Quality assurance in the surgical treatment of gastric cancer

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PART II

INFLUENCE OF HOSPITAL VOLUME ON OUTCOMES OF GASTRIC CANCER SURGERY

CHAPTER 5

ASSOCIATION BETWEEN HOSPITAL VOLUME AND QUALITY OF GASTRIC CANCER SURGERY IN THE CRITICS TRIAL

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ABSTRACT

Background: Studies investigating the association between hospital volume and quality of gastric cancer surgery are lacking. In the present study, the effect of hospital volume on quality of gastric cancer surgery was evaluated by analysing data from the CRITICS (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) trial.

Methods: Patients who underwent gastrectomy with curative intent in the Netherlands were selected from the CRITICS trial database. Annual hospital volume of participating centres was derived from the Netherlands Cancer Registry. Hospital volume was categorized into very low (1–10 gastrectomies per year per institution), low (11–20), medium (21–30) and high (31 or more), and linked to the CRITICS database. Quality of surgery was analysed by surgicopathological compliance (removal of at least 15 lymph nodes), surgical compliance (removal of indicated lymph node stations) and the Maruyama Index. Postoperative morbidity and mortality was also compared between hospital categories.

Results: Between 2007 and 2015, 788 patients were included in the CRITICS study, of whom 494 were analysed. Surgicopathological compliance was higher (86.7 *versus* 50.4 per cent; $P < 0.001$), surgical compliance was greater (52.9 *versus* 19.8 per cent; $P < 0.001$) and median Maruyama Index was lower (0 *versus* 6; $P = 0.031$) in high-volume hospitals compared with very low-volume hospitals. There was no statistically significant difference in postoperative complications or mortality between the hospital volume categories.

Conclusion: Surgery performed in high-volume hospitals was associated with better surgical quality than surgery carried out in lower-volume hospitals.

INTRODUCTION

Surgical resection remains the only curative treatment for locally advanced gastric cancer.[1] Despite improvements in surgical techniques and perioperative care, the mortality rate after gastrectomy in the Western world is still around 5 per cent.[2] The 5-year survival rate after gastrectomy with an adequate D2 lymph node dissection does not exceed 50 per cent.[3]

Since Luft and colleagues in 1979 suggested that high-volume hospitals have better outcomes for surgical procedures than low-volume hospitals, hospital volume has become a point of debate.[4] Studies have assessed the association between hospital volume and short- and long-term outcomes for a wide range of diseases including oesophageal and gastric cancer.[5–7] Postoperative mortality is often used as an outcome measure.[8–11] The relationship between hospital volume and improved short- and long-term outcomes has led to centralization of gastric cancer surgery in England in 2001 and in Denmark in 2003.[12,13] In the Netherlands, the Dutch Health Care Inspectorate incorporated a minimum volume of ten gastric resections per year per institution in 2012, and 20 per year per institution from 2013.

Studies investigating the relationship between hospital volume and quality of surgery are scarce, as detailed information regarding surgical quality is often lacking in retrospective studies. The present study aimed to assess the association between hospital volume and quality of gastric cancer surgery using data from a large international multicentre RCT, the CRITICS study. In this trial, patients with resectable gastric cancer underwent three preoperative cycles of epirubicin, cisplatin/oxaliplatin and capecitabine (ECC/EOC), followed by surgery and then either three further cycles of ECC/EOC or concurrent chemoradiotherapy. Information on surgical quality, including lymph node station removed during gastrectomy, was registered.

METHODS

Patients with a histologically proven stage Ib–IVa (AJCC 6th edition) gastric adenocarcinoma were included in the CRITICS trial. The bulk of the tumour had to be located in the stomach, although extension into the gastro-oesophageal junction was allowed. Inoperable patients, those with distant metastases, and patients with T1 N0 disease (determined by endoscopic ultrasonography) were not eligible. The study protocol for the CRITICS trial has been published previously.[14,15] For the present analysis, patients included in the CRITICS trial who underwent gastric resection with curative intent in a Dutch hospital were selected from the study database.

