

Effect of complication grade on survival following curative gastrectomy for carcinoma

Nan Jiang, Jing-Yu Deng, Xue-Wei Ding, Li Zhang, Hong-Gen Liu, Yue-Xiang Liang, Han Liang

Nan Jiang, Jing-Yu Deng, Xue-Wei Ding, Li Zhang, Hong-Gen Liu, Yue-Xiang Liang, Han Liang, Department of Gastric Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Tianjin 300060, China

Nan Jiang, Jing-Yu Deng, Xue-Wei Ding, Li Zhang, Hong-Gen Liu, Yue-Xiang Liang, Han Liang, Key Laboratory of Cancer Prevention and Therapy, Tianjin 300060, China

Author contributions: Jiang N, Liang H and Deng JY performed the study; Deng JY, Ding XW, Zhang L and Liu HG designed the study and analyzed data; Jiang N, Liang H, and Liang YX wrote the manuscript; Deng JY, Ding XW and Zhang L revised the manuscript.

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Correspondence to: Han Liang, MD, Department of Gastric Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Huanhuxi Road, Hexi District, Tianjin 300060, China. tjlianghan@gmail.com

Telephone: +86-22-23340123 Fax: +86-22-23340123

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Abstract

AIM: To elucidate the potential impact of the grade of complications on long-term survival of gastric cancer patients after curative surgery.

METHODS: A total of 751 gastric cancer patients who underwent curative gastrectomy between January 2002 and December 2006 in our center were enrolled in this study. Patients were divided into four groups: no complications, Grade I, Grade II and Grade III complications, according to the following classification systems: T92 (Toronto 1992 or Clavien), Accordion Classification, and Revised Accordion Classification. Clinicopathological features were compared among

the four groups and potential prognostic factors were analyzed. The Log-rank test was used to assess statistical differences between the groups. Independent prognostic factors were identified using the Cox proportional hazards regression model. Stratified analysis was used to investigate the impact of complications of each grade on survival.

RESULTS: Significant differences were found among the four groups in age, sex, other diseases (including hypertension, diabetes and chronic obstructive pulmonary disease), body mass index (BMI), intraoperative blood loss, tumor location, extranodal metastasis, lymph node metastasis, tumor-node-metastasis (TNM) stage, and chemotherapy. Overall survival (OS) was significantly influenced by the complication grade. The 5-year OS rates were 43.0%, 42.5%, 25.5% and 9.6% for no complications, and Grade I, Grade II and Grade III complications, respectively ($P < 0.001$). Age, tumor size, intraoperative blood loss, lymph node metastasis, TNM stage and complication grade were independent prognostic factors in multivariate analysis. With stratified analysis, lymph node metastasis, tumor size, and intraoperative blood loss were independent prognostic factors for Grade I complications ($P < 0.001$, $P = 0.031$, $P = 0.030$). Age and lymph node metastasis were found to be independent prognostic factors for OS of gastric cancer patients with Grade II complications ($P = 0.034$, $P = 0.001$). Intraoperative blood loss, TNM stage, and chemotherapy were independent prognostic factors for OS of gastric cancer patients with Grade III complications ($P = 0.003$, $P = 0.005$, $P < 0.001$). There were significant differences among patients with Grade I, Grade II and Grade III complications in TNM stage II and III cancer ($P < 0.001$, $P = 0.001$).

CONCLUSION: Complication grade may be an independent prognostic factor for gastric cancer following curative resection. Treatment of complications can improve the long-term outcome of gastric cancer patients.

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Key words: Gastric cancer; Complication grade; Gastrectomy; Overall survival; Prognosis

Core tip: Only a few studies have determined the potential impact of surgical complications, especially the grade of complications, on long-term survival of patients with gastric cancer. We found that complication grade might be an independent prognostic factor for patients with gastric cancer after gastrectomy. It can be used to stratify the risk for gastric cancer prognosis. Meticulous surgery is needed and new methods should be considered to decrease the amount of intraoperative blood loss.

