Quality assurance in the surgical treatment of gastric cancer

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CHAPTER 3

SURGICAL MORBIDITY AND MORTALITY AFTER NEOADJUVANT CHEMOTHERAPY IN THE CRITICS GASTRIC CANCER TRIAL

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ABSTRACT

Background: In order to determine the optimal combination of perioperative chemotherapy and chemoradiotherapy for Western patients with advanced resectable gastric cancer, the international multicentre CRITICS trial (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) was initiated. In this trial, patients with resectable gastric cancer were randomised before start of treatment between adjuvant chemotherapy or adjuvant chemoradiotherapy following neoadjuvant chemotherapy plus gastric cancer resection. The purpose of this study was to report on surgical morbidity and mortality in this trial, and to identify factors associated with surgical morbidity.

Methods: Patients who underwent a gastrectomy with curative intent were selected. Logistic regression analyses were used to assess risk factors for developing postoperative complications.

Results: Between 2007 and 2015, 788 patients were included in the CRITICS trial, of whom 636 patients were eligible for current analyses. Complications occurred in 296 patients (47%). Postoperative mortality was 2.2% (n=14). Complications due to anastomotic leakage was cause of death in 5 patients. Failure to complete preoperative chemotherapy (OR=2.09, *P*=0.004), splenectomy (OR=2.82, *P*= 0.012), and male sex (OR=1.55, *P*=0.020) were associated with a greater risk for postoperative complications. Total gastrectomy and oesophago-cardia resection were associated with greater risk for morbidity compared with subtotal gastrectomy (OR=1.88, *P*=0.001 and OR=1.89, *P*=0.038).

Conclusion: Compared to other Western studies, surgical morbidity in the CRITICS trial was slightly higher whereas mortality was low. Complications following anastomotic leakage was the most important factor for postoperative mortality. Important proxies for developing postoperative complications were failure to complete preoperative chemotherapy, splenectomy, male sex, total gastrectomy, and oesophago-cardia resection.

INTRODUCTION

Gastric cancer is the fourth most common malignancy worldwide with nearly one million new cases per year, and the third leading cause of cancer death with an estimated 723.000 deaths in 2012.[1] Survival remains poor with only 25% of all gastric cancer patients surviving the first five years.[2]
Surgery is the only curative treatment for locally advanced gastric cancer. In the Western world, a gastrectomy is considered high-risk surgery with surgical morbidity rates of 39% and mortality rates of approximately 5%.[3, 4] Even after an adequate gastric resection with a D2 lymphadenectomy, survival remains poor with a 5-year survival around 50%.[5]

Several studies have been performed to improve survival for locally advanced gastric cancer with (neo-) adjuvant chemotherapy and/or radiotherapy. Two randomised studies, the Intergroup 0116 trial and the MAGIC trial, changed current clinical practice for resectable gastric cancer in the Western world.[6, 7] In the Intergroup 0116 trial, a survival benefit was shown with adjuvant chemoradiotherapy compared to surgery alone, whereas in the MAGIC trial peri-operative chemotherapy improved survival over surgery alone.[6, 7] A direct comparison of the results from these two trials was not possible due to the differences in study design and eligibility criteria. To determine the optimal approach for adjuvant therapy after gastrectomy in patients with gastric cancer, the CRITICS (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) trial was initiated. In this multicentre trial, patients with resectable gastric cancer were treated with three cycles of preoperative chemotherapy, followed by surgery with adequate lymph node dissection, followed by either three cycles of chemotherapy (standard arm) or concurrent chemoradiation (experimental arm), according to the results of randomisation before the start of treatment.[8]
The purpose of the present analyses was to evaluate surgical morbidity and mortality in the CRITICS trial and to identify risk factors for postoperative complications.