Hospital volume

Annual hospital volume was defined as the number of gastrectomies per hospital per year. All participating hospitals in the CRITICS trial in the Netherlands gave permission to share the number of gastric resections per year during the study period of the CRITICS trial (2007–2015). Annual hospital volume was calculated from the Netherlands Cancer Registry. Gastrectomies included partial gastric resection, total gastric resection, gastrectomy with *en bloc* resection of surrounding organs/structures, and gastric resection not otherwise specified. Gastrectomies for benign diseases are not registered in the Netherlands Cancer Registry. Patients were categorized based on the date of primary resection. For patients who underwent multiple operations, the procedure that included the gastrectomy was used. Annual hospital volume was linked anonymously with data from the CRITICS trial.

Hospitals were ranked by annual hospital volume of gastrectomies ranging from very low (1–10), low (11–20), medium (21–30) to high (31 or more). As centralization of gastric cancer surgery took place during the study interval, hospitals could migrate between categories over the years, but each patient was categorized in one volume category based on the date of surgery.

Surgery

All patients were assigned to receive three cycles of ECC/EOC at 3-weekly intervals before operation. Surgery was performed 3–6 weeks after the last chemotherapy cycle. Both open and minimally invasive procedures were allowed. Total gastrectomy was performed for tumours in the upper part of the stomach. Subtotal resection of the stomach was advised for tumours in the middle or distal part of the stomach. Transhiatal oesophagus–cardia resection with gastric tube reconstruction was allowed for proximal tumours infiltrating the oesophagus. Lymph node dissection involving removal of lymph node stations 1–9 and 11 (lymph node locations and numbering according to the Japanese Research Society for the study of Gastric Cancer), with a minimum of 15 lymph nodes, a so-called D1+ lymph node dissection, was mandatory according the study protocol.[16] The definition of a D1 lymph node dissection was removal of stations 3–6 during partial gastrectomy and stations 1–6 during total gastrectomy. A D0 dissection comprised gastrectomy with a less than D1 dissection. A D2 lymph node dissection included removal of stations 1, 3, 5–9 for partial gastrectomy and stations 1–11 for total gastrectomy. The definition of D3 dissection was removal of lymph node stations 1–14. Splenectomy or resection of the pancreatic tail was not performed unless the tumour invaded these organs.

Central data review

The extent of lymphadenectomy was determined by two expert gastric surgeons. The resected lymph node stations (1–16) and type of lymph node dissection (D0, D1, D1+, D2 or D3) were scored based on the operative reports and the data recorded in the case report form. If the number of lymph node stations removed was not mentioned specifically, an estimate of the nodal stations removed was made based on the operative report, whenever possible. Removal of lymph nodes along the left gastric artery was defined as removal of lymph node station 7. If no assumptions could be made, the extent of lymphadenectomy was scored as unknown. If all removed stations were unknown, the patient was excluded from the analysis. If information on removal was unknown for a single lymph node station, the station was scored as not removed. The proportion of patients with an estimated number of nodal stations resected was not recorded.

Outcome measures of surgical quality

Surgicopathological compliance was defined as the removal of a minimum of 15 lymph nodes, and surgicopathological non-compliance as the removal of fewer than 15 lymph nodes.

The Maruyama Index of Unresected Disease (MI) is based on eight variables (sex, age, type of cancer, depth of invasion, maximum diameter, tumour location (upper, middle or lower third of stomach), position (anterior, posterior, circular, around lesser or greater curvature) and histological type). In the present study, the MI was calculated with the Maruyama computer program, as in the Intergroup 0116 trial and the Dutch Gastric Cancer Trial.[17–19] The lower the MI, the better the surgical quality. The proportion of patients with a MI below 5 was also calculated as a MI lower than 5 has been associated with improved disease-free and overall survival.[18–20] To quantify the likelihood of unresected nodal disease, the MI is defined as the sum of Maruyama computer program predictions of lymph node stations 1–12 that were not removed by the surgeon. When a patient underwent gastric resection with removal of lymph node stations 1–8, the MI was calculated by adding up the likelihood that each of the other lymph node stations was affected (stations 9–12).

