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EPIDEMIOLOGY, SURGICAL MANAGEMENT AND EARLY POSTOPERATIVE OUTCOME IN A COHORT OF GASTRIC CANCER PATIENTS OF A TERTIARY REFERRAL CENTER IN RELATION TO MULTI-CENTER QUALITY ASSURANCE STUDIES

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The aim of the study was to analyze epidemiologic parameters, treatment-related data and prognostic factors in the management of gastric cancer patients of a university surgical center under conditions of routine clinical care before the onset of the era of multimodal therapies. By analyzing our data in relation with multi-center quality assurance trials [German Gastric Cancer Study – GGCS (1992) and East German Gastric Cancer Study – EGGCS (2004)] we aimed at providing an instrument of internal quality control at our institution as well as a base for comparison with future analyses taking into account the implementation of evolving (multimodal) therapies and their influence on treatment results.

Material and methods. Retrospective analysis of prospectively gathered data of gastric cancer patients treated at a single institution during a defined 10-year time period with multivariate analysis of risk factors for early postoperative outcome.

Results. From 04/01/1993 through 03/31/2003, a total of 328 gastric cancer patients were treated. In comparison with the EGGCS cohort there was a larger proportion of patients with locally advanced and proximally located tumors. 272 patients (82.9%) underwent surgery with curative intent; in 88.4% of these an R0 resection was achieved (EGGCS/GGCS: 82.5%/71.5%). 68.2% of patients underwent preoperative endoluminal ultrasound (EUS) (EGGCS: 27.4%); the proportion of patients undergoing EUS increased over the study period. Diagnostic accuracy of EUS for T stage was 50.6% (EGGCS: 42.6%). 77.2% of operated patients with curative intent underwent gastrectomy (EGGCS/GGCS: 79.8%/71.1%). Anastomotic leaks at the esophagojejunostomy occurred slightly more frequently (8.8%) than in the EGGCS (5.9%) and GGCS (7.2%); however, postoperative morbidity (36.1%) and early postoperative mortality (5.3%) were not increased compared to the multi-center quality assurance study results (EGGCS morbidity, 45%); EGGCS/GGCS mortality, 8%/8.9%). D2 lymphadenectomy was performed in 72.6% of cases (EGGCS: 70.9%). Multivariate analysis revealed splenectomy as an independent risk factor for postoperative morbidity and ASA status 3 or 4 as an independent risk factor for early postoperative mortality. The rate of splenectomies performed during gastric cancer surgery decreased substantially during the study period.

Conclusions. Preoperative diagnostics were able to accurately predict resectability in almost 90% of patients which is substantially more than the corresponding results of both the EGGCS and the GGCS. In the future, more wide-spread use of EUS will play an increasing role as stage-dependent differentiation of therapeutic concepts gains acceptance. However, diagnostic accuracy of EUS needs to be improved. Our early postoperative outcome data demonstrate that the quality standard of gastric cancer care established by the EGGCS is being fulfilled at our institution in spite of distinct characteristics placing our patients at higher surgical risk. Besides being a valuable instrument of internal quality control, our study provides a good base for comparison with ongoing analyses on future developments in gastric cancer therapy.

Key words: gastric cancer, quality control, perioperative morbidity, early postoperative mortality, risk, factor

Despite its incidence being on a steady decline, gastric cancer remains the fourth most common cancer world wide and the second most common cause of cancer-related death (1, 2). In the Western hemisphere, many patients present with locally unresectable or metastatic cancer and thus cannot be cured from their disease. Moreover, multimodal therapy has been implemented into gastric cancer treatment with curative intent in recent years due to the results of several randomized-controlled trials (3, 4). However, surgical removal of the tumor remains the one principal and indispensable modality in the treatment of limited gastric cancer. First of all, this includes complete (R0) tumor resection with gastrectomy and subtotal gastric resection achieving equal results as long as resection margins are histologically negative (5). Depending on the histological tumor growth pattern according to Laurén's classification system, a safe distance of either 5 cm (for Laurén's intestinal-type tumors) or 8 cm (for diffuse-type tumors) should be observed which means that most diffuse-type tumors should be treated by gastrectomy.

There is still debate as to the issue of adequate lymphadenectomy in gastric cancer surgery. Both of the two European randomized gastric cancer trials (6, 7) have failed to demonstrate a survival benefit for the entire group of patients undergoing D2-lymphadenectomy while showing increased postoperative morbidity and mortality as compared to the D1 group. However, since it was shown to offer a (though statistically non-significant) survival benefit for the subgroup of patients with advanced lymph node involvement (N2) in the Dutch gastric cancer trial and for the subgroup of patients with UICC stage II and IIIA tumors in the (prospective, though non-randomized) German Gastric Cancer Study (GGCS 1992) (27), D2 lymph node dissection is considered standard of care for all patients in Germany because available diagnostic methods do not permit preoperative identification of these subgroups to date.

