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Insufficiency risk of esophagojejunal anastomosis after total abdominal gastrectomy for gastric carcinoma

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Abstract *Background:* The outcome and quality of surgical treatment in gastric cancer are closely associated with specific postoperative morbidity and mortality, in addition to an oncosurgically adequate resection status. In this context, a preventive concept of decreasing the insufficiency rate of esophageal anastomosis may have a great impact. *Method:* Over a time period of 12 months (from 1 January 2002 to 31 December 2002), 1,199 patients (from 80 East German hospitals) with gastric carcinoma, carcinoma of the esophago-gastral junction, or gastrointestinal stroma tumor (GIST) were enrolled in this prospective multicenter observational study with the aim of evaluating their early postoperative outcome. By means of a logistic regression analysis, independent variables, which alter significantly the healing of esophagojejunal anastomosis, were determined; in addition, their clinical impact on preventive management to lower the insufficiency rate of esophageal anastomosis was investigated. *Results:* In 1,139 patients, histological investigation revealed gastric carcinoma. Out of these patients, 1,031 subjects underwent surgical intervention (90.5%) and 891 individuals underwent resection (86.4%). In 813 patients, radical resection (subtotal resection and gastrectomy) was executed (78.9%), whereas in 726 cases, R₀ resection was achieved (81.5%). Gastrectomy was the preferred procedure in 649 patients, resulting in a gastrectomy rate of 62.9% relating to all patients who underwent operation

(curative and palliative intention, 80.3% and 19.7%, respectively). The insufficiency rate of esophagojejunal anastomosis was 5.7% (37/649). Neither the comparison between the various procedures for the reconstruction of the esophagojejunal passage and anastomosing techniques after gastrectomy nor that between gastrectomies with curative and palliative intention revealed any significant difference. Dysphagia and gastric outlet syndrome due to a stenosis were determined as independent variables by a logistic regression analysis of all preoperative and intraoperative variables. In all patients with gastric carcinoma, both parameters were recorded in 9.9% (113/1,139) and 6.7% (76/1,139), respectively. *Conclusion:* Dysphagia and gastric stenosis, which significantly influence the healing of esophagojejunal anastomosis after gastrectomy, are considered characteristics of an advanced tumor growth and a pretherapeutic lack of an adequate nutrition. This emphasizes the necessity of an early diagnosis of gastric cancer in order to lower perioperative morbidity. In addition, dysphagia is commonly associated with an obstruction of the upper gastrointestinal tract, which can lead to nutritional deficits, and thus deserves specific care during preventive management.

Keywords Gastric carcinoma · Gastrectomy · Esophagojejunal anastomosis · Anastomotic insufficiency · Prevention

Introduction

Gastric carcinoma is associated with 5-year survival rates of between 8 and 85% after R₀ resection, depending on tumor stage [1, 2]. The outcome after surgical treatment is significantly influenced by postoperative mortality and morbidity (e.g., mortality has been reported from various surgical centers to be between 0 and 15%) [3–7]. Perioperative morbidity is determined by the occurrence of infectious complications (such as wound infection, pneumonia, or urinary tract infections), the number of red blood units or required surgical revisions, and the insufficiency rate at the esophagojejunal anastomosis as considerable factors. Various authors from surgical centers with adequate caseloads have reported rates ranging from 1.3 to 15.9% [8–16]. Unfortunately, data obtained in prospective or multicenter

studies are rare or missing and are dominated by results from retrospective studies [9–11, 13, 15, 16].

Based on prospectively documented cases with gastrectomy due to gastric cancer in a database with a representative case number for descriptive statistics, the aims of the study were: (1) to determine the frequency and influencing factors of the insufficiency of esophagojejunal anastomosis in a multicenter clinical observational study and (2) to derive a preventive concept.

