidemiology and Biostatistics, University Hospital Rotterdam-Dijkzigt and Erasmus University Rotterdam, The Netherlands

SUMMARY. **In a retrospective study, the results after resection of carcinoma of the gastric cardia in the era without neoadjuvant therapy or extended lymph node dissection were evaluated. All 184 patients who underwent resection between January 1983 and December 1993 were included. Recurrence of disease, survival and prognostic factors were determined. The overall cumulative 5-year recurrence rate was 71% and the survival rate 23%. Multivariate analysis identified locoregional lymph node and distant metastases as the crucial prognosticators of recurrence of disease and survival. These results were similar to those from a previous study concerning our patients operated during the years 1983–88. The prognosis of a resected cardiacarcinoma has remained unchanged in our hands over the past 10 years. These results stress the importance of exploring new ways, such as the use of new diagnostic tools, to optimize preoperative patient selection and more aggressive treatment regimens to improve final outcome.**

INTRODUCTION

Treatment of adenocarcinoma of the gastric cardia carries poor survival rates. Metastatic disease is present in many patients at the time of diagnosis of the disease. Nevertheless, even when the patient cannot be cured, resection is often considered the most effective means of palliation.

Previously, we reported in a smaller series on the outcome after resection of carcinoma of the gastric cardia.[1] We decided to evaluate the data of all patients that had been operated on for this disease in the decade before the introduction of novel treatment options such as neoadjuvant therapy and extended lymph node dissection to detect any improvements in outcome compared with the previous report. If present, such improvements should mainly be attributed to advances in perioperative care. If not, this would be a strong argument in favor of exploring new ways of patient selection and treatment, using new diagnostic and therapeutic options.

Also, in the present study, an analysis was performed to identify independent factors influencing outcome after surgery. Such factors should be looked for in the preoperative work-up in an attempt to tailor the treatment to the patient.

Address correspondence to: Dr L P S Stassen (present address) Department of Surgery, Reinier de Graaf Gasthuis, Postbus 5012, 2600 GA Delft, The Netherlands.
Tel: (+31) 15 2604026; Fax: (+31) 15 2603599.

PATIENTS AND METHODS

A tumor was defined as an adenocarcinoma of the gastric cardia when it was confined to the cardia, when it was located in the fundus of the stomach and had reached the cardia, or when such tumor had crossed over to the distal esophagus. By definition, carcinoma arising in Barrett's esophagus was not included.[2] By some, the last carcinoma is considered clinically and epidemiologically a separate entity.[3]

Between 1 January 1983 and 31 December 1993, 184 patients underwent resection of their cardia carcinoma at the Department of General Surgery, Erasmus University Hospital, Rotterdam, The Netherlands. For this study, the information of the database of the Rotterdam Esophageal Tumor Study Group was used. In the same period, in 38 additional cases, resection was not performed because of the presence of metastatic lymph nodes at the celiac axis (22 cases), peritoneal metastases (14 patients), or liver metastases (two cases). These patients were excluded from the study.

In 177 patients, partial or subtotal esophagectomy was performed: in 133 with removal of the cardia and

in 44 with removal of the entire stomach. In seven cases, resection was limited to a total gastrectomy. Before 1987, esophagectomy was performed by laparotomy and separate thoracotomy with an intrathoracic anastomosis. Thereafter, the transhiatal approach with blunt dissection of the upper two-thirds of the esophagus and a cervical esophagogastrostomy with creation of a stomach tube has been preferred.[4] Perigastric lymph nodes and those around the distal esophagus and celiac axis were removed. No extended lymph node dissection was performed.

Some of our patients received radiotherapy. Before 1987, preoperative radiation therapy was given in our institution by protocol to patients with tumor invasion of the esophagus. This included 43 patients of the present series. This policy was based on studies in which a combined modality treatment strategy of preoperative radiation therapy and surgery was used for patients with esophageal cancer, suggesting superiority to surgery alone.[5,6] Until 1987, post-operative radiation therapy was administered to patients with a T3 or T4 tumor status and patients with positive lymph nodes or residual tumor at the resection margins. Later prospective studies showed no beneficial effects of pre- or post-operative radiation therapy on recurrence of disease or on survival after resection of a carcinoma of the esophagus or the cardia.[7–9] Therefore, after 1986, only selected patients in whom a macroscopically irradical resection was performed underwent post-operative radiation.