Gastric cancer surgery is complex and bears a substantial risk of morbidity and mortality, making an instrument of quality control indispensable for all institutions involved in these procedures. The multi-center German Gastric Cancer Study (GGCS 1992) (8) demonstrated an in-hospital mortality of 8.9% after gastric cancer surgery and an anastomotic leak rate of 7.2% after gastrectomy. An analysis of the records of 18.365 gastric cancer patients performed by the American College of Surgeons also demonstrated a 7.2% mortality risk after gastric cancer surgery even though only 4.7% of these operations involved D2 lymphadenectomy (9). The East-German Working Group for Quality Assurance and Regional Development in Surgery in collaboration with the Institute for Quality Assurance in Surgery at the Otto-von-Guericke University Medical School, Magdeburg, Germany, analyzed the data of 1.199 gastric cancer patients treated in 80 German institutions representing all levels of care between January 1st and December 31st, 2002. In this analysis, an 8.0 per cent in-hospital mortality rate and a 5.9 per cent anastomotic leak rate was demonstrated (EGGCS 2002) (10). These two multi-center trials have defined a reference level for gastric cancer surgery in the area of the participating hospitals which permits evaluating the own institution's quality of care for gastric cancer patients, though bearing in mind that patient characteristics may differ in one or more aspects. However, this requires a regular and systematic analysis of the own surgical quality data in comparison with the results of the multi-center quality assurance trials. Moreover, in order to achieve patient numbers sufficient for a valid analysis in a single institution, data collection over several years is usually necessary.

Thus, it was the aim of the present study to analyze epidemiological and treatment-associated data as well as the results of surgical treatment for gastric cancer in our institution (which has been one of the hospitals participating in the EGGCS) over a defined time span in order to provide a baseline for comparison with similar analyses that are scheduled at regular intervals in the future. Furthermore, these data will be used for research into the influence of the introduction of novel (multimodal) therapies for treatment of gastric cancer in our patients. In order to achieve maximum comparability with the EGGCS data and to acquire data from a purely surgically treated patient cohort (i.e., outside of multimodal concepts), we selected the time span from April 1st, 1993, through March 31st, 2003 for our analysis. During this period multimodal therapies were not yet established for gastric cancer in Germany. Furthermore, this time span includes the EGGCS data collection period. In addition to summarizing our surgical

results in comparison with the GGCS and EGGCS data, a multivariate analysis of risk factors for early postoperative morbidity and 30-day-mortality was carried out.

MATERIAL AND METHODS

For this systematic retrospective single-center observational study the records of all patients treated for gastric cancer at the Department of General, Abdominal, and Vascular Surgery at Magdeburg University Medical School Hospital between 04/01/1993 and 03/31/2003 were reviewed. Eligible patients were determined using ICD-10 and OPS codes recorded in the hospital´s computer-based clinical archive. All records retrieved were manually reviewed and relevant demographic, disease-associated, and treatment-associated data were entered into an electronic database. Descriptive statistics regarding demographic and disease-associated parameters were calculated for the entire patient cohort while only patients who had undergone a surgical procedure with curative intent were included in the analysis of surgery-associated data and parameters related to postoperative course.

In addition, all patients undergoing surgery with curative intent whose tumors were completely removed (negative resection margins – R0) were included in a multivariate analysis of potential factors influencing early postoperative outcome (ASA classification, tumor location (cardia/fundus region; corpus region; antrum/pylorus region), splenectomy, pancreatic resection, extent of lymphadenectomy (none/D1/D2/D3), duration of surgery). Outcome parameters analyzed included overall postoperative morbidity, surgical complications, postoperative ileus, and 30-day mortality. In detail, logistic regressions and Fisher's exact tests were performed for categorical data, Mann-Whitney-U tests for continuous variables. A p value of ≤ 0.05 was considered to indicate significance. All analyses were done using SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

The study was undertaken according to the 1964 Declaration of Helsinki guidelines for Biomedical Research and the standards of the Institutional Review Board.

RESULTS

Demographic data (tab. 1)

328 patients were treated for histologically proven gastric cancer during the period specified above. Median age was 65 (26-93) years. There were 123 men (37.5%) and 205 women (62.5%). Male patients were significantly younger at diagnosis (median: 64 years) than female patients (median: 68 years; p=0.007).

Tumor-related data

Of the 328 gastric carcinomas 151 (45.8%) were located in the fundus/cardia region, 42 (12.8%) were located in the corpus region and 91 (27.7%) were located in the antrum/pylorus region of the stomach. 21 tumors (6.4%) involved the entire stomach; in 11 patients the tumors were cancers of the gastric stump after prior gastric resection. For 12 patients no data on tumor location are recorded. The share of the tumors located in the proximal stomach (cardia/fundus region) remained almost con-