METHODS

CRITICS protocol
The protocol of the CRITICS trial has been published previously.[8] Patients with a histologically proven stage Ib-IVa (AJCC 6th edition) gastric adenocarcinoma were eligible for inclusion.[9] The bulk of the tumour had to be located in the stomach (determined by gastroscopy and/or endoscopic ultrasound), although extension into the gastro-oesophageal junction (GEJ) was allowed. The most important exclusion criteria were medical inoperability, distant metastases, and an uT1N0 tumour (determined with endoscopic ultrasound). Randomisation was performed before start of treatment.
Prior to surgery, all patients received three cycles of epirubicin, cisplatin or oxaliplatin, and capecitabine (ECC/EOC) at three-weekly intervals. Surgery was planned three to six

weeks after the last chemotherapy cycle. The principle of surgery was a wide resection of the tumour bearing part of the stomach en bloc with the N1 and N2 lymph nodes according a so-called D1+ lymph node dissection (lymph node stations 1-9 and 11) and with a minimum of 15 lymph nodes removed.[10] For tumours in the upper part of the stomach, a total gastrectomy was recommended with removal of lymph node station of 1-9 and 11. For tumours in the middle or distal part of the stomach, a subtotal resection of the stomach was recommended with removal of lymph node station of 1-9 and 11 apart from lymph node stations 2 and 4s. A trans-hiatal oesophagus-cardia resection was defined as resection of the distal part of the oesophagus and the upper part of the stomach (cardia) through the abdominal cavity with removal of lymph node station of 1-9 and 11 apart from lymph node stations 4d and 6. This type of resection with gastric tube reconstruction was allowed for tumours extending into the oesophagus.
Adjacent organs were removed only in case of there was suspicion of tumour involvement. If possible, a macroscopic margin of 5 cm was obtained to the proximal as well as the distal end.
Within twelve weeks after surgery, patients were treated with either adjuvant chemotherapy (three courses of ECC/EOC) or adjuvant chemoradiotherapy (radiotherapy combined with capecitabine and cisplatin), according to the upfront randomisation.

Patient selection and comorbidity
Patients who underwent a gastric resection with curative intent were selected from the CRITICS patient cohort. Curative intention of the gastrectomy was reviewed by two expert gastric surgeons based on the surgery report.
Co-morbidity was recorded in the Case Report Form (CRF) and was defined as the presence of at least one disease of the cardiovascular system, the gastrointestinal system, the genitourinary system, the central nervous system, the endocrine system, allergies, any musculoskeletal diseases, or other medical diseases. Co-morbidity was divided into three subgroups: none, presence of 1 or 2 co-existing diseases, and presence of three or more co-existing diseases.

Postoperative complications and postoperative mortality
Postoperative complications were blinded reported in the CRF without registration of grading of the complications. Postoperative complications were categorised in the CRF as surgery related complications (such as anastomotic leakage, bleeding, and ileus), infectious complications (such as abscess, sepsis, and abdominal wound infection), and general complications (such as pulmonary, cardiovascular, and thrombo-embolic). No uniform definitions of surgery related, infectious complications, and general complications were described in the study protocol of the CRITICS trial. Re-intervention due to a complication was defined as a re-intervention done for the management of a postoperative complication and was recorded in the CRF. Re-intervention was the equivalent of a Clavien-Dindo IIIA or IIIB grade.[11] Postoperative mortality was defined as death within 30 days after surgery or during hospital stay, if this exceeded 30 days.

Statistical analyses

Uni- and multivariate logistic regression analyses were used to assess risk factors for developing a postoperative complication. The chi-squared test was used to compare categorical data between total gastrectomies, subtotal gastrectomies, and oesophagocardia resections and the non-parametric Kruskal-Wallis test was used for numerical data. For all statistical analyses SPSS program 21.0 was used. A $P < 0.05$ was considered statistically significant.

RESULTS

Patient and surgical characteristics

The CRITICS gastric cancer trial was a multicentre (56 centres) randomised clinical trial, conducted in the Netherlands, Sweden, and Denmark from January 2007 to April 2015. In total, 788 patients were randomised of whom 152 patients did not meet the selection criteria for the current analyses (*Figure 1*). Consequently, 636 patients who underwent gastric cancer resection with curative intent were selected for the current analyses.