Patients and methods

The study was designed as a prospective multicenter observational study led by the Institute for Quality Control in Operative Medicine, University Hospital, Otto-von-

Table 1 Characteristics of the study “Quality Control in Gastric Carcinoma 2002 (Primary Tumor Growth)—general aspects and patients

Category	Data
Type of study	Clinical observation
Epidemiological classification	Patient cohort (gastric cancer) Case series (abdominal gastrectomy)
Data	
Documentation	Prospective (standardized documentation form, electronic database)
Evaluation	Retrospective (computer-based statistical tests)
Study period	1 January 2002 to 31 December 2002
Participating hospitals	80
Number of patients (<i>n</i>)	
Gastric carcinoma	1,139
Abdominal gastrectomy	586
Sex ratio (male:female)	59.5:40.5
Patients' age [median (range)]	68 (14–100)
Number of patients per hospital enrolled in the study [median (range)]	12 (1–62)
Profile of factors tested for a statistically significant impact on anastomotic healing	Body mass index Medical history (weight loss, dysphagia, anemia) ASA Physical Status Classification System Comorbidity Perioperative prophylaxis with antibiotics Emergency intervention Surgical intervention Intention (curative vs palliative) Duration Reconstruction of the upper gastrointestinal tract Technique of anastomosis Extent of lymphadenectomy Intraoperative complications Resection status and TNM staging

Guericke University (Magdeburg, Germany). Data were obtained from 80 East German hospitals of all levels of clinical care, such as regional and university hospitals, through a time period of 12 months (1 January 2002 to 31 December 2002). All patients with a primary and malignant gastric tumor growth [such as gastric carcinoma, carcinoma of the esophagogastral junction, or gastrointestinal stroma tumor (GIST)] who were admitted to one of the participating surgical departments were enrolled in the study. Exclusion criteria were tumor recurrence and other histological entities.

Study participation was voluntary; no hospitals were excluded. The participating surgical departments committed a complete prospective documentation of all consecutive patients meeting the inclusion criteria independent of therapeutic modalities (conservative or operative). To control the completeness of documentation, spot checks comparing the data with lists of clinic documentation systems were performed. The rate of registration was >95%.

Precise descriptions of the study design and performance have been summarized by Meyer et al. [17].

For specific aims, all subjects who underwent total abdominal gastrectomy due to gastric carcinoma, including esophagojejunal anastomosis, were investigated.

The patients were evaluated with regard to the following:

- Total number, age, and sex
- Operative vs. conservative (nonoperative) treatment
- Curative vs. palliative intention of surgical intervention
- Various surgical procedures
- Reconstruction
- Type of anastomosis (Table 1).

In particular, the patients who underwent total abdominal gastrectomy were investigated, since this group of patients formed the case series with the greatest case number and relatively homogenous characters, including the criterion of an esophagojejunal anastomosis. Anastomotic insufficiency was defined as a radiologically and/or endoscopically detectable leakage of the stapler or suture area at the esophagojejunal anastomosis and was related to the type of reconstruction of the upper gastrointestinal tract after gastrectomy, anastomosis technique, and therapeutic intention (curative vs. palliative).

Statistics

Descriptive statistics of the data were achieved using SPSS for Windows (Version 12.0). All available preoperative and intraoperative variables with possible correlation to anastomotic healing were investigated (see Table 1). Logistic regression was performed as a setup procedure. A univariate analysis of all investigated parameters was followed by a multivariate analysis to elucidate independent variables as appropriate, which influence the development of anastomotic insufficiency.

Results

Through the 12 months of 2002, 1,199 patients from 80 hospitals with gastric carcinoma, carcinoma of the esophagogastral junction, or GIST who were diagnosed by histological investigation were prospectively documented using a standardized protocol. Out of all these patients, gastric carcinoma was diagnosed in 1,139. One-thousand thirty-one individuals (90.5%) underwent surgical intervention [nonsurgical treatment, $n=108$ (9.5%)]. Altogether, 649 patients were approached with total gastrectomy, resulting in a gastrectomy rate of 62.9% (649/1,031). Considering the group of resected patients ($n=891$), the rate was 72.8%, whereas the gastrectomy rate related to the subjects with radical resection, such as subtotal resection or gastrectomy, was 79.8%. Out of the 726 resected patients with curative intention, 527 (72.6%) underwent gastrectomy (Table 2).