Post-operative histologic tumor classification was performed according to the TNM criteria for carcinoma of the stomach as established by the International Union Against Cancer/American Joint Committee on Cancer[10] (Tables 1 and 2). In this system, positive lymph nodes around the stomach or the distal intra-abdominal esophagus and within 3 cm of the tumor are classified as N1 nodes. N2 lymph nodes are situated perigastric, but more than 3 cm from the tumor, or around the celiac trunk, left gastric artery, splenic artery or common hepatic artery. Para-aortic and paraesophageal lymph nodes and those along the proper hepatic artery or in the splenic hilus are considered to be distant metastases.

Both locoregional recurrences and distant metastases were considered manifestations of recurrent disease. Survival rates and rates of recurrence were calculated on an actuarial basis with the Kaplan–Meier method. Comparison between these curves was made with the use of the log-rank test. Multivariate Cox regression analysis was carried out to identify independent prognostic factors. Intercurrent death-corrected survival was calculated by considering the patients who died of causes unrelated to their carcinoma as having been withdrawn from the study at the date of death; $p = 0.05$ (two-sided) was considered the limit of significance. Patient follow-up was complete.

Table 1. Stage of disease according to the 1992 pTNM classification of stomach carcinoma

IA	T1N0M0
IB	T1N1M0, T2N0M0
II	T1N2M0, T2N1M0, T3N0M0
IIIA	T2N2M0, T3N1M0, T4N0M0
IIIB	T3N2M0, T4N1M0
IV	T4N2M0, TxNxM1

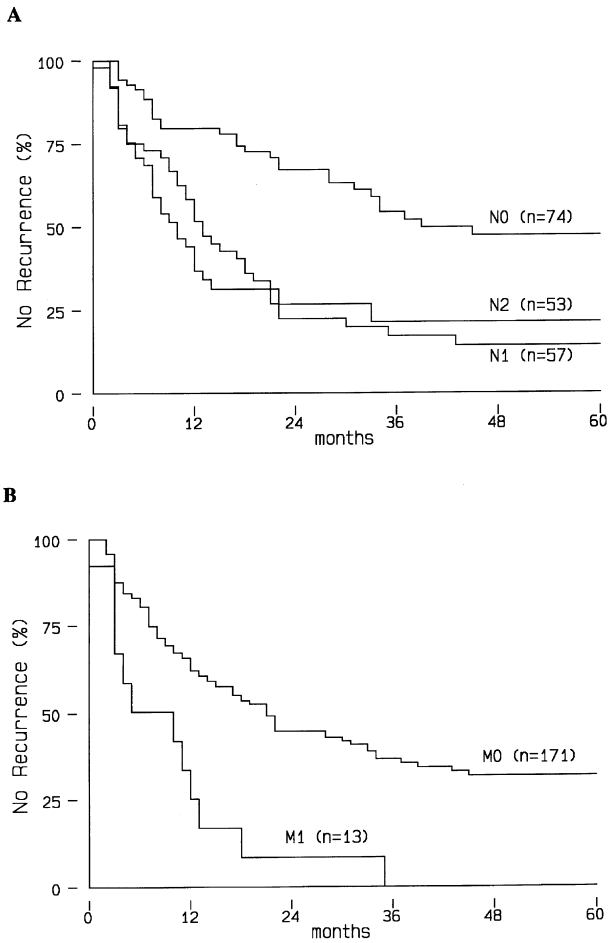

Fig. 1—Kaplan–Meier curves representing cumulative recurrence-free survival rates after resection of adenocarcinoma of the gastric cardia. Percentages (actuarial) without recurrence according to (A) N-category and (B) M-category. Percentages at 1, 2, 3, 4 and 5 years for the total study group are, respectively, 59%, 42%, 33%, 29% and 29%.

