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Adenocarcinoma of the Esophagogastric Junction

Results of Surgical Therapy Based on Anatomical/Topographic Classification in 1,002 Consecutive Patients

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Objective
To assess the outcome of surgical therapy based on a topographic/anatomical classification of adenocarcinoma of the esophagogastric junction.

Summary Background Data
Because of its borderline location between the stomach and esophagus, the choice of surgical strategy for patients with adenocarcinoma of the esophagogastric junction is controversial.

Methods
In a large single-center series of 1,002 consecutive patients with adenocarcinoma of the esophagogastric junction, the choice of surgical approach was based on the location of the tumor center or tumor mass. Treatment of choice was esophagectomy for type I tumors (adenocarcinoma of the distal esophagus) and extended gastrectomy for type II tumors (true carcinoma of the cardia) and type III tumors (subcardial gastric cancer infiltrating the distal esophagus). Demographic data, morphologic and histopathologic tumor characteristics, and long-term survival rates were compared among the three tumor types, focusing on the pattern of lymphatic spread, the outcome of surgery, and prognostic factors in patients with type II tumors.

Results
There were marked differences in sex distribution, associated intestinal metaplasia in the esophagus, tumor grading, tumor growth pattern, and stage distribution between the three tumor types. The postoperative death rate was higher after esophagectomy than extended total gastrectomy. On multivariate analysis, a complete tumor resection (R0 resection) and the lymph node status (pN0) were the dominating independent prognostic factors for the entire patient population and in the three tumor types, irrespective of the surgical approach. In patients with type II tumors, the pattern of lymphatic spread was primarily directed toward the paracardial, lesser curvature, and left gastric artery nodes; esophagectomy offered no survival benefit over extended gastrectomy in these patients.

Conclusion
The classification of adenocarcinomas of the esophagogastric junction into type I, II, and III tumors shows marked differences between the tumor types and provides a useful tool for selecting the surgical approach. For patients with type II tumors, esophagectomy offers no advantage over extended gastrectomy if a complete tumor resection can be achieved.

In the Western world, the prevalence of adenocarcinoma of the esophagogastric junction is rising at an alarming rate.[1] Because of its borderline location between the esophagus and stomach, many discrepancies exist in the literature regarding the cause and classification of these tumors. This is reflected in the vastly differing surgical approaches and long-term survival rates after surgical resection reported in the literature.[2–8]

To clarify these issues, we have proposed dividing tumors into three types based on purely topographic anatomical criteria[9–11]:

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- **Type I:** adenocarcinoma of the distal esophagus, which usually arises from an area with specialized intestinal metaplasia of the esophagus (i.e., Barrett esophagus) and may infiltrate the esophagogastric junction from above;
- **Type II:** true carcinoma of the cardia arising immediately at the esophagogastric junction;
- **Type III:** subcardial gastric carcinoma that infiltrates the esophagogastric junction and distal esophagus from below.

At a recent consensus conference of the International Gastric Cancer Association and the International Society for Diseases of the Esophagus, all participating experts agreed that this classification should form the basis for defining, assessing, and reporting treatment of adenocarcinoma of the esophagogastric junction.[11,12]

Since 1982, we have selected the surgical approach based on this classification and have treated type I tumors as esophageal cancer and type II and III tumors as gastric cancer. In this article we report an analysis of a large and homogeneously classified population of consecutive patients with adenocarcinoma of the esophagogastric junction treated according to these guidelines, with a focus on the pattern of lymphatic spread, the outcome of surgical treatment, and prognostic factors in patients with type II tumors.

METHODS

Patient Population and Classification

Between July 1982 and October 1999, 1,002 patients (205 women, 797 men; mean age 61 years) with adenocarcinoma of the esophagogastric junction underwent surgical resection with curative intent at the Department of Surgery, Technische University Munich. Adenocarcinoma of the esophagogastric junction was defined as a tumor whose center is within 5 cm proximal and distal of the anatomical cardia.[9–12] Patients with systemic metastases on preoperative staging or poor general status precluding an extensive surgical procedure were excluded.

