

RAPID COMMUNICATION

Risk factors for operative morbidity and mortality in gastric cancer patients undergoing total gastrectomy

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INTRODUCTION

Gastric cancer is the second leading cause of cancer-related death worldwide^[1]. It ranks first among all causes of death from cancer in China, with an annual mortality rate of approximately 25.2 per 100 000 people^[2].

Despite the best efforts of clinicians, gastric cancer is usually diagnosed at a fairly advanced stage in most countries^[3]. Complete surgical resection is the only potentially curative treatment for gastric cancer^[4,5].

In most Western countries, there has been a rapid rise in the incidence of tumors at or close to the gastroesophageal junction over the past 20 to 30 years^[3]. Based on tumor location and growth pattern, a total gastrectomy is the procedure of choice for patients with middle and proximal third gastric cancer^[6].

Preoperative preparation, anesthesiology, operative techniques, and postoperative care have improved considerably in recent years. However, total gastrectomy has been reported to have higher morbidity and mortality rates than subtotal gastrectomy^[7-9].

The aim of this study is to document the frequency and nature of operative morbidity and mortality after total gastrectomy, and to identify factors that are predictive of complications and death.

MATERIALS AND METHODS

We retrospectively reviewed the records of 125 consecutive patients who underwent total gastrectomy for gastric cancer at the Second Affiliated Hospital of Zhejiang University School of Medicine between January, 2003 and March, 2008. The median age of the patients was 60 (range 29-78). All patients had histologically confirmed gastric cancer, without previous or coexisting cancer. None had received preoperative chemotherapy or radiation therapy. Abdominal terminolateral esophagojejunal anastomosis

Abstract

AIM: To study the risk factors for morbidity and mortality following total gastrectomy.

METHODS: We retrospectively reviewed the records of 125 consecutive patients who underwent total gastrectomy for gastric cancer at the Second Affiliated Hospital of Zhejiang University School of Medicine between January 2003 and March 2008.

RESULTS: The overall morbidity rate was 20.8% (27 patients) and the mortality rate was 3.2% (4 patients). Morbidity rates were higher in patients aged over 60 [odds ratio (OR) 4.23 (95% confidence interval (CI) 1.09 to 12.05)], with preoperative comorbidity [with vs without, OR 1.25 (95% CI 1.13 to 8.12)], when the combined resection was performed [combined resection vs total gastrectomy only, OR 2.67 (95% CI 1.58 to 5.06)].

CONCLUSION: Age, preoperative comorbidity and combined resection were independently associated with the rate of morbidity after total gastrectomy for gastric cancer.

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Key words: Gastric cancer; Total gastrectomy; Morbidity; Mortality; Risk factor

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was performed with staples in every patient. Criteria for exclusion from this study were surgery for gastric stump carcinoma and other nonresective palliative operations for gastric cancer including bypass procedures. Roux-en-Y oesophagojejunostomy with or without a Paulino pouch was performed in all patients after radical or palliative total gastrectomy. A D2 or D2+ lymph node dissection was performed in patients with radical total gastrectomy. All patients received prophylactic antibiotics starting half an hour before the laparotomy and continuing for over 72 h.

From these data, risk factors were analyzed with postoperative morbidity and mortality. Analyzed risk factors included sex, age, American Society of Anesthesiologists (ASA) grade, tumor site, tumor size, pTNM stage, intraoperative transfusion volume, intraoperative loss of blood, preoperative comorbidity, operative time, combined organ resection, and procedure. Classification of pTNM stage followed the 5th edition of the International Union Against Cancer (UICC) criteria. The operative time was defined as the time between initiation of skin incision and the completion of wound closure. Postoperative hospital stay was defined as the number of days in hospital from operation to discharge. Combined organ resection was referred to as splenectomy, pancreaticosplenectomy, transverse colectomy, cholecystectomy, and hepatic segment resection.