RESULTS

Of the 184 patients in this study, 157 were men and 27 women, with a mean age at operation of 62 years (range 35–85). Average length of follow-up was 26 months.

The distribution according to the subclasses of the postoperative TNM staging system is given in Table 2.

Table 2. Recurrence and survival rates after resection of adenocarcinoma of the gastric cardia

TNM* subclasses	Number of patients	Recurrence†			Survival		
		2 year (%)	5 year (%)	p-value	2 year (%)	5 year (%)	p-value
T1	8	56 (2)	56 (2)		54 (3)	36 (2)	
T2	36	47 (12)	70 (4)	0.46	65 (15)	25 (4)	0.37
T3	136	61 (37)	73 (13)		40 (45)	21 (13)	
T4	4	67 (1)	67 (1)		25 (1)	25 (1)	
N0	74	33 (36)	52 (15)	< 0.001	69 (41)	38 (15)	< 0.001
N1/2	110	77 (16)	85 (5)		27 (23)	15 (5)	
M0	171	55 (51)	68 (20)	< 0.001	48 (63)	25 (20)	< 0.005
M1	13	92 (1)	100 (0)		8 (1)	0 (0)	
R0	149	54 (46)	69 (19)	0.03	49 (57)	25 (19)	0.02
R1	31	73 (6)	82 (1)	(trend)	28 (7)	16 (1)	(trend)
R2	4	100 (0)	100 (0)		0 (0)	0 (0)	
G1	5	0 (4)	50 (2)		100 (4)	50 (2)	
G2	64	49 (23)	76 (5)	0.07	54 (28)	18 (5)	0.09
G3	105	65 (23)	71 (12)	(trend)	38 (30)	24 (12)	(trend)
G4	10	73 (2)	73 (1)		23 (2)	23 (1)	
Stage							
IA	8	56 (2)	56 (2)		54 (3)	35 (2)	
IB	18	26 (10)	61 (3)		88 (12)	32 (3)	
II	52	34 (25)	50 (10)	< 0.001	64 (28)	38 (10)	< 0.001
IIIA	57	79 (8)	85 (4)	(trend)	32 (14)	13 (4)	(trend)
IIIB	35	67 (6)	74 (1)		25 (6)	25 (1)	
IV	14	93 (1)	100 (0)		7 (1)	0 (0)	

* Defined according to the criteria for carcinoma of the stomach as established by the International Union Against Cancer/American Joint Committee on Cancer.[10]
† Cumulative (actuarial) percentage.
p-values from log-rank test. Numbers in parentheses give numbers of patients at risk after 2 and 5 years.

Recurrence

Recurrence of disease was found in 102 patients. All recurrences appeared within 4.5 years after operation. No difference in recurrence rate was observed between the different levels of tumor penetration (T-stage, Table 2). The recurrence rate was significantly higher in the presence of positive locoregional lymph nodes than when these were absent ($p < 0.001$, Fig. 1A). No difference was observed between positive nodes at the N1 or N2 location. None of the patients with metastases remained free of disease compared with 32% of those without ($p < 0.001$, Fig. 1B). With decreasing grade of radicality of resection, with decreasing grade of differentiation of the tumor or with increasing TNM stage, a trend towards a higher recurrence rate was observed.

Survival

The in-hospital mortality rate was 4.3% (eight patients). Of our study group, 121 patients died during follow-up, of whom only 14 without evidence of recurrent disease. The overall 5-year survival rate was 23%. This differed only slightly from the intercurrent death-corrected rate of 27%, indicating that only few patients died without prior recurrence of disease.

Five-year survival in relation to the TNM classification was as follows (Table 2): no difference was observed between the different T-stages; 38% of the patients without involvement of the lymph nodes survived 5 years compared with 15% with positive nodes (N1 or N2) ($p < 0.001$, Fig. 2A); 25% of the patients without metastases were alive after 5 years, but none of those in whom metastases were present ($p < 0.001$, Fig. 2B). The median survival for patients with N0 nodal status was 30 months compared with 12 months for those with N1 or N2 status; these figures were 18 and 9 months in cases of a M0 and M1 classification respectively.