Table 1. Age and ASA status

	Full analysis set (n=328)			Male (n=205)			Female (n=123)		
Age median (range)	65 (26-93) years			64 (32-83) years			68 (26-93) years		
ASA risk	n	per cent of full analysis set	per cent of patients for whom ASA status is recorded	n	per cent of full analysis set	per cent of patients for whom ASA status is recorded	n	per cent of full analysis set	per cent of patients for whom ASA status is recorded
I	24	7,3	9	19	9,3	11,1	5	4,1	5,3
II	150	45,7	56,4	92	44,9	53,8	58	47,2	61,1
III	83	25,3	31,2	53	25,9	31	30	24,4	31,6
IV	9	2,7	3,4	7	3,4	4,1	2	1,6	2,1
Status not recorded	62	18,9		34	16,5		28	22,8	

stant throughout the study period (1993-1995: 50.8%; 1998-2003: 45.1%; p=0.361). Histologically, there were 315 (96%) adenocarcinomas including 59 (18%) signet ring cell carcinomas, 12 (3.7%) poorly differentiated carcinomas and 1 case (0.3%) of adenosquamous carcinoma.

pTNM and UICC stage distribution as provided by final postoperative histology from patients whose tumors were removed (n=272) is depicted in tab. 2 and fig. 1. During the second half of the study period significantly more tumors were diagnosed as being early T-stage (pT1 or pT2) (1993-1997: 43.4%, 1998-2003: 60.3%; p=0.007). This resulted in fewer patients diagnosed as having UICC stage III and stage IV tumors in the second half of the study period (1993-1997: 59.3%; 1998-2003: 48.7%), although this was not statistically significant (p=0.087).

Diagnostics

Data on preoperative gastroscopy were available for 303 patients (92.4%). In 259 cases (85.5%) the diagnosis of gastric carcinoma was confirmed histologically at endoscopy. Histology at endoscopy was negative in 27 patients (8.9%). No attempt at obtaining a histological diagnosis is documented in 17 cases (5.6%).

Data on preoperative transabdominal ultrasound are available for 304 of the 328 patients (92.7%). This diagnostic tool was used in 269 (88.5%) and ommitted in 35 (11.5%) of these patients. Of the 269 patients undergoing preoperative ultrasound 167 (62.1%) patients were diagnosed to have sonomorphologic evidence of a gastric tumor.

For 308 of 328 patients (93.3%) data on preoperative determination of tumor T-stage via endoluminal ultrasound (EUS) are documented. Of these, all except 98 patients (31.8%) underwent preoperative EUS. The proportion of patients undergoing preoperative EUS increased in the second half of the study period (1993-1997: 45.5%; 1998-2003: 77.7%; p<0.001). Endosonographic T-stage (uT-stage) could be determined in 166 cases (79%). In 14 patients (6.7%) no evidence of tumor within the stomach was found at EUS and no uT-stage could be determined in 34 cases (10.2%). Table 3 shows the distribution of EUS-determined (uT) and histopathological (pT) tumor stages as well as their concordance. EUS was able to predict the tumor T-stage at final histopathology in 91 (50.6%) cases. EUS accuracy for T-stage was best for locally advanced tumors (pT3: 75%; pT4: 54.5%) while EUS tended to overestimate the T-stage of early-stage tumors. Lymph node involvement (pN1/2 vs pN0) was correctly predicted by EUS in 58.4% of cases.

Data on preoperative abdominal and thoracic computed tomography (CT) scan are documented for 309 patients (94.2%). Of these, 246 (79.6%) underwent preoperative CT scan. CT scans revealed distant metastatic disease in 47 cases (19.1%) with hepatic metastases being diagnosed in 32 cases, pulmonary metastases in 6 cases and metastases at different locations in 9 cases.

Table 2. pTNM classification and histopathological grading

n (%)	pT	pN	M	G
0	–	77 (28,3%)	197 (72,4%)	–
1	45 (16,5%)	93 (34,2%)	47 (17,3%)	13 (4,8%)
2	98 (36%)	70 (25,7%)	–	70 (25,7%)
3	96 (35,4%)	23 (8,5%)	–	175 (64,4%)
4	30 (11%)	–	–	5 (1,8%)
X	–	7 (2,6%)	25 (9,2%)	–
Unknown	3 (1,1%)	2 (0,7%)	3 (1,1%)	9 (3,3%)
Total	272 (100%)	273 (100%)	272 (100%)	272 (100%)

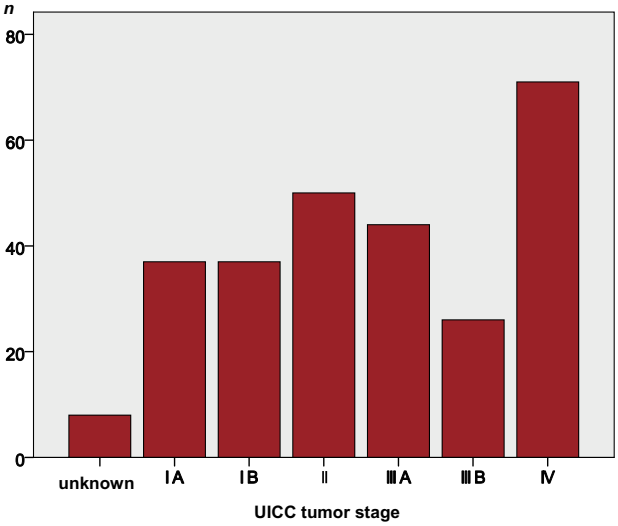

Fig. 1. UICC tumor stages of patients undergoing resection with curative intent

Table 3. Relation of tumor (T) stage as determined by EUS (uT) and histopathology (pT) of patients for whom uT-stage is recorded