The case series of total, exclusively abdominal gastrectomy comprised 586 patients, out of whom 475 individuals (81.1%) were surgically approached with curative intention and 111 subjects were surgically approached with (18.9%) with palliative intention. The spectrum of various types of anastomoses was dominated by a Roux-Y loop ($n=526$; 89.8%), subdivided into 380 cases (72.2%) without a pouch and 146 cases (27.8%) with a pouch. The following most frequently used types of anastomosis were: omega loop in 27 patients (4.6%; without a pouch, $n=12$; with a

Table 2 Characteristics of the study “Quality Control in Gastric Carcinoma 2002 (Primary Tumor Growth)”—number of surgical interventions

Category	Data
Treatment (n ; $n_{\text{total}}=1,139$)	
Operative	1,031 (90.5%)
Conservative (nonoperative)	108 (9.5%)
Patients with surgical intervention (n ; $n_{\text{total}}=1,031$)	
No resection	140 (13.6%)
Resections	891 (86.4%)
Gastrectomies	
Including extended gastrectomies	649 (62.9%)
Only abdominal	586 (56.8%)
Resections and intention (n ; $n_{\text{total}}=891$)	
Curative	726 (81.5%)
Palliative	165 (18.5%)
Total gastrectomy (including extended gastrectomies)	
Total (n)	649
Percentage in all [n (%)]	
Patients	649/1,139 (57.0%)
Patients with surgical intervention	649/1,031 (62.9%)
Resected patients	649/891 (72.8%)
Curatively resected patients	527/726 (72.6%)

Table 3 Characteristics of the study “Quality Control in Gastric Carcinoma 2002 (Primary Tumor Growth)—total abdominal gastrectomy

Category	Data
Total abdominal gastrectomy and intention [<i>n</i> (%)]	
Total	586 (100.0%)
Curative	475 (81.1%)
Palliative	111 (18.9%)
Total abdominal gastrectomy and reconstruction [<i>n</i> (%)]	586 (100.0%)
Interposition of a segment of the small intestine (Longmire)	25 (4.3%)
Roux loop	
Without pouch	380 (64.8%)
With pouch	146 (24.9%)
Omega loop	
Without pouch	12 (2.0%)
With pouch	15 (2.6%)
Others	8 (1.4%)
Total abdominal gastrectomy and type of anastomosis [<i>n</i> (%)]	586 (100.0%)
Stapler	550 (93.9%)
Suture by hand	
One layer	31 (5.3%)
Two layers	5 (0.8%)

pouch, *n*=15) and interposition of a small intestine segment by Longmire in 25 cases (4.3%). Stapler anastomosis dominated the profile of surgical techniques (*n*=550, 93.9%). Hand sewing of the anastomosis (*n*=36) was infrequently used: one layer, *n*=31 (86.1%); two layers, *n*=5 (13.9%) (Table 3).

The overall insufficiency rate of esophagojejunal anastomosis in abdominal gastrectomy was 5.5% (32/586), with no significant difference between the various types of surgical reconstruction of the upper gastrointestinal tract and various techniques for the esophagojejunal anastomosis. Related to the type of surgical reconstruction of the upper gastrointestinal tract, the insufficiency rates were as follows: Roux-Y loop without a pouch, 5.3% (20/380) vs. 6.2% with pouch (9/146); interposition of a segment of the small intestine by Longmire, 0% (0/25); and omega loop with and without a pouch, *n*=0 (0/15) and 8.3% (1/12), respectively.