As with recurrence of disease, there was a trend towards increasing survival with increasing TNM stage ($p < 0.001$). The same trend was observed with decreasing histopathologic grade of differentiation and decreasing radicality of the operation.

Multivariate analysis

T-, N- and M-category, histopathologic grade, radicality of resection, sex and age were independently evaluated in a multivariate analysis. N- and M-category were both significantly related to recurrence and survival (Table 3). Male sex and older age were also identified as risk factors for death.

DISCUSSION

'No news': perhaps this should be the rather disappointing message from the present study.

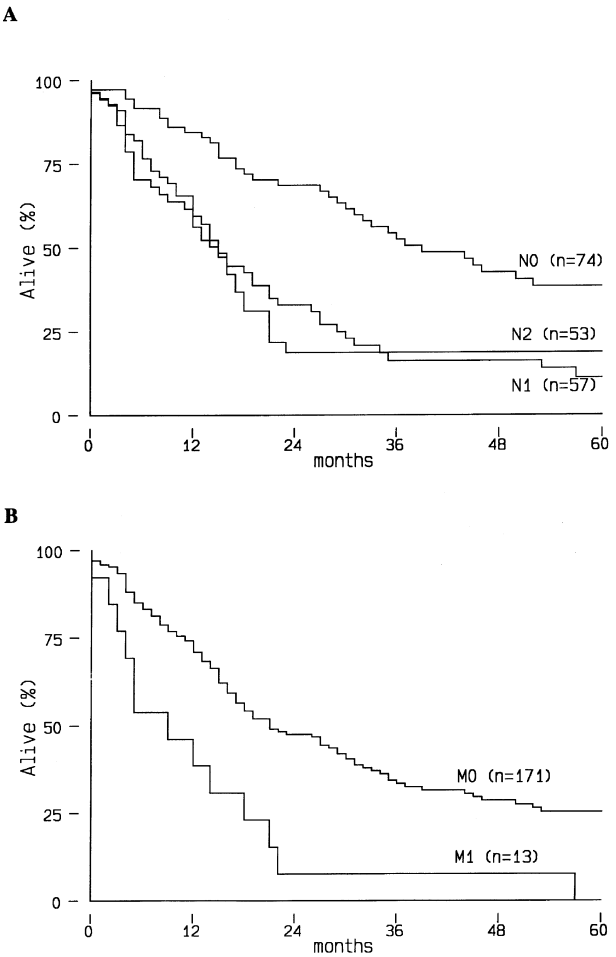

Fig. 2—Kaplan–Meier curves representing cumulative survival rates after resection of adenocarcinoma of the gastric cardia. Survival according to (A) N-category and (B) M-category. Survival percentages at 1, 2, 3, 4 and 5 years for the total study group are, respectively, 69%, 44%, 31%, 27% and 23%.

Table 3. Multivariate analysis of factors predicting recurrence or death after resection of adenocarcinoma of the gastric cardia

Prognostic factor	Relative risk (RR)	p-value
Recurrence		
Nodal status		
N0	1	
N1	2.4	< 0.001
N2	3.0	< 0.001
Metastases		
M0	1	
M1	2.0	0.03
Sex		
Male	1	
Female	0.6	0.08
Survival		
Nodal status		
N0	1	
N1	2.2	< 0.001
N2	2.7	< 0.001
Metastases		
M0	1	
M1	2.2	0.02
Histologic grade	1.4*	0.04 (trend)
Sex		
Male	1	
Female	0.5	0.01
Age		
< 56 years	1	
56–69 years	1.6	0.05
> 69 years	2.1	0.01

Reference categories are indicated by RR = 1. p-values refer to comparisons with the reference categories.
* Compared with one histologic grade higher.