n (%)	per cent of pT)	er cent of pT)	per cent of pT)	per cent of pT)	per cent of pT)	Total (per cent of pT)
pT0	0	0	0	0	0	0
pT1	3 (10)	11 (36,7)	12 (40)	4 (13,3)	0	30 (16,7)
pT2	2 (2,9)	2 (2,9)	26 (37,7)	36 (52,1)	3 (4,3)	69 (38,3)
pT3	4 (7,1)	0	1 (1,8)	42 (75)	9 (16,1)	56 (31,1)
pT4	3 (13,6)	0	0	7 (31,8)	12 (54,5)	22 (12,2)
Unknown	2 (66,7)	0	0	1 (33,3)	0	3 (1,7)
Total	14 (7,8)	13 (7,2)	39 (21,7)	90 (50)	24 (13,3)	180 (100)

Management

50 patients (15.3%) were managed conservatively or underwent palliative gastroenterostomy or gastrostomy due to unresectability of their disease that was revealed at preoperative imaging or at laparotomy (23 patients, 7%). Two more patients underwent limited resection of the gastric wall; in one of these patients, this procedure was carried out for palliation of tumor obstruction in the presence of extensive lymphatic metastases, the other patient had a pT1 tumor and multiple comorbidities that rendered radical resection impossible. The records of 4 patients (1.2%) do not contain data on the type of surgery.

The remaining 272 patients (82.9%) underwent surgical removal of their cancers with curative intent. The proportion of patients operated on with curative intent remained almost constant during the study period (1993-1997: 81.2%; 1998-2003: 83.5%; p=1). For 223 patients (82.9% of patients undergoing radical surgery) data on the extent of lymphadenectomy are recorded; of these, 162 (72.6%) underwent at least D2 lymphadenectomy. The median number of lymph nodes removed was 18 (range: 1-68). The type of procedures carried out and the extent of lymphadenectomy are depicted in tab. 4. The proportions of patients undergoing gastrectomy or subtotal gastric resection did not change during the study (p=1).

For 21 of the patients operated on with curative intent no data are available as to whether an R0-resection was achieved. Of the remaining 251 patients, a resection with his-

Table 4. Types of surgery in gastric cancer patients

Procedure	n	Per cent of total	Per cent of resections with curative intent	Per cent of patients for whom extent of lymphadenectomy is recorded
Palliative procedure without resection	50	15,3		
Local tumor excision (atypical gastric wall resection)	2	0,6		
Gastric resection with curative intent	272	82,9	100	
– Gastrectomy (including 13 procedures including resection of the lower esophagus through a transhiatal or transthoracal approach)	210	64	77,2	
– Subtotal gastric resection/Billroth-I-type reconstruction	16	4,9	5,9	
– Subtotal gastric resection/Billroth-II-type reconstruction	45	13,7	16,5	
– Proximal gastric resection (resection of the gastric cardia and fundus)	1	0,3	0,4	
– Lymphadenectomy: * D1	61	18,6	29	27,4
* D2	161	49,1	59,2	72,2
* D3	1	0,3	0,4	0,4
* Extent not recorded	53	16,2	19,5	0
Unknown	4	1,2		
Total	328	100		

tologically negative margins (R0) was achieved in 222 cases (88.4%). Thirty of 268 patients for whom final T status of their tumors has been recorded had tumor growth beyond the stomach (pT4). Of these, an R0 resection was achieved in 22 patients (88%) and a postoperative R1 or R2 status resulted in 3 patients (12%) while no postoperative R status is recorded for 5 of these 30 patients.

One hundred six patients (40.2%) underwent splenectomy and 23 patients (8.7%) underwent pancreatic resection as part of their gastric cancer surgery while data regarding splenectomy or pancreatic resection are lacking for 8 and 9 patients, respectively. Hepatic resection was carried out in 42 cases (16%), diaphragmatic resection in 20 cases (7.4%) and colonic resection in 7 cases (2.6%). The splenectomy rate during gastric cancer surgery decreased significantly in the second half of the study period (1993-1997: 58.7%; 1998-2003: 26.6%; $p<0.001$) while the rate of pancreatic resections remained constant ($p=0.828$; fig. 2). The number of lymph nodes removed was not significantly different between patients undergoing gastric cancer surgery with or without splenectomy; however, there were significantly more tumors classified as pN2 or pN3 among the patients undergoing splenectomy (without splenectomy: 28.9%; with splenectomy: 44.2%; $p=0.016$). Moreover, the proportion of patients with pT4-tumors was greater in the cohort undergoing splenectomy (14.4%) than among the patients undergoing gastric cancer surgery without splenectomy (8.6%) though this difference did not reach statistical significance ($p=0.154$).