Operative complications analyzed in this study included both immediate postoperative minor complications and major complications that occurred during the same hospitalization. Late complications, such as gallstone formation, anemia, dumping syndrome, and weight loss, were not included in the scope of this study. Bleeding was defined by the need for postoperative transfusion. A fluid collection was defined by the presence of septic fluid in the abdominal cavity causing fever higher than 38°C and verified by computer tomography (CT) or B-type ultrasound. Wound infection included the presence of septic fluid or pus at the incision leading to delayed suture removal or the need for wound re-suture. Pleural effusion was defined by the presence of fluid in the thoracic cavity requiring drainage. Pulmonary embolus was verified by pulmonary angiography. Pulmonary infection was verified by chest X-ray. The diagnosis of fungus infection and urinary tract infection was determined by sample microbiology culture.

Operative mortality in this study included all hospital deaths within 30 d.

Statistical analysis

The χ^2 test, Fisher's exact test and a binary logistic regression model were used for statistical analysis. $P < 0.05$ (two sided) was regarded as significant. SPSS® version 11.5 (SPSS, Chicago, IL, USA) was used for data analysis.

RESULTS

The postoperative morbidity of the 125 patients studied

Table 1 Postoperative morbidity

Morbidity	No. of patients
Pulmonary infection	7
Wound infection	4
Abdominal abscess	3
Intra-abdominal bleeding	3
Upper digestive tract bleeding	3
Duodenal stump leakage	3
Jejunum stump leakage	1
Chylous leaks	2
Pulmonary embolus	2
Arrhythmia	4
Pleural effusion	4
Ascite	3
Urinary tract infection	2
Fungus infection	3
Total	44

is listed in Table 1. The overall morbidity rate was 20.8% (27 patients), and the mortality rate was 3.2% (4 patients) and mean postoperative stay was 18.34 d. Univariate analysis showed that age, sex, extension of resection (combined or not), perioperative transfusion, and preoperative comorbidity were all significantly associated with operative morbidity (Table 2). Multiple logistic regression analysis identified older age [odds ratio (OR) 4.23 (95% confidence interval (CI) 1.09 to 12.05)], preoperative comorbidity [with *vs* without, OR 1.25 (95% CI 1.13 to 8.12)] and combined resection [combined resection *vs* total gastrectomy only, [OR 2.67 (95% CI 1.58 to 5.06)] as independent predictors of a higher operative morbidity rate.

Four patients (3.2%) with preoperative comorbidity died in hospital. All four had undergone palliative or radical total gastrectomy without combined organ resection. The first of these patients died of a pulmonary infection with preoperative chronic bronchitis. The second patient, who died of sudden cardiac arrest, had preoperative coronary heart disease for 5 years. The third patient died of multiple organ dysfunction syndrome (MODS) with preoperative complete right bundle-branch heart block. The fourth patient, who died of heart failure, had preoperative pleural effusion.

DISCUSSION

Gastric cancer is the second leading cause of cancer-related death worldwide^[1]. It ranks first among all causes of death from cancer in China, with an annual mortality rate of approximately 25.2 per 100 000^[2]. In most Western countries, there has been a rapid rise in the incidence of tumors at or close to the gastrooesophageal junction over the past 20 to 30 years^[3]. Based on tumor location and growth pattern, a total gastrectomy is the procedure of choice in patients with middle and proximal third gastric cancer^[4].

Although morbidity and mortality rates for gastrectomy for gastric cancer were different in past studies, many recent studies show that they have now decreased significantly to less than 23% and 6%, respectively^[8,10-14]. Total gastrectomy has been reported

Table 2 Factors related to operative morbidity *n* (%)

	No. of patients	No. with complications	<i>P</i> ¹	<i>P</i> ²
Age (yr)			0.005	< 0.01
< 60	62	7 (11.29)		
≥ 60	63	20 (31.75)		
Sex			0.038	
Male	86	23 (26.74)		
Female	39	4 (10.26)		
ASA			0.154	
1	37	5 (16.51)		
2-3	88	22 (25)		
Tumor size (cm)			0.821	
≤ 3	19	5 (26.32)		
≤ 6	45	10 (22.22)		
> 6	61	12 (19.67)		
Tumor site			0.887	
Upper	46	9 (19.56)		
Middle	24	4 (16.67)		
Low	17	4 (23.53)		
Two thirds or more	38	10 (26.32)		
pTNM stage			0.135	
I - II	27	3 (11.11)		
III-IV	98	22 (22.45)		
Transfusion (U)			0.036	
0	71	8 (11.27)		
≤ 3	34	8 (23.53)		
≥ 4	20	7 (35)		
Operative hemorrhage (mL)			0.947	
≤ 400	45	10 (22.22)		
≤ 800	54	12 (22.22)		
> 800	26	5 (19.23)		
Operative time (h)			0.214	
≤ 4	75	19 (25.33)		
> 4	50	8 (16)		
Combined resection			0.009	0.012
Yes	47	16 (34.04)		
No	78	31 (39.74)		
Procedure			0.585	
Palliative	28	5 (17.86)		
Radical	97	22 (22.68)		
Comorbidity			0.003	0.011
With	56	19 (33.93)		
Without	69	8 (11.59)		