The recurrence and survival rates are unchanged compared with an earlier series at our institute comprising patients operated during the years 1983 to 1988.[1] Nor are they essentially better than those reported in earlier series from other authors. In these studies on resected adenocarcinoma of the gastric cardia or gastroesophageal junction, the 5-year survival rates after resection ranged from 10% to 29%.[11–15]

Lymph node involvement and the presence of distant metastases were identified in multivariate analysis as independent factors influencing recurrence of disease and survival. This is a common finding in other series, concerning patients with cardia-carcinoma,[11] esophageal carcinoma[16,17] or both.[18–20] In these series, 5-year survival rates of patients with negative nodes ranged from 36% to 58%, compared with 38% in the present series.

Because of a growing interest in lymph node dissection and the expectation that the presence of positive nodes at the N2 location would carry a worse prognosis than cases with positive N1 nodes, the results were analyzed according to lymph node status. No difference in recurrence or survival rates could be demonstrated between N1 or N2 positive nodes. We should realize, however, that this apparent absence of difference might be due to the fact that no true extended lymph node dissection was carried out. As a result of this, the N-classification was probably not entirely accurate.

The predominance of men and age distribution correlate with other series data.[18,21] In our series, a better prognosis for women is observed. This corresponds to the findings of a large Japanese series on esophageal and cardia carcinoma.[19] This phenomenon cannot be confirmed by other series.[16,22,23] Its relevance therefore remains uncertain.

In general, we consider the presence of metastases a contraindication for resection. Nevertheless, 13 patients classified in the pTNM staging as having distant metastases underwent resection. Most of these metastases were lymph nodes that were discovered when a considerable part of the resection had already been carried out, or that were found post-operatively in the resection specimen. However, in four cases, metastases were apparent at an early stage of the operation. Resection was nevertheless carried out, as it was considered the best palliation in these patients with the combination of invalidating dysphagia, relatively young age and good physical condition.

What, then, is new? Do options exist to improve the future outcome after resection of a cardiacarcinoma?

Many efforts are put into optimizing preoperative tumor staging. Proper preoperative patient selection enables us to give the best treatment to each patient. Of special importance is the detection of metastases or positive lymph nodes and of a locally irresectable tumor. The presence of distant metastases is generally believed to be a contraindication for resection. Preoperative finding of this condition or of a locally irresectable tumor would avoid an unnecessary laparotomy. Renewed attention has been focused on the identification of suspect locoregional nodes. It has been suggested that patients with a gastric carcinoma and positive nodes might benefit from an extended lymphadenectomy.[24] If this is confirmed by future studies, preoperative identification could result in a policy of extended dissection in these selected cases.

In the past decade, several new diagnostic tools have been proven effective in enhancing the accuracy of preoperative staging, such as endoscopic ultrasonography (EUS) and laparoscopy combined with laparoscopic ultrasound (LUS). In diagnosing the T and N classification, EUS is superior to conventional staging by abdominal ultrasound or computed tomography (CT) scanning.[25–27] The sensitivity and specificity of EUS in detecting locoregional lymph node involvement range from 75% to 85% and from 70% to 88% respectively.[26,28,29] A novel approach is the use of a curved-array echoendoscope.[30] This facilitates EUS-guided biopsies of suspected lesions because the full length of the needle can be visualized.

For detecting distant lymph node metastases such as those at the celiac axis, CT scanning remains superior to EUS.[31] Van Overhagen et al.[32] found that these metastases and those in the supraclavicular region can be equally accurately assessed by conventional ultrasound or CT.

The value of laparoscopy, combined with laparoscopic ultrasound (LUS), lies in visualization of small intra-abdominal or peritoneal lesions and in improved detection of liver metastases, direct tumor extension and lymph node metastases in the retroperitoneum. Laparoscopy is more sensitive and accurate than ultrasonography and CT scanning with regard to evaluation of the hepatic status in patients with esophageal and cardia cancer.[33] It is also superior to conventional ultrasound in detecting intra-abdominal metastases and superior to CT and ultrasound in detecting peritoneal lesions.[27,33] In a series on esophageal and cardia carcinoma, 38 out of 179 patients with a normal or equivocal ultrasound (US) or CT were found to have intra-abdominal tumor spread at laparoscopy that prohibited resection.[34] In a recent series, LUS provided a better N-and M-staging than CT or endoscopic ultrasonography. The authors stress the importance of adequate staging to improve selection for operation or inclusion in neoadjuvant chemotherapy trials.[35]

Evidently, preoperative tumor staging has improved. This alone will not improve the outlook for our patients, but it enables us better to select patients for new therapeutic options.