Based on the anatomical location of the tumor center or, in patients with advanced tumors, the tumor mass, all tumors were prospectively classified into the categories noted above.[9–12] The assignment was purely morphologic/topographic and was made based on the findings of contrast radiography, endoscopy with orthograde and retroflexed views of the esophagogastric junction, computed tomography, and intraoperative findings.

The prospectively collected data included demographic parameters, histomorphologic tumor characteristics, the presence of associated intestinal metaplasia in the distal esophagus (Barrett esophagus), the type of resection, postoperative 30-day death rate, the depth of tumor invasion (pT), the pN category, the number and location of positive and removed lymph nodes, the pM category, and 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 the goal of achieving complete macroscopic and microscopic tumor resection. In general, a radical transmediastinal or transthoracic en bloc esophagectomy with resection of the proximal stomach was the procedure of choice in patients with type I tumors.[13] An extended total gastrectomy with transhiatal resection of the distal esophagus was performed in patients with type III tumors.[14] In patients with type II tumors, an attempt was usually made to achieve complete tumor resection by means of an extended gastrectomy with transhiatal resection of the distal esophagus. If, based on preoperative staging or the intraoperative findings, complete tumor resection by a transabdominal approach appeared unlikely, an esophagectomy with proximal gastric resection was performed.[15] A subgroup of patients with locally advanced tumors (uT3/4NxM0) underwent resection after neoadjuvant cisplatin-based polychemotherapy in a prospective and ongoing phase II study.

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. 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.[12] 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. Reconstruction after transmediastinal or transthoracic esophagectomy was performed with a narrow gastric tube or colon interposition and a cervical or high intrathoracic anastomosis.

Extended total gastrectomy always included 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).[14] A pancreas-preserving splenectomy was performed only in patients with frank infiltration or lymph node metastases at the splenic hilum.[15] Dissection of the left retroperitoneal paraaortic and left renal hilum nodes was performed only in patients who had enlarged nodes at these areas on preoperative or intraoperative staging. An end-to-side esophagojejunostomy performed with a circular stapler and Roux-en-Y bile diversion was the reconstruction procedure of choice after extended total gastrectomy.

Table 1. DEMOGRAPHIC AND MORPHOLOGIC TUMOR CHARACTERISTICS

	Total (n = 1,002)	Type I Tumors (n = 361)	Type II Tumors (n = 271)	Type III Tumors (n = 370)	*P*
Age at presentation (years, mean ± SD)	61.0 ± 11.3	60.1 ± 10.5	60.4 ± 11.3	62.6 ± 11.9	NS
Male:female ratio	3.9:1	9.0:1	5.4:1	2.1:1	<.01
Prevalence of associated intestinal metaplasia in the distal esophagus (Barrett esophagus)	31.0%	76.9%	9.8%	2.0%	<.01
Prevalence of G3/G4 (undifferentiated) tumors	60.2%	51.0%	55.4%	71.6%	<.01
Prevalence of tumors with intestinal growth pattern	53.7%	78.9%	41.3%	38.1%	<.01

Histopathologic Assessment of the Removed Specimen and Lymph Nodes

Resection specimens were assessed by an experienced pathologist. All removed lymph nodes were counted, assessed separately, and identified according to their location. 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).[16,17] A particular effort was made to identify areas with intestinal metaplasia in the distal esophagus and in the region of the cardia in all resection specimens and to classify the tumor growth pattern according to the criteria of Lauren[18] into intestinal and nonintestinal.

Follow-Up

The survival status of our patients was ascertained between October and December 1999. Survival data were available for 949 of the 1,002 patients (94.7%), with a median follow-up of the surviving patients of 68 months (range 1–193).

Statistical Analysis

Data are shown as prevalence or mean (± standard deviation). Continuous data were compared by the Mann-Whitney test, ordinal data by the chi-square test. Survival was analyzed by the Kaplan-Meier method, and prognostic factors were assessed by log-rank and Cox regression analyses. $P < .05$ was considered significant.