Surgical compliance was defined as the removal of lymph node stations 1–9 and 11, with exception of stations 2 and 4s in subtotal gastric resections, and stations 4d and 6 in gastric tube reconstructions. Surgical non-compliance was defined as no removal of the indicated lymph node stations.

The definition of surgical contamination was removal of one or more lymph node stations outside the intended extent of resection.

Postoperative complications and mortality

Complications were recorded in the case report form, and classified as surgery-related (such as anastomotic leakage, bleeding and ileus), infectious (for example abscess, sepsis and abdominal wound infection) and general complications (such as pulmonary, cardiovascular and thromboembolic). Postoperative mortality was defined as death within 30 days of surgery and/or during the hospital stay.

Missing data

Patients were excluded from the surgicopathological analyses if the total number of lymph nodes sampled was not reported by the pathologist. They were excluded from the analyses of surgical compliance, surgical contamination and MI if the exact location of the lymph node stations removed could not be retrieved from the surgery report.

Statistical analysis

Comparisons were done using the χ^2 test for categorical data, and the non-parametric Kruskal–Wallis test for numerical data. An independent-samples medians test was carried out to compare medians. To test whether type of hospital (academic *versus* community hospital) was a possible confounder, an interaction test was performed for categorical outcomes and a univariable general linear model for numerical outcomes. $P < 0.050$ was considered statistically significant. All analyses were carried out using SPSS® version 21.0 (IBM, Armonk, New York, USA).

RESULTS

Between January 2007 and April 2015, 788 patients were included in the CRITICS trial, of whom 631 were treated in Dutch hospitals (*Fig. 1*). Some 494 of 631 patients underwent a gastric resection with curative intent. Data were available from 492 patients for the analysis of surgicopathological compliance, and from 480 patients for the analyses of surgical compliance, surgical contamination and MI.

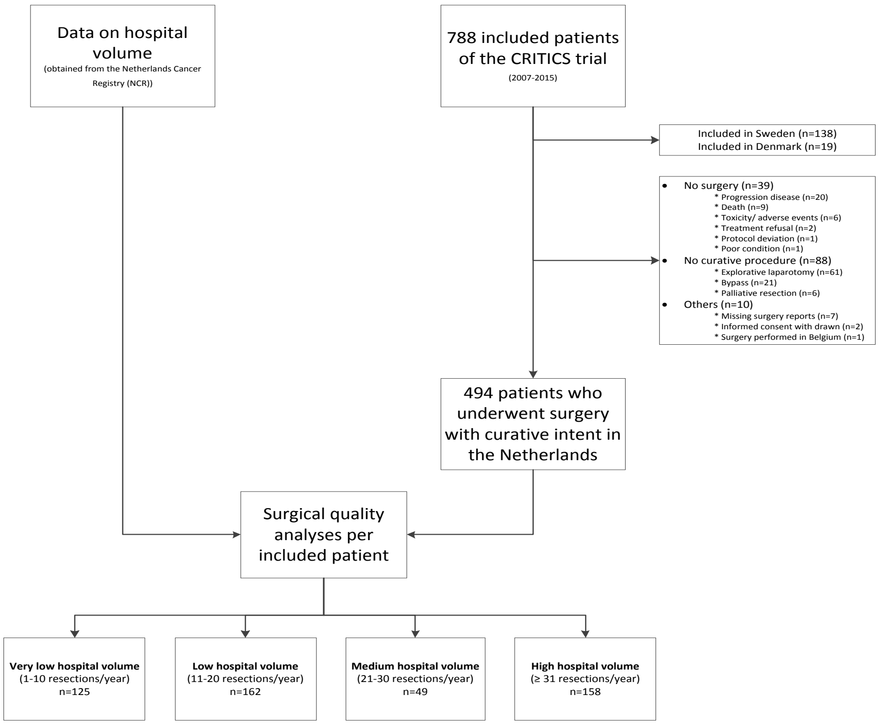

Fig. 1 Study flow chart. Data on hospital volume for patients who has surgery with curative intent in the Netherlands were obtained from the Netherlands Cancer Registry