One of the developments that seems of interest for patients with a cardiacarcinoma is neoadjuvant therapy. Concomitant preoperative radiotherapy and chemotherapy or pre- and post-operative chemotherapy can be considered neoadjuvant. Unfortunately, no reports have been published yet of its use in patients with a cardiacarcinoma. Promising data, however, are available on the combination of preoperative radiotherapy and chemotherapy for esophageal cancer. Leichman et al.[36] took the lead by publishing the concept in 1984. Since then, several groups have published their results using this treatment in both adenocarcinoma and squamous cell carcinoma of the esophagus.[37–39] The majority of these trials report a survival advantage of the therapy group over controls. Comparison between studies is difficult because of differences in preoperative staging, drugs used and estimation of response. Nevertheless, especially the observation that in a subset of patients complete disappearance of the tumor occurs, which is associated with a substantial survival benefit, is intriguing.[38–40] The feasibility of disease control and downstaging is currently being assessed for gastric cancer in the large Medical Research Council MAGIC (pre- and post-operative gastric infusional chemotherapy) Trial.

Another concept that might prove to be of benefit for our patients is extended lymph node dissection. Until now, it is theoretically promising, but its impact in the treatment of gastroesophageal cancer still has to be established. Favorable reports from Japan are well known, yet even from this country the question is raised as to whether extended lymph node dissection is truly of therapeutic benefit or merely represents a staging procedure.[41] Of course, more accurate staging is of great importance. Not only by enhancing the comparability of studies, but also by revealing differences in survival or recurrence that would have remained unnoticed with less secure staging (for example, a survival difference between N1 and N2 node-positive patients). Averbach and Jacquet[24] suggest that in stages II and IIIA gastric cancer a therapeutic advantage of extended (D2) dissection can be expected as the resection line in such dissection encompasses the N2 lymph nodes. Especially when these are free of tumor, the margin of resection is improved. On the contrary, in a limited (D1, perigastric nodes only) lymph node dissection, the resection is carried out through tissue harboring cancer in half of the patients.[42] Nevertheless, the problem of increased post-operative morbidity and

mortality has not yet been solved, thereby remaining an important argument against extended lymphadenectomy.

Finally, also concerning the possible prevention of gastric and cardia carcinoma, intriguing knowledge is emerging. This is the possible relation between *Helicobacter pylori* infection and gastric cancer that should not remain unmentioned. McFarlane and Munro[43] comprehensively summarized the possible sequence from *H. pylori* infection to the development of gastric carcinoma. The majority of patients infected will remain asymptomatic with chronic active gastritis. A minority will progress to atrophic gastritis, which can subsequently lead to intestinal metaplasia, dysplasia and cancer. What determines which route the infection in the individual will follow is yet to be determined. The strain of *H. pylori*, the age at acquisition of the infection and genetic and environmental factors probably all play a role. The unraveling of the sequence after infection and the influence of other factors thereupon may contribute to the prevention of gastric carcinoma.

In conclusion, the results of the present series compared with a previous series of our institute illustrate that the prognosis of our patients after resection of adenocarcinoma of the gastric cardia has remained unchanged over the past decade. This disappointing message emphasizes the importance of exploring new ways to improve these results. Enhancing the accuracy of preoperative tumor staging in combination with the application of new treatment regimes such as neoadjuvant therapy and extended dissection in selected patients might improve the outlook after resection of this disease. In order to define the exact value of such new treatment regimes, participation in prospective randomized studies, of which several are already under way, is mandatory.