RESULTS

Of the 1,002 patients with resected adenocarcinoma of the esophagogastric junction, 361 (36%) had type I tumors, 271 (27%) had type II tumors, and 370 had type III tumors. A comparison of the demographic data and histomorphologic tumor characteristics showed marked discrepancies between the three types. The preponderance of the male sex, the prevalence of associated intestinal metaplasia in the distal esophagus (Barrett esophagus), and the prevalence of an intestinal tumor growth pattern decreased from type I to type III tumors ($P < .01$), whereas the prevalence of undifferentiated tumors increased from type I to type III tumors ($P < .01$) (Table 1).

Table 2 shows the distribution of the surgical procedures. Primary resection was performed in 827 of the 1,002 patients (82.5%), and 175 of the 1,002 (17.5%) underwent resection after neoadjuvant polychemotherapy. An esophagectomy (transmediastinal or transthoracic) with resection of the proximal stomach was the primary procedure in patients with type I tumors; extended total gastrectomy with transhiatal resection of the distal esophagus was performed in 97.8% of patients with type III tumors. An extended total

Table 2. SURGICAL APPROACH

	Type I Tumors (n = 361)	Type II Tumors (n = 271)	Type III Tumors (n = 370)	Total
Primary resection	290 (80.3%)	210 (77.4%)	327 (88.4%)	827
Resection after neoadjuvant polychemotherapy	71 (19.7%)	61 (22.6%)	43 (11.6%)	175
Esophagectomy				
Transthoracic	66	5	1	72
Transmediastinal	266	43	6	315
Extended gastrectomy	29	223	363	615

Table 3. POSTOPERATIVE 30-DAY DEATH RATES

	1982–1991	1992–1999	Total
Transthoracic esophagectomy	3/30 (10%)	2/42 (4.8%)	5/72 (6.9%)
Transmediastinal esophagectomy	12/144 (8.3%)	3/171 (1.8%)	15/315 (4.8%)
Extended gastrectomy	13/304 (4.3%)	5/311 (1.6%)	18/615 (2.9%)
Total	28/478 (5.6%)	10/524 (1.9%)	38/1002 (3.8%)

gastrectomy with transhiatal resection of the distal esophagus also predominated in patients with type II tumors. The mean number of removed lymph nodes was higher in patients with type II (34.7 ± 15.8) and type III (41.9 ± 20.1) tumors compared with patients with type I tumors (24.9 ± 13.6).

As shown in Table 3, the overall postoperative 30-day death rate for the 17-year study period was 3.8%. Postoperative deaths were significantly lower in patients who underwent resection between 1992 and 1999 (1.9%) than for those who had surgery before 1992 (5.6%) ($P < .05$). Overall, transthoracic esophagectomy was associated with a significantly higher postoperative 30-day death rate compared with extended total gastrectomy ($P < .05$).

On histopathologic assessment of the resected specimens, early tumors (pT1) and the pN0 category were significantly more common in patients with type I tumors than in those with type II or III tumors ($P < .01$, Table 4). Compared with patients with type III tumors, pN0 and pM0 categories were more common in patients with type I and II tumors. This resulted in higher R0 resection rates in patients with type I and II tumors than in patients with type III tumors.

The overall 5- and 10-year survival rates for the entire population of 1,002 patients with resected adenocarcinoma of the esophagogastric junction were 32.3% and 24.3%, respectively. On multivariate analysis, a complete macroscopic and microscopic tumor resection (R0 resection, $P < .001$), the pN0 category ($P < .001$), and the pT1 category ($P < .01$) were the dominating independent prognostic factors. The 5- and 10-year survival rates in patients with an R0 resection were 38.7% and 28.3%, respectively, compared with 13.7% and 11.6% in patients with a R1/R2 resection (Fig. 1).