Values in parentheses are percentages. ¹ χ^2 test; ²Multiple regression analysis.

to have higher morbidity and mortality rates than subtotal gastrectomy^[7-9]. In our study, the morbidity and mortality rates for total gastrectomy was 20.8% and 3.2%, respectively. The most common complication was pulmonary infection, in accordance with other reports^[9,12].

In keeping with other studies showing that postoperative morbidity and mortality rates are associated with age, sex and combined resection^[15], univariate analysis in our study demonstrated that age, sex, and combined resection contributed to postoperative complications. Furthermore, besides combined resection, age was an independent contributor to postoperative complications, because elderly patients may harbor occult heart disease, and have reduced respiratory and liver function reserves.

Opelz *et al*^[16] reported that homologous blood

transfusion was associated with immunosuppression in renal allograft transplantation. Clinical evidence of a relationship between perioperative transfusion and postoperative septic complications has been reported in some studies of gastric cancer^[17-20]. Although the exact mechanism of immunosuppression is still to be elucidated, reduced tumor necrosis factor- α levels, interleukin 10 (IL-10) induction, impairment of natural killer cells, increases in certain other cytokines, complement activation, decreased macrophage function, decreased CD4/CD8 ratio, and decreased IL-2 secretion are all involved^[21-23]. Our univariate analysis also showed that perioperative transfusion was associated with postoperative morbidity.

Our study found that preoperative comorbidity was an independent predictor of postoperative morbidity, and that all of the 4 patients who died in hospital were preoperatively suffering from respiratory or cardiac disease. This relationship was also reported in other studies^[9,24,25]. Thus, we believe that prior treatment of preoperative comorbid conditions is critical to the postoperative recovery of patients with gastric cancer.

There are some common drawbacks to undertaking any retrospective study, including sample insufficiency and operations performed by different surgeons, which apply to this study. This study also demonstrates that relatively low morbidity and mortality rates for total gastrectomy can be achieved in a large-volume hospital by experienced surgeons with careful perioperative treatment.

COMMENTS

Background

Gastric cancer is the second leading cause of cancer-related death worldwide. In most Western countries, there has been a rapid rise in the incidence of tumors at or close to the gastroesophageal junction. A total gastrectomy is the procedure of choice for patients with middle and proximal third gastric cancer. However, total gastrectomy has been reported to have higher morbidity and mortality rates than subtotal gastrectomy. It is significant to identify factors that are predictive of complications and death.

Research frontiers

Although morbidity and mortality rates for gastrectomy for gastric cancer were different in past studies, many recent reports show that they have now decreased significantly to less than 23% and 6%, respectively. Furthermore, some reports showed that several risk factors were associated with the complications and death.

Innovations and breakthroughs

Age, preoperative comorbidity and combined resection were independently associated with the rate of morbidity after total gastrectomy for gastric cancer. Perioperative transfusion was also associated with postoperative morbidity.

Applications

This study demonstrates that relatively low morbidity and mortality rates for total gastrectomy can be achieved in a large-volume hospital by experienced surgeons and with careful perioperative treatment.

Terminology

Immunosuppression is defined as deliberate prevention or diminution of the host's immune response. It may be nonspecific as in the administration of immunosuppressive agents (drugs or radiation) or by lymphocyte depletion or may be specific as in desensitization or the simultaneous administration of antigen and immunosuppressive drugs.

Peer review

To document the frequency and nature of operative morbidity and mortality after total gastrectomy, the authors retrospectively reviewed the records of 125

consecutive patients who underwent total gastrectomy for gastric cancer. As a clinical experience, the results may provide some helpful information for the readers.

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