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INTRODUCTION

Gastric cancer is the second most common cause of cancer-related death worldwide^[1]. D2 lymphadenectomy has become the standard treatment for curable gastric cancer, however, it always brings a simultaneous increase in surgical complications^[2]. Western countries have published complication rates ranging from 35% to 46%, and mortality rates from 4% to 16% after D2 lymph node dissection^[3]. Many studies have indicated that, in gastric cancer, the presence or absence of complications is an important factor that could influence the prognosis of patients following curative gastrectomy^[4]. Accurate grading of complications is essential to analyze surgical outcomes, but methods for classification of complications are not uniform and the traditional classification is too complicated. To date, few studies have determined the potential impact of surgical complications, especially the complication grade, on long-term survival of patients with gastric cancer. Hence, the aim of this study was to reclassify the complications and investigate whether the grade of complications in patients undergoing curative gastrectomy could provide a new survival prognostic factor.

MATERIALS AND METHODS

Patients

A total of 1750 patients with gastric cancer underwent surgery at Tianjin Medical University Cancer Institute and Hospital between January 2002 and December 2006 and were entered into a prospectively maintained database. Eligibility criteria for inclusion in this study were as follows: (1) gastric adenocarcinoma identified

by histopathological examination; (2) histologically confirmed R0 resection; (3) availability of complete follow-up data; (4) radical resection and D2 lymphadenectomy performed; and (5) patients with ≥ 15 lymph nodes retrieved. The exclusion criteria were: (1) patients who underwent palliative surgery; and (2) patients who had distant metastasis or peritoneal dissemination that was confirmed during the operation. Based on these criteria, 999 patients out of 1750 were excluded from this study. Among those excluded, 315 had < 15 lymph nodes harvested for pathological examination, 210 had undergone palliative gastrectomy, 237 had D0 and D1 lymph node resection, 27 had died within 1 mo after surgery, 70 had distant metastasis before gastrectomy, 30 had peritoneal dissemination before gastrectomy, and 110 were lost to follow-up. Ultimately, 751 patients were included in the analysis.

Three hundred and five patients had postoperative complications. Complications were defined as any deviation from the normal postoperative course. There were 214 men and 91 women aged 23-82 years (mean: 62.5 ± 11.8 years).

Complication classification

Complications were classified according to the following: T92, Accordion Classification, and Revised Accordion Classification^[5-7]. The 751 patients were divided into four groups: no complications; Grade I (required only minor invasive procedures that could be done at the bedside); Grade II (required treatment with drugs other than those allowed for minor complications; no general anesthesia; required management by an endoscopic, interventional procedure or reoperation without general anesthesia); and Grade III (general anesthesia or single-organ failure; general anesthesia and single-organ failure or multisystem organ failure).

Surgical treatment and perioperative management

D2 lymphadenectomy was performed according to the guidelines for lymph node stations^[8]. The choice of surgical procedure for reconstruction was made by the surgeon. Resection margin was pathologically confirmed as negative. Postoperative adjuvant chemotherapy and neoadjuvant chemotherapy were implemented according to the tumor stage, physical condition, and willingness of the patient. Chemotherapeutics consisted of 5-fluorouracil, leucovorin and oxaliplatin. Radiotherapy was not used in the present study.

Evaluation of clinicopathological variables and survival

The clinicopathological features included sex, age (≤ 65 and > 65 years), other diseases (including hypertension, diabetes and chronic obstructive pulmonary disease), BMI (normal and abnormal), laboratory findings (white blood cell count and serum albumin), tumor size (< 5 and ≥ 5 cm), intraoperative blood loss (< 200 and ≥ 200 mL), tumor location, histology, extranodal metastasis (positive and negative), serosal invasion, lymph node

metastasis, TNM stage, postoperative chemotherapy, and type of gastrectomy. The tumors were staged according to the Union for International Cancer Control (UICC) Classification System, 7th edition, whereas lymphadenectomy and lymph node stations were defined according to the Japanese Classification of Gastric Carcinoma, 3rd English edition. Tumors were classified into two groups based on histology: differentiated type including papillary, well or moderately differentiated adenocarcinoma; and undifferentiated type including poorly differentiated or undifferentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma.