On univariate analysis of the R0-resection patients, the long-term prognosis of patients with type I and II tumors was significantly better than that of patients with type III tumors (Fig. 2). On multivariate analysis, the tumor type and the surgical approach (esophagectomy or extended

Table 4. COMPARISON OF THE pT, pN, pM, AND R CATEGORIES

	Type I Tumors (n = 361)	Type II Tumors (n = 271)	Type III Tumors (n = 370)
T Category			
pT1	90 (24.9%)	38 (14%)	26 (7%)
pT2	101 (27.9%)	155 (57.2%)	116 (31.4%)
pT2a	NA	82 (30.3%)	49 (13.2%)
pT2b	NA	73 (26.9%)	67 (18.2%)
pT3	137 (38%)	55 (20.3%)	164 (44.3%)
pT4	33 (9.1%)	23 (8.5%)	64 (17.3%)
N Category			
pN0	132 (36.6%)	85 (31.4%)	77 (20.8%)
pN+	229 (63.4%)	186 (68.6%)	293 (79.2%)
pN1	229 (63.4%)	80 (29.5%)	108 (29.2%)
pN2	NA	61 (22.5%)	167 (45.1%)
pN3	NA	45 (16.6%)	18 (4.9%)
M Category			
pM1	55 (15.2%)	44 (16.2%)	104 (28.1%)
pM1a(lymph)	16 (4.4%)	NA	NA
pM1b	39 (10.8%)	NA	NA
R Category			
R0	273 (75.6%)	205 (75.6%)	254 (68.6%)
R1/2	88 (24.4%)	66 (24.4%)	116 (31.4%)

NA, not applicable.
Patients with type I tumors were staged according to the UICC/AJCC guidelines for esophageal cancer, patients with type II and type III tumors according to the UICC/AJCC criteria for gastric cancer.

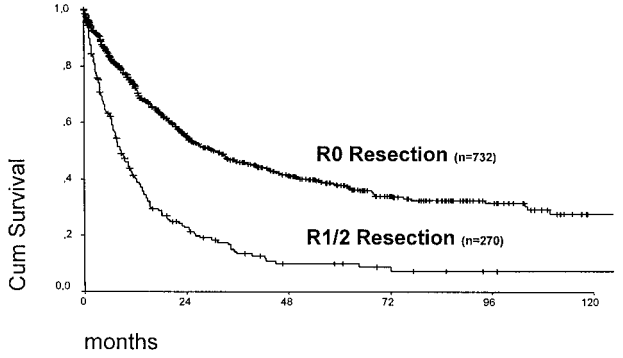

Figure 1. Overall 10-year survival rates of 1,002 consecutive patients with resected adenocarcinoma of the esophagogastric junction. Complete macroscopic and microscopic tumor resection (R0) vs. microscopic or macroscopic residual disease after resection (R1/2), $P < .001$.

gastrectomy) had no independent effect on long-term survival.

In the patients with type II tumors (n = 271), there were no significant differences in the distribution of the pT, pN, pM, and R categories between those who underwent an esophagectomy with proximal gastric resection and those who underwent an extended total gastrectomy with transhiatal resection of the distal esophagus. Multivariate analysis of prognostic factors in this subgroup of patients identified an R0 resection ($P < .001$) and a pN0 category ($P < .001$) as the predominating independent predictors of long-term survival (Fig. 3). In the R0-resection patients with type II tumors, there was no significant difference in long-term survival between those who underwent an esophagectomy with proximal gastric resection and those who underwent an extended total gastrectomy and transhiatal resection of the distal esophagus (Fig. 4).