The proportion of patients who completed preoperative chemotherapy was not statistically significantly different between the four categories of hospital volume, varying between 82.1 and 91.2 per cent (overall $P = 0.141$). Most patients underwent surgery in a low-volume (162, 32.8 per cent) or high-volume (158, 32.0 per cent) hospital, followed by a very low-volume (125, 25.3 per cent) or a medium-volume hospital (49, 9.9 per cent) hospital. *Table 1* shows patient, tumour and treatment related characteristics in relation to hospital type. The mean and median number of gastrectomies performed per hospital annually were 22.2 and 18.0 respectively.

Table 1. Patient, tumour and surgical characteristics according to hospital volume

	Very low volume (*n* = 125)	**Low volume (*n* = 162)**	**Medium volume (*n* = 49)**	**High volume (*n* = 158)**	***P*†**
Age (years)*	61 (35–81)	63 (28–82)	63 (37–78)	63 (33–78)	0.327‡
Sex ratio (M : F)	81 : 44	107 : 55	39 : 10	104 : 54	0.267
Co-morbidity					0.205
None	18 (14.4)	19 (11.7)	7 (14)	14 (8.9)	
1–2	70 (56.0)	81 (50.0)	21 (43)	73 (46.2)	
≥ 3	37 (29.6)	62 (38.3)	21 (43)	71 (44.9)	
Tumour location					0.005
Proximal stomach	32 (25.6)	63 (38.9)	18 (37)	59 (37.4)	
Middle stomach	35 (28.0)	40 (24.7)	11 (22)	59 (37.3)	
Distal stomach	58 (46.4)	59 (36.4)	20 (41)	40 (25.3)	
Type of resection					0.379
Total gastrectomy	48 (38.4)	71 (43.8)	27 (55)	74 (46.8)	
Subtotal gastrectomy	65 (52.0)	73 (45.1)	16 (33)	71 (45.0)	
Oesophagus–cardia resection	12 (9.6)	18 (11.1)	6 (12)	13 (8.2)	
Surgical approach					0.036
Open	111 (88.8)	128 (79.0)	35 (71)	122 (77.2)	
Minimally invasive	10 (8.0)	28 (17.3)	12 (24)	31 (19.6)	
Conversion	1 (0.8)	6 (3.7)	2 (4)	3 (1.9)	
Missing	3 (2.4)	0 (0)	0 (0)	2 (1.3)	
Tumour category					0.022
pT0/pTis/pT1	25 (20.0)	38 (23.5)	14 (29)	31 (19.6)	
pT2	59 (47.2)	65 (40.1)	9 (18)	58 (36.7)	
pT3	37 (29.6)	45 (27.8)	18 (37)	55 (34.8)	
pT4	4 (3.2)	14 (8.6)	8 (16)	14 (8.9)	

Table 1 continues

	Very low volume (*n* = 125)	Low volume (*n* = 162)	Medium volume (*n* = 49)	High volume (*n* = 158)	*P*†
Node category					0.625
pN0	64 (51.2)	76 (46.9)	26 (53)	79 (50.0)	
pN1	47 (37.6)	61 (37.6)	12 (24)	52 (32.9)	
pN2	12 (9.6)	21 (13.0)	8 (16)	21 (13.3)	
pN3	2 (1.6)	4 (2.5)	3 (6)	6 (3.8)	
Splenectomy					0.539
Yes	5 (4.0)	3 (1.9)	1 (2)	7 (4.4)	
No	120 (96.0)	159 (98.1)	48 (98)	151 (95.6)	
Distal pancreatectomy					0.462
Yes	4 (3.2)	4 (2.5)	1 (2)	1 (0.6)	
No	121 (96.8)	158 (97.5)	48 (98)	157 (99.4)	