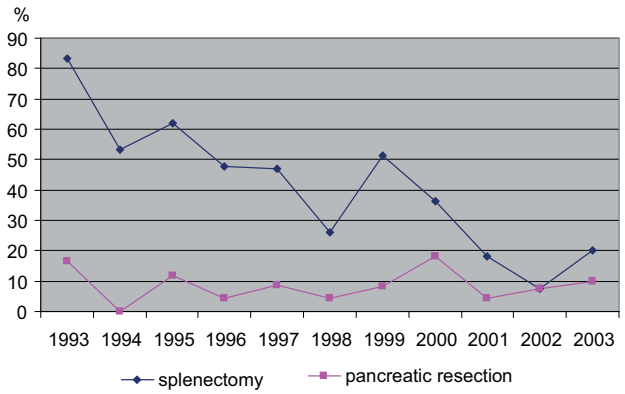

Fig. 2. Splenectomies and pancreatic resections performed during gastric cancer surgery (per cent of all surgical procedures with curative intent)

Restitution of intestinal passage after gastric resection was made in the form of a Roux-en-Y anastomosis in the majority of patients (n=209). For 22 patients, an omega-loop type reconstruction is recorded. Esophagojejunostomy was predominantly carried out in the form of a stapled anastomosis (n=154); in 22 cases this anastomosis was hand-sewn. However, the exact type of anastomosis is not recorded in 96 cases.

The median number of erythrocyte concentrate units administered intraoperatively was 2 (range: 0-10). Median duration of surgery was 210 (range: 27-560) minutes.

Postoperative course

The median duration of postoperative ICU stay was 4 (range: 0-94) days. Median in-hospital stay was 20 (range: 8-115) days. Postoperative complications recorded are shown in tab. 5. Total postoperative morbidity was 36.1% and remained grossly constant throughout the study period.

Fourteen (5.3%) of 264 patients for whom these data are available (i.e., 97.1% of all patients undergoing surgery with curative intent) died within 30 days after surgery. Thirty-day mortality and total postoperative morbidity were not significantly different between the group of patients undergoing gastrectomy or subtotal gastric resection ($p=0.198$ and $p=0.281$, respectively). There was a trend towards more cases of postoperative peritonitis within the gastrectomy cohort though this did not reach statistical significance (9.3% vs. 3.4%; $p=0.089$).

The influence of potential risk factors (ASA status, pT stage, tumor location, splenectomy, pancreatic resection, and extent of lymphadenectomy) on outcome parameters (overall morbidity, surgical complications, postoperative ileus, and 30-day mortality) was analyzed within a multivariate model. This analysis yielded ASA status 3 and 4 to be independently associated with 30-day mortality ($p=0.033$). Moreover, splenectomy was independently associated with the rate of surgical complications ($p=0.001$). This effect was mainly due to an increased rate of postoperative pleural effusions in the splenectomy group (without splenectomy: 0.8%; with splenectomy: 13.9%), but there were also more anastomotic leaks in the cohort of patients undergoing

Table 5. Postoperative complications in surgically treated gastric cancer patients

	Percentage of data availability	n (per cent of patients for whom data are available)
Complications not directly related to surgery		
urinary tract infection	96,30	22 (8,4)
pneumonia	96,30	29 (11,1)
pancreatitis	90,10	5 (2)
myocardial infarction	90,10	2 (0,8)
sepsis	96,30	10 (3,8)
Surgical complications		
anastomotic leak	96,30	23 (8,8)
peritonitis	96,30	21 (8)
wound infection	96,30	35 (13,4)
bleeding	96,30	32 (12,2)
ileus	96,30	4 (1,5)
seroma formation	96,30	9 (3,4)
complete wound rupture	96,30	4 (1,5)

splenectomy (without splenectomy: 6.1%; with splenectomy: 11.1%). Furthermore, logistic regression yielded a direct association between duration of surgery and the rate of postoperative ileus (p=0.018). All other potential risk factors tested were not shown to be independently associated with any of the outcome parameters.

DISCUSSION

Despite recent advances in our knowledge about molecular characteristics of various cancers, the ongoing development of new antineoplastic drugs and the rapid implementation of multimodal concepts in cancer therapy associated with it, surgical tumor removal remains an indispensable component of potentially curative therapy for gastric cancer. However, the morbidity and mortality of these surgical procedures cannot be neglected. Reports in the surgical literature have demonstrated an overall morbidity around 30% after gastric resections. Postoperative mortality has been reported to be in the range of 1.6 through 8.9% (11-15).