In total, 87 patients (13.7%) were not able to complete neoadjuvant chemotherapy. The majority of these patients had problems due to toxicity (n=74, 85.1%), followed by intercurrent disease (n=5, 5.7%), stomach bleeding/ perforation (n=3, 3.4%), poor condition (n=2, 2.3%), progression of the disease (n=1, 1.1%), refusal of patient (n=1, 1.1%), or death (n=1, 1.1%).

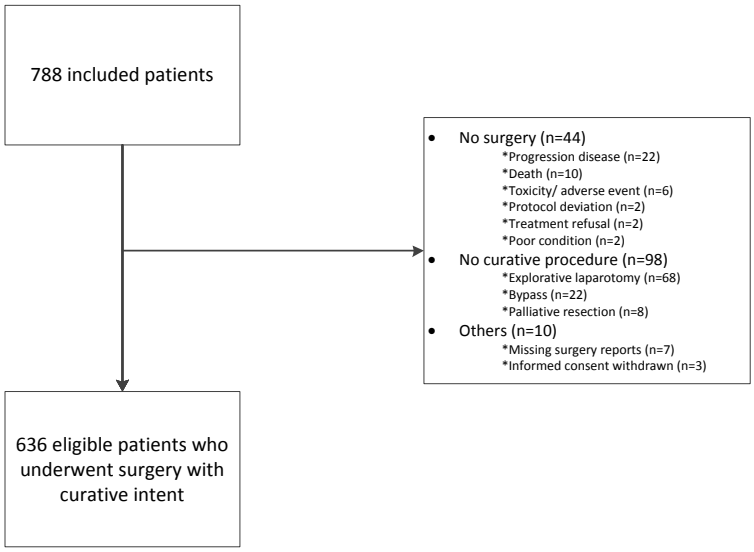

Figure 1. Study flow chart

Patient and surgical characteristics are shown in *Table 1*. Most patients underwent a total (n=318, 50.0%) or a subtotal gastrectomy (n=255, 40.1%), whereas a small group had an oesophago-cardia resection (n=63, 9.9%). Forty-nine patients with an antrum tumour had a total gastrectomy due to more extensive growth of diffuse type tumours. One patient with a proximal tumour underwent a proximal gastric resection. Usually, surgery was performed with an open approach (n=530, 83.3%); a laparoscopic procedure was performed in 101 patients (15.9%). The conversion rate was 11.9% (n=12). Reasons for conversion were direct tumour ingrowth in adjacent organs (n=9), perforation of meso-colon (n=1), perforation of duodenum (n=1), and hemodynamic instability (n=1). Thirty-eight patients underwent a splenectomy (6.0%) due to tumour ingrowth (65.5%), or bleeding (34.5%). Three patients in the subtotal gastrectomy group underwent a splenectomy, due to bleeding (n=2) or ingrowth of tumour (n=1). Sixteen patients underwent a distal pancreatectomy (2.6%) of whom half had a splenectomy as well. After excluding the patients of whom the location of the resected lymph node stations were not extractable from the surgery report (n=14), the majority of patients (n=544, 87.5%) underwent a D1+ lymph node dissection or more. In most of the patients (n=460, 72.8%) at least 15 lymph nodes were removed. A median of 20 retrieved lymph nodes were reviewed by the pathologist.

Table 1. Patient and surgical characteristics

	Total (n=636)
Age (years)	62 (28-82)
Sex	
Male	429 (67.5)
Female	207 (32.5)
BMI	
<18	15 (2.4)
18-24	306 (48.1)
≥25	315 (49.5)
Co-morbidity	
None	85 (13.4)
1-2	327 (51.4)
≥3	224 (35.2)
Completion preop chemo	
Yes	549 (86.3)
No	87 (13.7)
Tumour localisation	
Proximal	224 (35.2)
Middle	187 (29.4)
Distal	225 (35.4)