Analysis of the pattern of lymphatic spread in patients with type II tumors showed the left (67.8%) and right (56.9%) paracardial region, the lesser curvature (67.8%), and the left gastric artery, splenic artery, and celiac axis

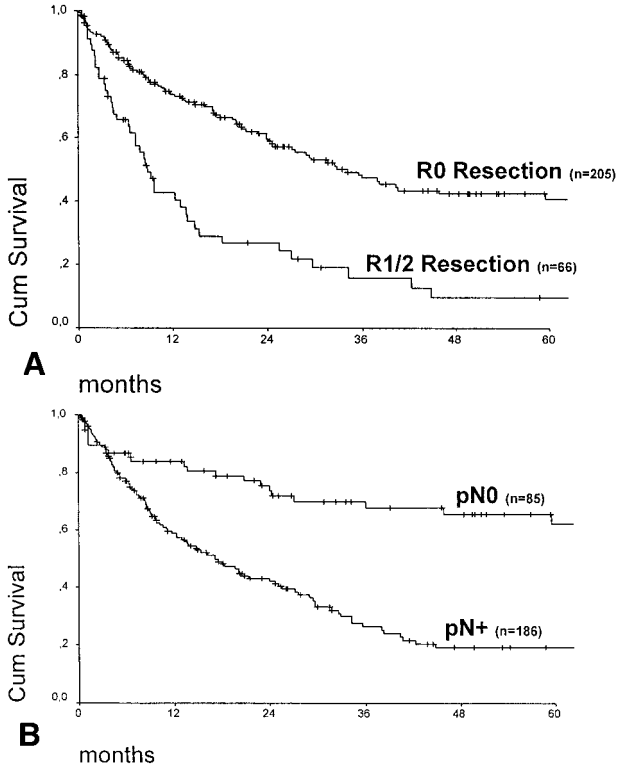

Figure 3. Survival rates of patients with true carcinoma of the cardia (type II tumors). Effect of R category (A, $P < .001$) and N category on survival (B, $P < .001$).

(26.8%) as the predominating areas of lymph node metastases, followed by the greater curvature (16.1%), the lower posterior mediastinum (15.6%), and the lymph nodes in the retropancreatic area toward the left renal hilum (Fig. 5).

DISCUSSION

There are no major controversies in the surgical therapy of patients with esophageal and gastric cancer, but the

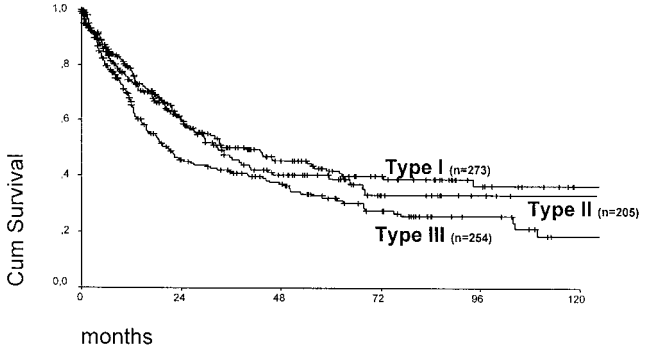

Figure 2. The 10-year survival rates of patients with R0-resected (no residual macroscopic or microscopic tumor) adenocarcinoma of the distal esophagus (type I tumors), true carcinoma of the cardia (type II tumors), and subcardial gastric cancer infiltrating the esophagogastric junction (type III tumors). Type I vs. type III, $P < .01$; type II vs. type III, $P < .05$; type I vs. type II, not significant.

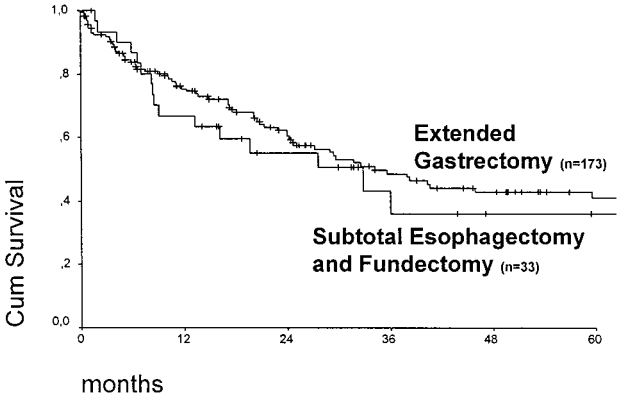

Figure 4. Survival rates of patients with R0-resected (no residual macroscopic or microscopic tumor) true carcinoma of the cardia (type II tumors) according to type of resection. No significant difference was found between extended gastrectomy and esophagectomy.