References

1. Blomjous J G A M, Hop W C J, Langenhorst B L A M, ten Kate F J W, Eykenboom W M H, Tilanus H W. Adenocarcinoma of the gastric cardia. Cancer 1992; 70: 569–574.
2. Husemann B. Cardia carcinoma considered as a distinct clinical entity. Br J Surg 1989; 76: 136–139.
3. Kalish R J, Clancy P E, Orringer M B, Appelman H D. Clinical, epidemiological, and morphologic comparison between adenocarcinomas arising in Barrett's esophageal mucosa and in the gastric cardia. Gastroenterology 1984; 86: 461–467.
4. Orringer M B, Sloan H. Esophagectomy without thoracotomy. J Thorac Cardiovasc Surg 1978; 5: 643–651.
5. van Andel J G, Dees J, Dijkhuis C M, et al. Carcinoma of the esophagus. Results of treatment. Ann Surg 1979; 190: 684–689.
6. van Andel J G, Dees J, Eijkenboom W M H, et al. Therapy of esophageal carcinoma. Results from the joint group on esophageal carcinoma in Rotterdam. Acta Radiol Oncol 1986; 25: 115–120.
7. Launois B, Delarue D, Campion J P, Kerbaol M. Preoperative radiotherapy for carcinoma of the esophagus. Surg Gynecol Obstet 1981; 153: 690–692.
8. Giuli R, Sancho-Garnier H. Diagnostic, therapeutic, and prognostic features of cancer of the esophagus: results of the international prospective study conducted by the EOSO group (790 patients). Surgery 1986; 99: 614–622.
9. Gignoux M, Roussel A, Paillot B, Gillet M. The value of preoperative radiotherapy in esophageal cancer: results of a study of the EORTC. World J Surg 1987; 11: 426–432.
10. International Union Against Cancer (UICC)/American Joint Committee on Cancer. TNM-Classification of Malignant Tumours, 4th edn, 2nd revision. Hermanek P, Sobin L H, eds. New York: Springer, 1992: 45–48.
11. Paolini A, Tosato F, Cassese M et al. Total gastrectomy in the treatment of adenocarcinoma of the cardia. Am J Surg 1986; 151: 238–243.
12. Husemann B, Gall F P, Bödeker H A. Altendorf chirurgische behandlung des kardiakarzinoms. Münch Med Wochenschr 1983; 125: 61–64.
13. Hölscher A H, Siewert J R. Surgical treatment of adenocarcinoma of the gastroesophageal junction: results of a European questionnaire (GEEMO). Dig Surg 1985; 2: 1–6.
14. Hennessy T P J, Keeling P. Adenocarcinoma of the esophagus and cardia. J Thorac Cardiovasc Surg 1987; 94: 64–68.
15. Ellis Jr F H, Gibb S P, Watkins Jr E. Limited esophagogastrectomy for carcinoma of the cardia: indications, technique, and results. Ann Surg 1988; 208: 354–361.
16. Elias D, Lasser P, Mankarios H, Cabanes P A, Escudier B, Kac J. Esophageal squamous cell carcinoma: the specific limited place of surgery defined by a prospective multivariate study of prognostic factors after surgical approach. Eur J Surg Oncol 1992; 18: 563–571.
17. Roder J D, Stein H J, Siewert J R. Prognostic markers in patients with carcinoma of the esophagus. Eur J Gastroenterol Hepatol 1994; 6: 663–639.
18. Moreaux J, Msika S. Carcinoma of the gastric cardia: surgical management and long-term survival. World J Surg 1988; 12: 229–235.
19. Iizuka T, Isono K, Kakegawa T, Watanabe H. The Japanese committee for registration of esophageal carcinoma cases: parameters linked to 10-year survival of resected esophageal carcinoma in Japan. Chest 1989; 96: 1005–1011.
20. Rahamim J, Cham C W. Esophagogastrectomy for carcinoma of the esophagus and cardia. Br J Surg 1993; 80: 1305–1309.
21. Papachristou D N, Fortner J G. Adenocarcinoma of the gastric cardia. The choice of gastrectomy. Ann Surg 1980; 192: 58–64.
22. Sugimachi K, Matsuura H, Kai H, Kanematsu T, Inokuchi K, Jingu K. Prognostic factors of esophageal carcinoma: univariate and multivariate analyses. J Surg Oncol 1986; 31: 108–112.
23. Müller J M, Erasmi H, Stelzner M, Zieren U, Pichlmaier H. Surgical therapy of esophageal carcinoma. Br J Surg 1990; 77: 845–857.
24. Averbach A M, Jacquet P. Strategies to decrease the incidence of intra-abdominal recurrence in resectable gastric cancer. Br J Surg 1996; 83: 726–733.
25. Botet J F, Lightdale C J, Zauber A G, Gerde H, Urmacher C, Brennan M F. Preoperative staging of esophageal cancer: comparison of endoscopic US and dynamic CT. Radiology 1991; 181: 419–425.
26. Fok M, Cheng S W K, Wong J. Endosonography in patient selection for surgical treatment of esophageal carcinoma. World J Surg 1992; 16: 1098–1103.
27. Hölscher A H, Dittler H J, Siewert J R. Staging of squamous esophageal cancer: accuracy and value. World J Surg 1994; 18: 312–320.
28. Murata Y, Suzuki S, Hashimoto H. Endoscopic ultrasonography of the upper gastrointestinal tract. Surg Endosc 1988; 2: 180–183.
29. Dittler H J, Siewert J R. Role of endoscopic ultrasonography in oesophageal cancer. Endoscopy 1993; 25: 156–158.
30. Hunerbein M, Dohmoto M, Rau B, Schlag P M. Endosonography and endosonography-guided biopsy of upper-GI-tract tumours using a curved-array echoendoscope. Surg Endosc 1996; 10: 1205–1209.
31. Tio T L, Cohen P, Coene P P, Udding J, Den Hartog Jager F C A, Tytgat G N J. Endosonography and computed tomography of esophageal carcinoma. Gastroenterology 1989; 96: 158–160.
32. van Overhagen H, Lameris J S, Berger M Y, et al. Improved assessment of supraclavicular and abdominal metastases in