Table 1 continues

	Total (n=636)
Type of resection	
Total gastrectomy	318 (50.0)
Subtotal gastrectomy	255 (40.1)
Oesophago- cardia resection	63 (9.9)
Lauren classification	
Intestinal	175 (27.5)
Diffuse	206 (32.4)
Mixed	34 (5.3)
Missing	221 (34.8)
ypT stage	
ypT0/pTis/pT1	133 (20.9)
ypT2	222 (34.9)
ypT3	217 (34.1)
ypT4	64 (10.1)
ypN stage	
ypN0	311 (48.9)
ypN1	214 (33.7)
ypN2	77 (12.1)
ypN3	34 (5.3)
Radicality	
R0	515 (81.0)
R1	66 (10.4)
Unknown	55 (8.6)
Approach	
Open	530 (83.3)
Minimally invasive	89 (14.0)
Conversion	12 (1.9)
Missing	5 (0.8)
Splenectomy	
Yes	38 (6.0)
No	598 (94.0)
Pancreatectomy	
Yes	16 (2.6)
No	624 (97.4)

Age is presented as median (range), other data are presented as n (%).
Abbreviations; BMI = Body Mass Index; Completion preop chemo = completion of preoperative chemotherapy.

Postoperative complications and postoperative mortality
The overall complication rate was 46.5% (n=296, *Table 2*). Approximately 60% (n=52) of the patients who did not complete preoperative chemotherapy (n=87) developed a postoperative complication. Surgery related complications in the total study population occurred in 142 patients (22.3%). Anastomotic leakage was the most frequent surgical complication (n=45, 7.1%), followed by bleeding (n=18, 2.8%), and ileus (n=18, 2.8%). Reinterventions due to a complication occurred in 13.4% (n=85) of the total study population. Of the patients who developed a complication, 56.3% and 57.2% of the patients of the chemotherapy and chemoradiotherapy arm, respectively, did complete adjuvant treatment, compared to 60.0% and 67.6% of the patients who did not develop a complication (*P*<0.001 and *P*=0.036*)*. Data of complications of the different surgical subgroups are given in *Table 2*.

Table 2. (Three most frequently occurring) complications of subtotal gastrectomies, total gastrectomies, oesophago-cardia resections, and total study population

	Subtotal gastrectomy (n=255)	**Total gastrectomy (n=318)**	**Oesophago-cardia resection (n=63)**	***P***	**Total (n=636)**
Complication overall	93 (36.5)	170 (53.5)	33 (52.4)	*<0.001*	296 (46.5)
Surgery related complications	40 (15.7)	85 (26.7)	17 (27.0)	*0.004*	142 (22.3)
Anastomotic leakage*	5 (2.0)	32 (10.1)	8 (12.7)	*<0.001*	45 (7.1)
Bleeding*	5 (2.0)	13 (4.1)	0 (0.0)	0.112	18 (2.8)
Ileus*	6 (2.4)	11 (3.5)	1 (1.6)	0.597	18 (2.8)
Infectious complications	37 (14.5)	98 (30.8)	13 (20.6)	*<0.001*	148 (23.3)
Abscess*	8 (3.1)	28 (8.8)	1 (1.6)	*0.005*	37 (5.8)
Sepsis*	7 (2.7)	24 (7.5)	4 (6.3)	*0.038*	35 (5.5)
Abdominal wound inf*	9 (3.5)	15 (4.7)	2 (3.2)	0.705	26 (4.1)
General complications	53 (20.8)	103 (32.4)	24 (38.1)	*0.001*	180 (28.3)
Pulmonary*	15 (5.9)	48 (15.1)	15 (23.8)	*<0.001*	78 (12.3)
Cardiovascular*	7 (2.7)	25 (7.9)	5 (7.9)	*0.024*	37 (5.8)
Pulmonary embolism*	1 (0.4)	6 (1.9)	4 (6.3)	*0.004*	11 (1.7)
Reintervention due to complication	18 (7.1)	55 (17.3)	12 (19.0)	*0.001*	85 (13.4)
Hospital stay (days)	10 (8-14)	12 (10-17)	12 (10-16.3)	*<0.001*	11 (9-16.3)