Location	Number of patients with positive nodes		% of N+ patients (n = 186)
lower mediastinum	29		15.6 %
left paracardial	126		67.8 %
right paracardial	106		56.9 %
lesser curvature	126		67.8 %
greater curvature	30		16.1 %
left gastric artery	28		
splenic artery	9	50	26.9 %
celiac trunc	13		
parapyloric	3		
hepaduodenal ligament	9		
left renal hilus	6		

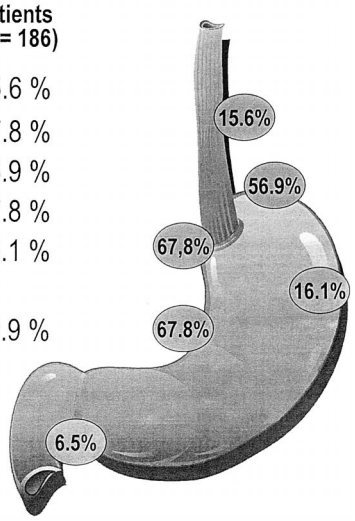

Figure 5. Distribution of lymph node metastases in patients with resected true carcinoma of the cardia (type II tumors) and positive lymph nodes (n = 186).

management of patients with adenocarcinoma of the esophagogastric junction 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.[2–8,19–24] At a recent consensus conference, experts agreed that a generally accepted classification of tumors arising at the esophagogastric junction is needed for a valid comparison of data from various centers and assessment of different diagnostic and therapeutic approaches.[12]

The classification of adenocarcinomas of the esophagogastric junction into type I, II, and III tumors, as suggested by our group, is now increasingly used worldwide.[25,26] Although this classification is based purely on anatomical/topographic parameters, the present analysis and the experience of other authors[24,25] show that it provides a useful tool for differentiating tumor entities arising in the vicinity of the esophagogastric junction and thus aids in the selection of the surgical approach. Type I tumors clearly constitute a distinct entity that requires a specific therapeutic approach as distal esophageal cancer. Most if not all of these tumors arise from areas of intestinal metaplasia in the distal esophagus (Barrett esophagus, which develops as a consequence of chronic gastroesophageal reflux). Because of effective endoscopic surveillance programs, such tumors are increasingly diagnosed at an early stage and may be amenable to limited surgical or endoscopic treatment. Similarly, type III tumors clearly represent a special form of proximal gastric cancer and require treatment according to the well-established gastric cancer guidelines. The relation of Type II tumors to distal esophageal or proximal gastric cancer, however, remains controversial. Because the classification system provides a clear definition of these tumors, an analysis of our large and prospectively documented and classified patient population with adenocarcinoma of the esophagogastric junction provides the basis for a discussion of these issues and an objective evaluation of various surgical strategies.

This analysis shows that in contrast to patients with type I tumors, intestinal metaplasia in the distal esophagus was documented in only 10% of patients with type II tumors and was rare in patients with type III tumors. This is in agreement with the findings of a recent report indicating that patients with type I tumors are more likely to have a long history of gastroesophageal reflux disease than are patients with type II or III tumors.[27] Although a subgroup of type II tumors may still have developed from microscopic foci of intestinal metaplasia at the esophagogastric junction,[28–30] our data clearly indicate major differences in the pathogenic pathway between type I tumors on the one hand and type II and III tumors on the other hand.

Most type II tumors resemble proximal gastric cancer more closely than they do distal esophageal adenocarcinoma. The present study found a significantly higher proportion of an intestinal-type growth pattern in type I tumors than in type II and III tumors. In contrast to a recent analysis of a smaller patient series,[31] we and others have previously also shown differences in the prevalence and pattern of mutations of the p53 tumor suppressor gene and histogenetic abnormalities between type I tumors and type II and III tumors.[32–34] Further, the prevalence of lymph node micrometastases in early tumor stages and the activity of tumor metabolism on positron emission tomography markedly differ between type I tumors and type II and III tumors.[35,36] Finally, lymphographic studies show that the main lymphatic pathways originating from the lower esophagus advance both up into the mediastinum and down along the celiac axis, whereas those from the gastric cardia and subcardial region preferentially make their way to the celiac axis.[37] This is reflected in the pattern of lymphatic spread of type II tumors, which differs from that of type I tumors but matches that of type III tumors.[20,21,38,39] Thus, there are

several pronounced differences between type I and type II tumors, whereas similarities between type II and III tumors predominate.