Although stapler anastomosis was insufficient in 29 of 550 cases (5.3%), hand sewing (one layer) caused an insufficiency rate of 9.7% (3 of 31 patients). In the five subjects who received two-layered hand-sutured anastomoses connecting the aboral end of the esophagus with the oral end of the jejunal loop, insufficiency or leakage was not observed. Comparing curative intention with palliative intention in surgical treatment, there was also no significant

difference in the postoperative development of anastomotic insufficiency: 5.1% (24/475) and 7.2% (8/111), respectively (Table 4).

The results of the univariate and multivariate analyses of all investigated variables (see Table 1) are summarized in Table 5. In the univariate analysis, we establish a significant connection of anastomotic insufficiency with preoperative dysphagia, gastric stenosis, positive (metastatic) lymph nodes, nicotine abuse, and multivisceral resection. In the following multivariate analysis, dysphagia and gastric stenosis proved to be independent, significantly influencing factors for the occurrence of postoperative insufficiency of the esophageal anastomosis with odds ratios of 3.408 and 3.762, respectively.

In the group of total abdominal gastrectomies, 6.7% (39/586) of the patients showed preoperative dysphagia and 5.1% (30/586) showed gastric stenosis. Patients with dysphagia suffered from an anastomotic leakage in 12.8% (5/39), whereas patients without dysphagia suffered from an anastomotic leakage in 4.9% (27/547). In addition, insufficiency rate in patients with gastric stenosis was 16.7% (5/30) and was therefore pronouncedly higher than the 4.9% (27/556) in patients without gastric stenosis.

Table 4 Characteristics of the study “Quality Control in Gastric Carcinoma 2002 (Primary Tumor Growth)—insufficiency of anastomosis

Category	Data
Anastomotic insufficiency and reconstruction [<i>n</i> (%); <i>n</i> _{total} =586 total abdominal gastrectomies]	NS (<i>P</i> =0.416)
Total	32/586 (5.5%)
Interposition of a segment of the small intestine (Longmire)	0/25 (0%)
Roux-Y loop	
Without pouch	20/380 (5.3%)
With pouch	1/146 (6.2%)
Omega loop	
Without pouch	1/12 (8.3%)
With pouch	0/15 (0%)
Anastomotic insufficiency and type of anastomosis [<i>n</i> (%); <i>n</i> _{total} =586 total abdominal gastrectomies]	NS (<i>P</i> =0.243)
Total	32/586 (5.5%)
Stapler	29/550 (5.3%)
Suture by hand	
One layer	3/31 (9.7%)
Two layers	0/5 (0%)
Anastomotic insufficiency and intention [<i>n</i> (%); <i>n</i> _{total} =586 total abdominal gastrectomies]	NS (<i>P</i> =0.357)
Total	32/586 (5.5%)
Curative	24/475 (5.1%)
Palliative	8/111 (7.2%)

NS Not significant

Table 5 Characteristics of the study “Quality Documentation in Gastric Cancer 2002 (Primary Tumor Growth)”—results of univariate and multivariate analyses for anastomotic insufficiency (only significant results)

Parameter	Univariate analysis (<i>P</i>)	Multivariate analysis (<i>P</i>)	Odds ratio
Dysphagia	0.003	0.005	3.408
Gastric stenosis	0.008	0.013	3.762
Positive lymph node status	0.018		
Nicotine abuse	0.019		
Multivisceral resection	0.022		

Discussion

The insufficiency of the esophagojejunal anastomosis after gastrectomy alters considerably the overall outcome in the surgical treatment of gastric cancer. Various authors have reported insufficiency rates to be between 1.3 and 15.9% [9–12, 14–16]. In the present study, this rate is 5.7%. The much comparable German Gastric Cancer Trial (GGCS)

found an insufficiency rate of 7.2% [8]. Although 19 hospitals were involved in the GGCS at the end of the 1980s, in particular and almost exclusively university hospitals (gastrectomies, $n=787$), 80 hospitals of various levels of clinical care participated in this study (gastrectomies, $n=586$).

Comparing the same parameter (the number of radical resections), gastrectomy rate is higher compared with GGCS: 72.1 vs. 47.7%; including the extended gastrectomies, the percentages are 79.8% in this study vs. 71.1% in the GGCS. Other authors report gastrectomy rates to be between 40 and 55% [18–21].