Duration of surgery, blood loss, and hospital stay are presented as median (25 percentile – 75 percentile), other data are presented as n (%). Abbreviations; Abdominal wound inf = abdominal wound infection.
**three most frequently occurring complications, a patient can be registered for more than one complication*

Postoperative mortality was 2.2% (n=14) in the total group, and 8.0% (n=7) in the group that did not complete preoperative chemotherapy (n=87). Cause of death of the 14 patients were complications due to anastomotic leakage (n=5), followed by duodenal stump leakage (n=2), bleeding after abdominal infection (n=2), intestinal ischemia (n=1), tumour perforation (n=1), pancreatitis (n=1), complications following pulmonic complications (n=1), and sudden cardiac arrest (n=1). Two patients (5.3%) died in the group of splenectomies (n=38) and two patients (12.5%) in the group of distal pancreatectomies (n=16), of whom one had a splenectomy as well. After developing a complicated postoperative course, postoperative mortality was highest in the group aged 70+ (n=5, 7.4%), compared to 5.3% (n=6) and 2.6% (n=3) in the group of 60-69 years and in the younger than 60 years group, respectively.

Risk factors for postoperative complications

Univariate analysis showed that patients who failed to complete preoperative chemotherapy (OR=1.85; CI=1.16-2.92; *P*=0.009) were more likely to develop complications (*Table 3*). Furthermore, patients who underwent a splenectomy (OR=2.98; CI=1.45-6.13; *P*=0.003), male patients (OR=1.58; CI=1.13-2.21; *P*=0.008), patients who underwent a pancreatectomy (OR=3.23; CI=1.02-10.27; *P*=0.046), and patients who underwent a total gastrectomy (OR=2.01; CI=1.44-2.82; *P*<0.001) or an oesophago-cardia resection (OR=1.98; CI=1.13-3.47; *P*=0.017) were more prone to develop complications. In multivariate analyses, all of these remained statically significant, except the pancreatectomy group.

Table 3. Uni- and multivariate logistic regression analyses of risk factors for postoperative complications*

		Univariate analysis			**Multivariate analysis****		
		OR	*P*	CI	OR	*P*	CI
Age							
	<60 years	1			1		
	60-69 years	1.14	0.482	0.80-1.62	1.03	0.891	0.70-1.51
	≥ 70 years	1.24	0.317	0.82-1.87	1.08	0.744	0.68-1.73
Sex							
	Male	1.58	*0.008*	1.13-2.21	1.56	*0.020*	1.07-2.26
BMI							
	<18	1			1		
	18-24	1.22	0.709	0.43-3.52	0.87	0.809	0.27-2.81
	≥25	1.43	0.511	0.50-4.10	1.12	0.847	0.35-3.65
Co-morbidity							
	none	1			1		
	1-2	1.12	0.651	0.69-1.81	1.09	0.748	0.64-1.85
	≥3	1.40	0.192	0.85-2.32	1.27	0.404	0.72-2.23