This affects the selection of the surgical approach to type II tumors. Because complete macroscopic and microscopic tumor resection (R0 resection) and the presence of lymph node metastases are the dominating independent prognostic factors, complete tumor removal and adequate lymphadenectomy must be the goal of any potentially curative surgical approach. The present study shows that in the vast majority of patients with type II tumors, these goals can be achieved by a transabdominal approach only with total gastrectomy, resection of the distal esophagus after wide splitting of the esophageal hiatus, and lymphadenectomy in the lower posterior mediastinum, in addition to a D2 lymph node dissection according to the principles of gastric cancer surgery.[14] Subtotal esophagectomy with fundectomy offers no survival benefit but is associated with significantly higher rates of death and complications and a compromised postoperative quality of life.[3,5,8,20] Resection of type II tumors using an abdominal approach only has been shown to be feasible and safe by several groups.[19,24,40] To ensure clear resection margins in the distal esophagus, intraoperative frozen sections should be used liberally.

Based on these data, an even more limited form of resection (locoregional resection of the distal esophagus, esophagogastric junction, and proximal stomach, with preservation of the distal stomach) may be justified in patients with early tumor stages.[25] Although proximal gastric resections with esophagogastrostomy have been abandoned because of subsequent uncontrollable reflux, reconstruction with jejunal or colon interposition, which would prevent this problem and the associated poor quality of life, could result in the renaissance of locoregional resections of such tumors.

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Discussion

DR. MURRAY F. BRENNAN (New York, New York): I am pleased to be asked to comment on Prof. Siewert's fine manuscript, although I must admit it is a little daunting to appear in the introduction with a citation for bad surgical results! Dr. Siewert and his group from Munich remain, as many of you know, the major force in gastric adenocarcinoma in the West.

Dr. Siewert is somewhat modest—he has clearly redefined adenocarcinoma of the esophagogastric junction, and today you heard a very thoughtful analysis of 1,000 patients admitted to their institution. In addition to describing their results, however, they show the marked fixed difference in sex distribution in these lesions, a recurring theme in the West, and about which I am sure you will hear more from the next discussant.

The extensiveness and thoroughness of the dissection is well outlined in the manuscript by the number of removed lymph nodes. The importance of a minimal number of lymph nodes to be examined to obtain accurate staging is emphasized. The impressive survival results are matched by minimal postoperative mortality, consistent with the value of specialized units.

As Dr. Siewert and others such as ourselves have shown, there is no benefit to an extended esophagectomy for type II and III tumors, both of which can be equally well managed by extended gastrectomy, although the subsequent discussants might not agree. Dr. Siewert clearly shows the difference in presentation of patients with type 1 as opposed to type 2 and 3 tumors. Type 1 tumors continue to exhibit intestinal metaplasia and are associated with a long history of gastroesophageal reflux, in contradistinction to the type 2 and type 3 tumors.

There is little to question in this manuscript. Perhaps the audience, Dr. Siewert, would be most interested in further insights into the increasing incidence of esophagogastric junction tumors, as it would appear that the current audience, myself included, as middle-class white Anglo-Saxons with reflux, contains many of the patients at most risk. In all groups, however, there is a 15% to 28% incidence of pathological M1 disease. Prof. Siewert, can you describe the indications for resection in the presence of M1 disease? What is the survival of pathologically M1 patients? Does operation influence that survival? If it does not, how hard do you try to confirm the diagnosis of M1 disease?

Finally, in the abstract there was a suggestion that neoadjuvant chemotherapy makes a difference. I wonder how confident you are with that data.