The majority of participating hospitals favored the Roux-Y loop without a pouch for the reconstruction of the upper gastrointestinal tract after gastrectomy, which was used in 380 patients (64.8%). Similarly, stapler anastomosis (93.9%) dominated hand-sewn anastomoses. Neither the comparison between the various procedures for the reconstruction of the upper gastrointestinal tract and the various anastomosing techniques after gastrectomy nor that between gastrectomies with curative and palliative intention revealed any significant difference in the occurrence of postoperative insufficiency in the esophagojejunal anastomosis. Therefore, identification

Table 6 Comparison of data from the literature on insufficiency rates of esophagojejunal anastomosis

Author	Year	Type of study	Number of patients	Anastomotic insufficiency	Remarks
Panieri and Dent [11]	2003	Retrospective	175	4.0%	No independent influencing factors
Yasuda et al. [15]	2001	Retrospective	97	14.0%	Tumors $\varnothing > 10$ cm, duration of Op, blood loss, carcinoembryonic antigen
Lang et al. [10]	2000	Retrospective	1,114	7.5%	Study period, 30 years; independent of reconstruction/radical approach
Schardey et al. [13]	1998	Retrospective	838	15.9%	Study period, 20 years; cardia, splenectomy, Op > 5 h, hand suture
Isozaki [9]	1997	Retrospective	404	8.2%	Lymphocytes, albumin
Zilling [16]	1997	Retrospective	174	11.5%	Case and work load (number of interventions), surgeon
Seufert [14]	1990	Prospective, randomized (hand suture vs stapler)	80	$n=1$ (Stapler)	No significant differences (duration of Op, morbidity, mortality, duration of hospital stay)
Schardey et al. [12]	1997	Prospective, randomized (oral decontamination vs placebo)	102 vs 103	2.9 vs 10.6%	Both groups with systemic prophylaxis with antibiotics
Böttcher et al. [8]	1994	Prospective	787	7.2%	Extended gastrectomy, surgeon, assistant
East German Study Group	2004	Prospective	586	5.5%	Dysphagia, gastric stenosis

Op Operation (synonyma and surgical intervention)

of further influencing factors in order to achieve a preventive effect is of great importance in univariate and multivariate logistic regression analyses (a list of selected reports is presented in Table 6). Important factors established in these papers are advanced tumor growth, extended surgical intervention, patient's nutritional status, and duration of the intervention. In addition, the caseload of a surgical center and the factor "surgeon" are considered as further criteria for the final outcome. However, there are only very few data on controlled studies that are available in the literature [12, 14].

This study elucidates that dysphagia and gastric stenosis are independent variables with a significant impact on the development of esophagojejunal anastomosis insufficiency. Both are characteristic aspects of an advanced tumor growth and underline the required early detection and diagnosis of gastric cancer.

In 52.5% ($n=598$) of the documented gastric cancer cases of this study, stages III and IV, according to the Union International Contre le Cancer classification, were diag-

nosed. In addition, dysphagia is the leading symptom of an obstruction of the upper gastrointestinal tract, which is frequently associated with a severe nutritional deficit. This might offer possible options for a preventive approach prior to gastric resection. First, the preoperative nutritional status should be objectively characterized beginning with the documentation of current nutritional aspects of a patient's medical history and a clinical examination of nutritional status. According to the literature, this can be completed by some special laboratory parameters, such as serum albumin level and lymphocyte count as well as physiological parameters (e.g., body impedance analysis). The influence of nutritional deficit on the complication rate and postoperative outcome has been investigated several times and has resulted in a significant impact of this relevant factor [22–24]. Thus, an adapted, short-term, hypercaloric preoperative nutritional supplementation [25] can improve the nutritional status prior to the surgical intervention and can be supportive in the prevention of esophagojejunal anastomosis insufficiency [26].

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