Table 3 continues

		Univariate analysis			Multivariate analysis**		
		OR	*P*	CI	OR	*P*	CI
Lauren classification							
	Intestinal	1			1		
	Diffuse	0.84	0.391	0.56-1.26	0.90	0.655	0.57-1.42
	Mix	1.13	0.756	0.53-2.34	1.33	0.485	0.60-2.94
ypTstage							
	ypT0/pTis/ pT1	1			1		
	ypT2	1.30	0.241	0.84-2.00	1.01	0.962	0.62-1.65
	ypT3	1.18	0.453	0.76-1.83	0.88	0.623	0.52-1.48
	ypT4	1.28	0.427	0.70-2.32	0.82	0.579	0.40-1.67
ypNstage							
	ypN0	1			1		
	ypN1	1.30	0.141	0.92-1.85	1.25	0.275	0.84-1.86
	ypN2	1.57	0.080	0.95-2.60	1.41	0.249	0.79-2.53
	ypN3	1.34	0.420	0.66-2.72	1.03	0.952	0.44-2.40
Preop chemo not completed							
	Yes	1.85	*0.009*	1.16-2.92	2.09	*0.004*	1.27-3.43
Splenectomy							
	Yes	2.98	*0.003*	1.45-6.13	2.82	*0.012*	1.26-6.32
Pancreatectomy							
	Yes	3.23	*0.046*	1.02-10.27	1.41	0.636	0.34-5.80
Type of gastrectomy							
	Subtotal gastrectomy	1			1		
	Total gastrectomy	2.01	*<0.001*	1.44-2.82	1.88	*0.001*	1.30-2.72
	Oesophago-cardia resection	1.98	*0.017*	1.13-3.47	1.89	*0.038*	1.04-3.46
Blood transfusion							
	Yes	1.30	0.272	0.82-2.06	1.15	0.572	0.70-1.90

**Postoperative complication(s); surgery related and/or infectious and/or general complication.*
***Adjusted for age groups, sex, BMI, co-morbidity, Lauren classification, pTstage, pNstage, preop chemo not completed, splenectomy, pancreatectomy, type of gastrectomy, and blood transfusion.*
Abbreviations; OR = odds ratio; CI = confidence interval; BMI = Body Mass Index; Preop chemoth not completed = preoperative chemotherapy not completed.

DISCUSSION

In this study, postoperative morbidity and mortality in the CRITICS trial were evaluated and risk factors for postoperative morbidity identified.

Overall morbidity rate in the CRITICS trial was nearly 47%, with a reintervention rate of 13%. This percentage is slightly higher compared to other earlier practice changing randomised gastric cancer trials, as the Medical Research Council (MRC) trial and the Dutch Gastric Cancer Trial (DGCT) (MRC trial: 46%, DGCT: 43%), taking into account that in the CRITICS trial a D2 lymphadenectomy is performed without removal of the spleen, and the pancreatic tail, and lymph node station 10.[12, 13] In the Italian Gastric Cancer Trial, however, a considerable lower overall morbidity (17.9%) was registered.[14] Since the start of the Dutch Upper Gastrointestinal Cancer Audit (DUCA) in 2011, a complicated course after a gastrectomy of approximately 20% was registered which remained constant until 2015.[15]
Postoperative mortality rate in the CRITICS trial was 2.2%. Postoperative mortality rates in previous randomised clinical trials were 10% in the MRC trial, 13% in the DGCT, and 2.2% in the Italian Gastric Cancer Trial, respectively.[12-14] The postoperative mortality in the CRITICS trial was also low, compared to the postoperative mortality registered by the DUCA from 2011 to 2015, varying between 3.5% and 7.5%, and the British audit AUGIS (Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland), varying between 1.9% and 4.5%.[15, 16]
Thus, the for current Western standards relative high morbidity rate did not result in a higher mortality rate. High accuracy of registering complications in the CRITICS trial and the more vulnerable status of patients due to preoperative chemotherapy could partly explain this postoperative complication rate. Furthermore, it might be explained by the relatively low severity of the complications and by the increasing quality of perioperative care over time.

In the current study postoperative mortality was most often caused by complications due to anastomotic and duodenal stump leakage. In literature anastomotic leakage after gastrectomy have been reported to occur in 1.2%-5.0% of the cases, with a related mortality rate of 21.1%.[17, 18] Recently it was shown that neoadjuvant chemotherapy prior to gastric resection was not associated with an increased risk of anastomotic leakage or short-term morbidity or mortality.[19] It could be, however, that the consequences, once an anastomotic leakage occurs, are greater in patients who underwent neoadjuvant chemotherapy than in patients who did not underwent neoadjuvant chemotherapy. At this moment the proven survival benefit of neoadjuvant therapy over surgery alone outweighs this possible disadvantage.[20]