PRESENTER DR. J. RÜDIGER SIEWERT (Munich, Germany): Three different questions. The first one, what are the reasons for the increasing incidence? It is impossible for me to give you a very good answer. The only one thing I would like to stress is that the explanation that everything is coming only from reflux disease is not adequate. It is not covering all the different types of adenocarcinomas of the gastroesophageal junction; the reflux problem is only proven for Barrett's and it is unproven for cardia and for subcardial tumors.

So I think we have to look for other reasons. There is a hypothesis in discussion that the eradication of *Helicobactor pylori* can increase the incidence of atrophic gastritis in the upper third of the stomach, but this is only a hypothesis. So at the end I must say I have not a very convincing explanation as to why these types of tumors show an alarming increase at the moment.

The second question is dealing with the early tumors and just beginning lymph node metastasizing. And indeed the question is arising, is there is a place for, let's say, a limited type of surgery. We feel there is a place for a limited type of surgery. All these patients are under endoscopic surveillance, and these patients coming with an early diagnosis want to have type of treatment other than the very radical extended total gastrectomy or subtotal esophagectomy. So we have decided to start a protocol in my department with proximal gastrectomy and distal esophageal resection, always including complete resection of the segment with intestinal metaplasia—this is very important.

The old type of proximal gastric resections have had problems of alkaline reflux and of very bad quality of life, but this is a problem of reconstruction. We have decided to perform a so-called Merendino procedure in this type of patient, meaning a small bowel interposition. We have now included about 30 patients in this protocol; we have had no mortality, and the quality of life and the functional studies postoperatively are very nice. So we think there is a place for a limited type of surgery with our interposition of small bowel or maybe of a segment of large bowel.

The last question was regarding neoadjuvant chemotherapy. We have experience with neoadjuvant chemotherapy, but we know that controlled trials are not available at this time. We are including only patients who are not reresectable (locally advanced tumors) in

this Phase II protocol. We have a response rate of 60%, and the patients having a benefit from neoadjuvant chemotherapy will have a second-line resection. At this time we see no place for adjuvant chemotherapy.

Dr. John Wong (Hong Kong, China): Dr. Siewert, it seems to me that you are proposing the use of a technique on the basis of an anatomical classification. I wonder if another way of approaching this might be not adhering to a rigid classification and prescribing an operation for it, but instead to establish the epicenter of the tumor, and then try to obtain an adequate margin on both sides, proximally and distally, whatever approach is appropriate to achieve this.

For an abdominal operation for type 2 cancers, my questions are: One, what proximal margins were you able to obtain? Two, are there difficulties with the anastomosis? Three, if so, is this associated with a higher leakage rate? And finally, since the proximal margin may not be adequate, what was the anastomotic recurrence rate?

Dr. Siewert: The transhiatal approach to the distal esophagus is very easy to do. If you are well trained with our procedure, then you will have no problems. One aspect is right, you must have more frequent frozen sections, because you have to ensure that you have a clear margin at the end of the operation. But you have to realize what the types of tumors are. Eighty percent show an intestinal tumor growth, so it is not necessary to have a wide safety margin, let's say, of 6 or 8 cm. It is enough to have a safety margin of 2 or 3 cm.

We have the experience that the anastomosis between the esophageal remnant and the small bowel is very easy to perform with a circular stapler device. I must say that we have seen a leakage rate far below under 5%. This complication is extremely rare. The problem is never the anastomosis. The problem is sometimes the interposed jejunum. So you have to ensure a good blood supply of the loop, and then you will have no problems with the anastomosis.

If we are seeing local recurrences—and this is extremely rare—then there are not local recurrences at the site of the anastomosis; much more frequently, we are seeing local recurrences coming from outside (extraluminal recurrences), meaning from the former tumor bed. This is a situation observed in our department in something around 20%. That is indeed a problem, but it is a problem of the locally advanced tumors at the first operations, it is not a problem of the type of resection or of the type of reconstruction.