esophageal and gastro-esophageal junction carcinoma with the combination of ultrasound and computed tomography. Br J Radiol 1993; 66: 203–208.
33. Watt I, Stewart I, Anderson D, Bell G, Anderson J R. Laparoscopy, ultrasound and computed tomography in cancer of the esophagus and gastric cardia: a prospective comparison for detecting intra-abdominal metastases. Br J Surg 1989; 76: 1036–1039.
34. Molloy R G, McCourtney J S, Anderson J R. Laparoscopy in the management of patients with cancer of the gastric cardia and esophagus. Br J Surg 1995; 82: 352–354.
35. Finch M D, John T G, Garden O J, Allan P L, Paterson-Brown S. Laparoscopic ultrasonography for staging gastro-esophageal cancer. Surgery 1997; 121: 10–17.
36. Leichman L, Steiger Z, Seydel H G, et al. Preoperative chemotherapy and radiation therapy for patients with cancer of the esophagus: a potentially curative approach. J Clin Oncol 1984; 2: 75–79.
37. Bessell J R, Devitt P G, Gill P G, Goyal S, Jamieson G G. Prolonged survival follows resection of oesophageal SCC downstaged by prior chemoradiotherapy. Aust N Z J Surg 1996; 66: 214–217.
38. Vogel S B, Mendenhall W M, Sombeck M D, Marsh R, Woodward E R. Downstaging of esophageal cancer after preoperative radiation and chemotherapy. Ann Surg 1995; 221: 685–695.
39. Walsh T N, Noonan N, Hollywood D, Kelly A, Keeling N, Hennessy T P J. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. N Engl J Med 1996; 335: 462–467.
40. Mathew G, Jamieson G G. Neoadjuvant therapy for esophageal cancer. Br J Surg 1997; 84: 1185–1187.
41. Noguchi M, Miyazaki I. Prognostic significance and surgical management of lymph node metastasis in gastric cancer. Br J Surg 1996; 83: 156–161.
42. Wanebo H J, Kennedy B J, Chmiel J, Steele Jr G, Winchester D, Osteen R. Cancer of the stomach. A patient care study by the American College of Surgeons. Ann Surg 1993; 218: 583–592.
43. McFarlane G A, Munro A. *Helicobacter pylori* and gastric cancer. Br J Surg 1997; 84: 1190–1199.