Multi-center quality assurance trials are used to determine the quality of care for a specific type of disease within a defined time span under general care conditions. Their results render information on how recent research findings are implemented into routine clinical care as part of an evidence-based treatment approach. Furthermore, they permit to define a quality standard of care against which the results at one's own institution can be measured. However, this requires a systematic analysis of epidemiological, disease-related, and treatment-related data as well as data on treatment-related complications. In order to achieve this, the present retrospective analysis of surgical care for gastric cancer patients at Otto-von-Guericke University Hospital was carried out. The 10-year time span chosen for our study ends in the year that data were collected for analysis in the multi-center East German Gastric Cancer study; thus, our results can well be measured against the quality standard established in this multi-center trial. Moreover, by choosing a study period ending before the wide-spread implementation of multimodal therapies for gastric cancer in Germany, it was possible to acquire data of a purely surgically treated patient cohort. The data presented here render a precise image of the clinical care situation for gastric cancer patients during the period specified in our institution as demonstrated by the high rates of data availability (>90% for most of the relevant parameters).

Demographic parameters (age, sex, ASA status) were not substantially different between our study and the EGGCS cohort.

Comparison of tumor-related parameters between our patients and the EGGCS data revealed a higher proportion of locally advanced (pT3/pT4-) tumors and proximally located tumors in our study cohort (fig. 3). Tumors located in the cardia/fundus region were 1.7 times more frequent than tumors located

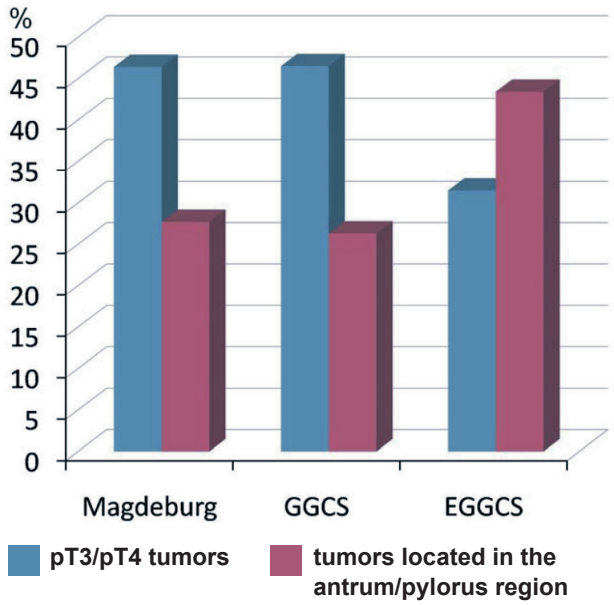

Fig. 3. Proportion of locally advanced (pT3/pT4) tumors and distally located tumors (antrum/pylorus region) within our study cohort, the German Gastric Cancer Study (GGCS) cohort and the East German Gastric Cancer Study (EGGCS) cohort

in the antrum/pylorus region of the stomach in our study while a reversed ratio (1:1.6) was present in the EGGCS patients. There were also more proximally located tumors in the cohort of the German Gastric Cancer Study (GGCS); moreover, the GGCS cohort comprised a proportion of pT3 and pT4 tumors that was almost precisely identical to our data (GGCS: 46.5%, EGGCS: 31.5%, present study: 46.4%) (10, 16). It is one of the distinct characteristics of the EGGCS that it included patients from institutions of all levels of care (community and district hospitals as well as high-volume academic cancer centers). In contrast, only patients from university hospitals were included in the GGCS and only patients from the Otto-von-Guericke University Hospital (Magdeburg) formed the cohort of the present study. Thus, the observed differences in tumor stage and location between the three studies are probably partly due to their different study population. Also, it is likely that the more wide-spread availability of out-patient endoscopy has lead to improved early-stage cancer diagnosis in recent years as compared to the GGCS study period. This is also emphasized by the observation that the proportion of locally advanced tumors decreased significantly in the second half of our study.

As in the two multi-center trials, endoscopy was the principal diagnostic method used for evaluation of local tumor growth and obtaining a pathohistological diagnosis while percutaneous ultrasound and computed tomography (CT) were the main modalities used for evaluation of systemic tumor spread in our study. As a growing proportion of patients are treated in the framework of multimodal concepts a precise determination of tumor infiltration depth into the gastric wall is gaining importance for which purpose EUS appears to be the most appropriate diagnostic modality. EUS was performed in more than two thirds of our patients but only in 27.4% of the EGGCS patients which reflects once again the different levels of care of participating hospitals (all levels of care vs. university hospital). Diagnostic accuracy of EUS for T-stage was higher than in the EGGCS (50.6% vs. 42.6%) but considerably lower than values reported in single-center EUS studies (15, 17). Thus, despite its high sensitivity and specificity for evaluation of local tumor extent, EUS is highly dependent on examiner experience which limits its diagnostic value in routine care. In the study by Willis et al. (15) all patients underwent EUS by a single examiner with an experience of more than 500 EUS exams. This resulted in 78% diagnostic accuracy for T-stage and 77% for N-stage. In contrast, studies evaluating EUS in routine clinical care (18, 19) yielded significantly lower diagnostic accuracy for both T-stage (46-50%) and for discrimination between node-negative and node-positive patients (65%) which lies in the range of the corresponding numbers observed in our study.