*Values in parentheses are percentages unless indicated otherwise; *values are median (range). Very low-volume hospitals: one to ten gastrectomies per year; low-volume hospitals, 11–20 per year, medium-volume hospitals, 21–30 per year; high-volume hospitals, at least 31 per year. † χ^2 test, except ‡Kruskal–Wallis test.*

Surgical quality

Surgicopathological compliance was achieved in 50.4 per cent of patients in very low-volume hospitals, compared with 86.7 per cent in high-volume hospitals ($P < 0.001$) (*Fig. 2a*). The median number of resected lymph nodes was 24 (range 1–66) in high-volume hospitals; this decreased to 21 (5–57), 18 (0–71) and 15 (1–53) in medium-, low- and very low-volume hospitals respectively ($P < 0.001$).

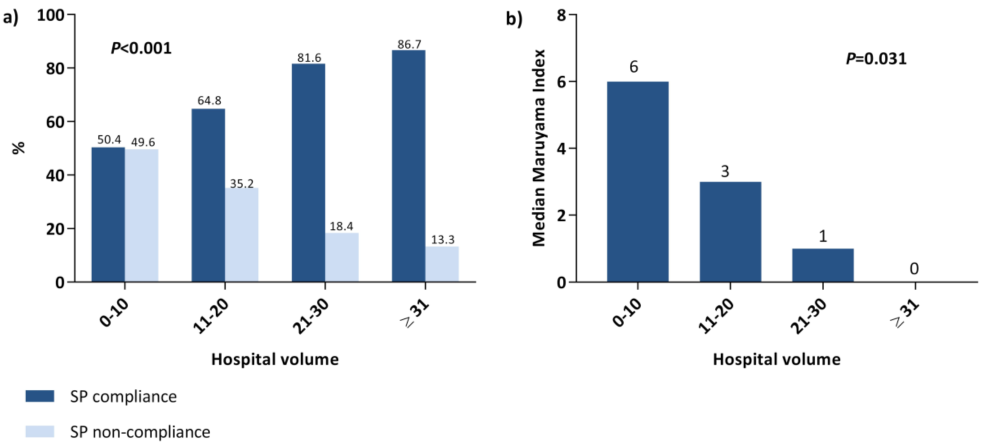

Fig. 2a) Surgicopathological (SP) compliance and b) Maruyama Index according to hospital volume. a P < 0.001 (χ^2 test), b P = 0.006 (independent-samples medians test)

D1+ lymph node dissection or more was performed in 69.0 per cent of the patients in very low-volume hospitals, compared with 87.3, 98 and 96.2 per cent of patients in low-, medium- and high-volume hospitals respectively. An inverse relationship between median MI and hospital volume was seen (*Fig. 2b*). The median MI was 6 (range 0–130), 3 (0–136), 1 (0–38) and 0 (0–93) in very low-, low-, medium- and high-volume hospitals respectively. A MI of 5 was achieved in 47.4 per cent (55 of 116 patients), 53.2 per cent (84 of 158), 57 per cent (28 of 49) and 68.2 per cent (107 of 157) respectively ($P = 0.004$). Type of hospital was not a confounder for surgicopathological compliance (interaction test $P = 0.536$) or for MI ($P = 0.545$).

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Surgical compliance was noted in 23 of 116 patients (19.8 per cent) in very low-volume hospitals compared with 83 of 157 (52.9 per cent) in high-volume hospitals ($P < 0.001$) (*Fig. 3a*). There were no significant differences between hospital volume categories regarding surgical contamination ($P = 0.670$) (*Fig. 3b*).