In the CRITICS trial, registration of specific complications was recorded in the CRF whereby a detailed overview of complications was obtained. However, as a consequence of not registering aspects as severity of comorbidity, seriousness and grading of the

complications (e.g. with a Clavidien-Dindo classification), more detailed analyses were not possible and this is a major shortcoming of the current study. On the other hand, in the current study it was possible to investigate the influence of postoperative morbidity on the completion of the adjuvant treatment; either chemotherapy or chemoradiotherapy. In both study arms developing a complication was associated with a smaller chance to complete adjuvant treatment, emphasizing the long-term effect and the impact of a postoperative course in this group of patients.

The group that did not complete preoperative chemotherapy in the current study was more than twice as likely to develop postoperative complications (OR=2.15, *P*=0.003) and had a higher postoperative mortality rate (8.0%), findings of which surgeons should be aware. Results showed that not completing preoperative chemotherapy in the CRITICS trial was mainly due to toxicity (85.1%), which stresses the major clinical implications of side effects of the chemotherapy in this group of patients. Recently it was shown that sarcopenia is associated with toxicity in gastric cancer patients undergoing neo-adjuvant chemotherapy.[21] It is well known that sarcopenic and frail patients are vulnerable to experience severe problems once a complication occurs.[22] In this trial sarcopenia and frailty were not reported as such, but the ability not to complete preoperative chemotherapy mainly due to toxicity could indicate such a condition. Patients who were able to complete their chemotherapy could have been fitter, physically stronger, and therefore less likely to develop a complication.

Previously, splenectomy has been described as an important risk factor for a complicated postoperative course and hospital mortality with even a significant adverse effect on survival.[23, 24] In the Dutch Gastric Cancer Trial pancreatic resections and splenectomies were routinely performed for D2 dissections in proximal tumours to obtain proper removal of lymph node stations 10 and 11, which occurred in 23% of the patients in the Dutch Gastric Cancer Trial.[23] The increased morbidity and mortality caused by pancreatic resections and splenectomies probably have offset the difference in survival between the D1 and D2 groups.[23] Recently, the randomised JCOG-0110 trial has proven that routine removal of the spleen should be avoided, as it increases morbidity without improving survival.[25] In the CRITICS trial only 6% of the patients underwent a splenectomy. Unfortunately, for adequate removal of all tumour tissue the increased risk for complications could not be avoided in these patients.

In bowel surgery, several studies suggested that male sex is a risk factor for developing postoperative complications.[26, 27] With respect to gastric cancer surgery, opposite results are shown. In accordance with the results of a recent retrospective study, our results showed an increased risk of postoperative complications for male gender, whereas another study showed that females were at high risk.[28, 29] Without a clear biological explanation for these findings and with the absence of grading of postoperative complications in the current study, this finding should be interpreted with caution.

The postoperative complication rate was significantly higher in the total gastrectomy group compared with the subtotal gastrectomy group. In the last decade of the 20th century, a French and an Italian randomised trial were performed to analyse the

differences between a total and a subtotal gastrectomy, resulting in a similar long-term survival but with a higher morbidity rate, a higher mortality rate, and a decreased quality of life for patients who underwent a total gastrectomy. It was thus recommended to perform a subtotal gastrectomy when possible.[24, 30] According to the current guidelines, for diffuse type of tumours, due to their composition of poorly cohesive tumour cells and poor differentiation, a total gastrectomy is recommended.[31] Results in this study showed differences between the two types of procedures all in favour of a subtotal gastrectomy with regard to the development of postoperative complications, the reintervention rate, and hospital stay. This emphasizes the concept that total gastrectomy should only be performed if the extension or the type of the tumour dictates so.

Overall, compared to other Western studies, surgical morbidity in the CRITICS trial was slightly higher whereas mortality was low. Complications following anastomotic leakage was the most important factor for postoperative mortality. Important proxies for developing postoperative complications were failure to complete preoperative chemotherapy, splenectomy, male sex, total gastrectomy, and oesophago-cardia resection.

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