In all trials it was observed that EUS diagnostic accuracy was better with locally advanced tumors than with early tumor stages and that a tendency towards overestimating tumor infiltration depth was present as was also the case in our cohort (tab. 3). Since multimodal therapies did not play a significant role in gastric cancer care in Germany during our study period (1993-2003), over- and underestimating T- and N-stage by EUS in our patients probably did not influence therapeutic decisions. However, these data demonstrate that in the era of increasing stage-dependent differentiation of therapies a high level of experience and appropriate instruments of quality control for preoperative diagnostics are needed. Corresponding data from our institu-

tion covering the time span after the period studied here (2003 and following years) are presently being analyzed.

The proportion of patients deemed resectable with curative intent after conclusion of preoperative diagnostics was 82.9% in our study which is almost identical to the corresponding values from the GGCS (82.7%) or the EGGCS (84.4%) study cohort. On the one hand this share is dependent on the actual tumor stage distribution in the cohort examined; on the other hand it also depends on diagnostic accuracy. For the future we expect an increasing share of resectable patients through a more wide-spread implementation of tumor screening methods which will lead to diagnosis in earlier tumor stages (as we were able to demonstrate within the time span of our study). At the same time improvements in preoperative radiological imaging and more wide-spread use of diagnostic laparoscopy will lead to an increasing proportion of unresectable patients being diagnosed preoperatively. The latter development may cause an overall decrease in the proportion of patients treated with curative intent; at the same time the rate of R0 resections among all patients undergoing surgery will increase. This can actually be observed when comparing the GGCS and EGGCS results with our study. The R0 resection rate among all patients undergoing surgery with curative intent was 71.5% in the GGCS and 88.4% in the present study. In the EGGCS (the data of which were collected during the last year of our study period) this rate was also lower (81.5%) than in our study (fig. 4) which may be once again due to the different levels of care of the participating institutions. The proportion of gastrectomies among all patients undergoing surgery with curative intent was almost identical to the corresponding value from the EGGCS cohort (77.2% vs 79.8%). There were slightly more anastomotic leaks of the esophagojejunostomy in our study than in the EGGCS (8.8% vs 5.9%); however, this was still acceptable in the light of corresponding numbers reported in the literature anastomotic leak rate up to 14%) (20, 21). Moreover, overall postoperative morbidity (36.1%; EGGCS: 45%) and early mortality (5.3%; EGGCS: 8%) were not increased compared to the EGGCS. It seems possible that the slightly higher rate of anastomotic leaks in our study is at least partly due to the difference in tumor characteristics between the EGGCS cohort and our patients (higher proportion of locally advanced and proximally located tumors in our study). In a multivariate analysis of the EGGCS data tumor stenosis and dysphagia (both of which are frequently associated with locally advanced tumors) were demonstrated to be independently associated with a higher risk of anastomotic leakage after gastrectomy (31).

D2 lymphadenectomy has gained widespread acceptance as standard of care in gastric cancer surgery in Germany (22). According to the results of the German and Dutch gastric cancer trials (6, 22, 23) it appears likely that D2 lymphadenectomy provides a survival benefit for a subgroup of patients that cannot be identified preoperatively with available diagnostic methods. The D2 lymphadenectomy rate was roughly identical to the D2 LAD rate in the EGGCS at 70%; however, it is expected that the ongoing analysis of the data of patients treated after 2003 will yield an increase in the D2 LAD rate. It is an accepted view in the oncology community that the lack of a survival benefit for the entire study population of the Dutch gastric cancer study is partly due to a substantially elevated postoperative morbidity (43% vs 25%) and mortality (10% vs 4%) in the patients undergoing D2 LAD as com-

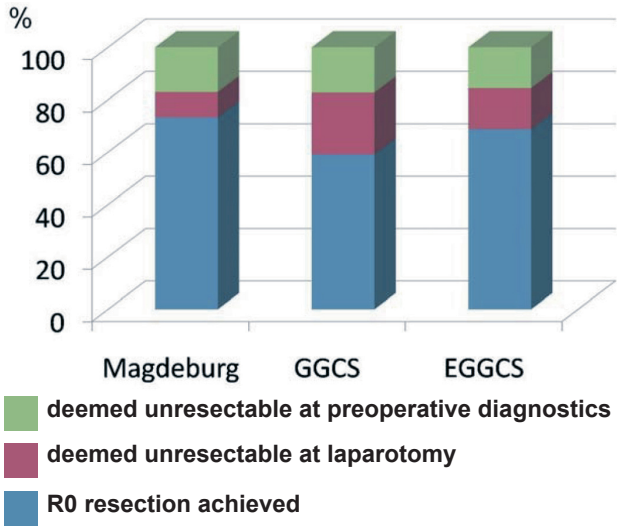

Fig. 4. Proportions of patients in whom an R0 resection was achieved (blue) and patients deemed unresectable at preoperative diagnostics (green) or at laparotomy (red) among our patients, the GGCS study cohort and the EGGCS study cohort

pared to the D1 LAD patients. A substantial part of this can probably be attributed to splenectomies and pancreatic resections frequently carried out in the D2 group in order to fully dissect lymph nodes along the splenic vessels and in the splenic hilum (lymph node stations 10 and 11) (24). In our multivariate analysis of risk factors associated with postoperative morbidity and mortality D2 lymphadenectomy could not be demonstrated to be an independent risk factor.