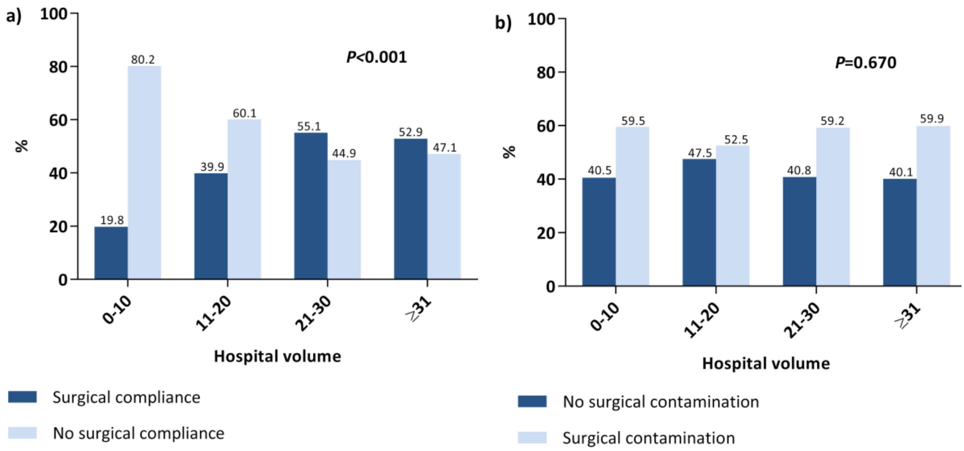

Fig. 3a) Surgical compliance and b) extent of surgical contamination according to hospital volume, a) P < 0.001, b) P = 0.670 (χ^2 test)

Postoperative complications and mortality

Postoperative complications were seen in 226 of the 494 patients (45.7 per cent) (*Table 2*). There were no differences in type of complications between hospital volume categories. The rate of reinterventions for complications was not statistically different. There were 11 postoperative deaths (2.2 per cent).

Table 2. Postoperative complications and mortality according to hospital volume

	Very low volume (*n* = 125)	Low volume (*n* = 162)	Medium volume (*n* = 49)	High volume (*n* = 158)	*P*†
Complication overall	53 (42.4)	77 (47.5)	27 (55)	69 (43.7)	0.447
Surgery-related complication	23 (18.4)	40 (24.7)	14 (29)	33 (20.9)	0.418
Anastomotic leakage	11 (8.8)	11 (6.8)	6 (12)	8 (5.1)	
Bleeding	2 (1.6)	2 (1.2)	2 (4)	4 (2.5)	
Ileus	3 (2.4)	5 (3.1)	1 (2)	5 (3.2)	
Infectious complication	27 (21.6)	34 (21.0)	10 (20)	30 (19.0)	0.946
Abscess	6 (4.8)	9 (5.6)	2 (4)	8 (5.1)	
Sepsis	6 (4.8)	9 (5.6)	1 (2)	5 (3.2)	
Abdominal wound infection	8 (6.4)	7 (4.3)	2 (4)	4 (2.5)	
General complication	35 (28.0)	53 (32.7)	15 (31)	39 (24.7)	0.455
Pulmonary	15 (12.0)	23 (14.2)	7 (14)	15 (9.5)	
Cardiovascular	4 (3.2)	10 (6.2)	4 (8)	8 (5.1)	
Thromboembolic	1 (0.8)	3 (1.9)	0 (0)	0 (0)	
Reintervention*	15 (12.0)	26 (16.0)	7 (14)	18 (11.4)	0.636
Postoperative death	2 (1.6)	7 (4.3)	1 (2)	1 (0.6)	0.149

*Values in parentheses are percentages unless indicated otherwise. *For management of a postoperative complication. Very low-volume hospitals: one to ten gastrectomies per year; low-volume hospitals, 11–20 per year, medium-volume hospitals, 21–30 per year; high-volume hospitals, at least 31 per year. †χ^2 test.*

DISCUSSION

In this study, gastrectomy for cancer performed in high-volume hospitals was associated with better surgical quality parameters compared with surgery undertaken in lower-volume hospitals.

Large multicentre studies investigating the association between hospital volume and surgical quality of gastric resections are scarce. Specific surgical information, such as removal of lymph node stations, is not usually available in national registries, although this is one of the essential parameters for evaluation of the quality of surgical care. Data from the CRITICS trial were used in the present study. No significant difference in overall survival between the two study arms was found in the intention-to-treat analysis in this RCT.[21] The strength and the uniqueness of the present study lie in the detailed data available. In an analysis of data from the Intergroup 0116 trial in 2007, Enzinger and colleagues observed no impact of hospital volume on overall long-term survival.[22]
However, the proportion of patients with an adequate lymph node dissection was limited, which may have obscured a potential benefit of high-volume surgery, as noted

by the authors.[22] The present authors recently showed that at least 15 lymph nodes were removed in 87 per cent of the patients in the CRITICS trial and that approximately 80 per cent underwent an adequate lymph node dissection.[23] The high surgical standard in the CRITICS trial support the present results.