It has to be admitted that the number of lymph nodes removed in our study (median 18) was relatively low and did not reach the cut-off level of 25 lymph nodes that was found to permit long-term follow-up analysis unhampered by stage migration (also known as the Will-Rogers phenomenon) in the GGCS (28). However, this may not be of major importance for our analysis of early postoperative outcome presented here. A minimum number of 15 lymph nodes is necessary for reliable N staging according to the relevant UICC guidelines (28, 29). In the MRC gastric cancer trial, the number of lymph nodes removed was 13 in the D1 group and 17 in the D2 group (30). The fact that no association between the extent of lymphadenectomy and early postoperative outcome could be demonstrated in our study also suggests that D2 lymphadenectomy can safely be performed in high-volume centers providing adequate perioperative (ICU) care. In contrast, splenectomy was identified to increase the rate of postoperative complications. The rate of splenectomies was fairly high at 40.2%; however, it decreased substantially during the study and was only 26.6% in the second half of the study period (1998-2003) (fig. 2).

Besides its immanent risk of increased morbidity, the oncologic usefulness of splenectomy has also been questioned since metastatic lymph nodes in the splenic hilum do not occur frequently (25). Thus, splenectomy or pancreatic resection is only recommended if necessary in order to achieve an R0 resection in cases of direct tumor invasion or obvious lymph node metastases (26). The reasons for splenectomy in our patients cannot be clearly identified retrospectively; however, there was a higher proportion of pT4 tumors and of tumors postoperatively diagnosed as having pN2 or pN3 lymph node status among the patients undergoing splenectomy. Thus, it is likely that splenectomy was performed due to direct tumor invasion rather than as a standard component of D2 lymphadenectomy at least in part of the patients.

The present study did not focus on long-term survival analysis. It was our aim to create a valid image representing the quality of purely surgical care for gastric cancer patients in our institution before the onset of the era of multimodal therapies and to compare our results with the standard of care established by multi-center quality assurance trials. Also, this study is meant as a baseline for a series of similar analyses scheduled at regular intervals for the future. This is supposed to permit a regular verification of the quality of care delivered by our hospital in relation to the defined standard. Moreover, it will provide information on the influence of new evolving therapies for gastric cancer on procedures and treatment results in our institution. Data of patients treated after 2003 are currently being analyzed; results will be presented in relation with the gastric cancer results of the All-German quality assurance trial "Gastric Cancer, Cancers of the GE junction, GIST 2007/2008" that was conducted by the Institute for Quality Assurance in Surgery at Otto-von-Guericke University Medical School, Magdeburg (Germany). Since first long-term follow-up results of the latter study will soon be available, these data will be included in the upcoming analysis together with follow-up data from our single-center experience, taking into account the growing proportion of patients treated within multimodal concepts.

CONCLUSIONS

Due to its status as a tertiary referral center our hospital treats gastric cancer patients with a number of distinct characteristics placing them at higher surgical risk compared to patients of the East German Gastric Cancer study cohort. In particular, our data indicate a higher proportion of patients with locally advanced and proximally located gastric tumors. We were able to demonstrate a decline of patients with advanced tumor stages over the 10 year time span of our study; a similar development could also be shown comparing patients from the German Gastric Cancer Study of 1992 (GGCS) cohort with the EGGCS patients. It is likely that this is partly due to

improved tumor screening and diagnostics in recent years. The increasing share of patients undergoing preoperative EUS in our study is in keeping with the world-wide trend towards stage-dependent differentiation of therapeutic concepts, fulfilling the role of a university hospital as leader in cancer care in our region.

However, the quality of EUS exams urgently needs to be improved since diagnostic accuracy was demonstrated to fall far behind other studies though these are specialized single-center trials specifically dealing with EUS and cannot easily be applied to the routine clinical care situation. Overall preoperative diagnostic accuracy regarding resectability was shown to be higher in our study than in both the GGCS or the EGGCS as demonstrated by the R0 resection rate of 88.4% (EGGCS: 81.5%; GGCS: 71.5%). Our early postoperative outcome data were grossly equal to the EGGCS results. In accordance with earlier studies dissection of the D2 lymph node compartment was not demonstrated by itself to increase surgical risk; however, splenectomy as part of gastric cancer surgery was shown to be an independent risk factor for increased postoperative morbidity. The splenectomy rate decreased substantially during the study period.

In summary, these results demonstrate that gastric cancer surgery at our institution fulfills the quality standard established by the EGGCS in patients having an increased risk factor profile. Data of patients treated after 2003 are currently being analyzed; results will be available for analysis in relation with the gastric cancer results of the All-German quality assurance trial "Gastric Cancer, Cancers of the GE junction, GIST 2007/2008". Besides being a valuable instrument of continuing internal quality assurance, this will permit to obtain information on the implementation of new evolving therapies in gastric cancer and their influence on the management of these patients at our institution.

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