Removal of 15 lymph nodes or more has been defined as a surgical quality parameter with proven impact on survival.[24] The cut-off point of 15 lymph nodes is currently under debate, as several studies have reported longer disease-free survival when a greater number of lymph nodes was removed.[25] However, the cut-off point of 15 lymph nodes is still widely used today. In the Intergroup 0116 trial, the number of resected lymph nodes did not differ between low-volume (0–5 gastrectomies per year), moderate-volume (6–13) and high-volume (at least 14) hospitals, whereas the present study showed a significant increase in number of lymph nodes sampled with increasing hospital volume.[22] In this context, it should be acknowledged that the proportion of total gastrectomies was greater in the higher-volume categories than in the very low-volume hospital in the present study. Furthermore, the awareness and dedication of the pathologist may play a role. The pathology technician is an important healthcare-related factor influencing the total number of lymph nodes reported, and *ex vivo* dissection of lymph nodes during gastrectomy optimizes lymph node yield.[26,27] In the CRITICS trial, gastrectomy specimens with *en bloc* lymph node stations were sent directly to the pathology department for processing. Awareness of the pathologist or technician was raised by giving feedback when fewer than 15 nodes were reported during the course of the trial. This emphasizes that lymph node yield is a quality indicator for the whole team and not only for the surgeon.

In the CRITICS trial, an adequate gastric resection was defined as a D1+ lymphadenectomy or more, determined more than 10 years ago at a time when the debate about the superiority of D2 dissection was still ongoing. An adequate gastric resection was performed in 98 and 96.2 per cent of the patients in medium- and high-volume hospitals, but in only 69.0 per cent in very low-volume hospitals. This is better than the adequacy in hospitals participating in the Intergroup 0116 trial, where even in high-volume hospitals (at least 14 resections/year), half of the patients underwent a D0 dissection and only 10 per cent had the intended D2 dissection.[22]

The MI is one of the most important surgical quality indicators in gastric cancer surgery, as shown in the Intergroup 0116 study and Dutch Gastric Cancer Trial.[19,20] The MI was strongly related to survival: a MI lower than 5 was associated with improved disease-free and overall survival.[18–20] In the Intergroup 0116 trial, the MI was less than 5 in only 13.6 per cent of patients in high-volume hospitals, compared with 68.2 per cent in high-volume hospitals in the present study.[22]

Postoperative complication rates were not significantly different between the hospital volume categories. It was expected that complication rates may be lower in high-volume hospitals. This expected difference may be counteracted by the higher percentage of patients with a co-morbidity score of 3 or more and the larger proportion who had a total gastrectomy in high-volume hospitals compared with lower-volume hospitals.[28] Postoperative mortality was low for each hospital volume category compared with rates in a retrospective French study that reported the impact of centre volume on postoperative mortality after gastric cancer surgery.[29] In that study, the postoperative mortality rate ranged from 4.3 to 10.2 per cent, and was 7.9 per cent in very high-volume hospitals (at least 60 resections/year); it should be noted that the majority of patients had a cardia tumour.

The experience of the surgeon rather than hospital volume as such is of importance. Recently it was shown that mortality after gastrectomy decreased as surgeon volume increased to 30 patients per year.[30] Although the surgeon still plays an important role in the curative treatment of gastric cancer, multimodal treatment and multidisciplinary teams including radiation oncologists, medical oncologists, gastroenterologists, pathologists and anaesthesiologists are key nowadays. Moreover, it should be noted that hospital volume was defined by operated patients only, which represents less than half of the patients with gastric cancer.

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