Clinicopathological features were compared among the four groups. We evaluated independent prognostic factors for patients with gastric cancer. Finally, we explored the possible independent prognostic factors associated with all grades of complications.

Follow-up

All patients were followed with a standardized protocol. The follow-up was conducted until November 2012 or death, and data were collected based on clinical review or telephone consultation after discharge. There were no patients lost to follow-up.

Statistical analysis

The analyses were performed with SPSS for Windows version 13.0. Actuarial survival rate was determined by the Kaplan-Meier method, with univariate comparisons between groups through the Log-rank test. Independent prognostic factors were identified using the Cox proportional hazards regression model. One-way analysis of variance or *t*-test was used in univariate analysis to identify possible factors associated with laboratory findings. $P < 0.05$ indicated significant differences.

RESULTS

Clinicopathological features

The patients were divided into four groups according to the complication grade (Table 1). There were 105 patients with Grade I complications, 106 with Grade II and 94 with Grade III. There were no significant differences in laboratory findings, tumor size, histology, serosal invasion, and type of gastrectomy among the four groups. Age > 65 years was more frequent in patients with Grade II complications, while male patients had gastric complications more frequently than female patients. Patients who had other diseases including hypertension, diabetes and chronic obstructive pulmonary disease were more prone to postoperative complications. Intraoperative blood loss ≥ 200 mL was more frequent in patients with Grade II and III complications than in those with Grade I complications. Tumor location in the upper third was more frequent in patients with Grade I and III complications. In patients with Grade II complications, 37.7% of tumors were located in the lower third. As the grade of complications increased, so

did extranodal metastasis, lymph node metastasis and TNM stage, while chemotherapy was more frequently performed in patients with Grade I than in those with other complications.

Prognostic value of complications in gastric cancer

The 5-year overall survival (OS) rates were 43.0%, 42.5%, 25.5% and 9.6% for no complications, and Grade I, Grade II and Grade III complications, respectively (Figure 1A). There was no difference between Grade I and no complications ($P = 0.882$). A total of 10 factors evaluated in the univariate analysis had a significant effect on survival: age, tumor size, intraoperative blood loss, tumor location, extranodal metastasis, serosal invasion, lymph node metastasis, TNM stage, type of gastrectomy, and grade of complications. In multivariate analysis, grade of postoperative complications was found to be an independent prognostic factor for OS in gastric cancer ($P < 0.001$) (Table 2).

Risk factors associated with all grades of complications

Multivariate analysis of factors associated with all grades of complications was performed (Table 3). In multivariate analysis, lymph node metastasis, tumor size, and intraoperative blood loss were independent prognostic factors for Grade I complications ($P < 0.001$, $P = 0.031$, $P = 0.030$). Age and lymph node metastasis were found to be independent prognostic factors for OS of gastric cancer patients with Grade II complications ($P = 0.034$, $P = 0.001$). Intraoperative blood loss, TNM stage, and chemotherapy were found to be independent prognostic factors for OS in gastric cancer patients with Grade III complications ($P = 0.003$, $P = 0.005$, $P < 0.001$).

Grade of postoperative complications according to TNM stage

The 5-year OS rates of the patients with Stage I disease were 83.3%, 57.1% and 50.0% for different grades of postoperative complications, respectively ($P = 0.213$). The 5-year OS rates of patients with Stage II disease were 67.9%, 47.8% and 13.6% for different grades of postoperative complications, respectively ($P < 0.001$, Figure 1B). The 5-year OS rates of patients with Stage III disease were 25.8%, 18.0% and 8.0% for different grades of postoperative complications, respectively ($P = 0.001$, Figure 1C). The 5-year OS rates of patients with Stage IV disease were 0%, 6.7% and 0% for different grades of postoperative complications, respectively ($P = 0.303$) (Table 4).

DISCUSSION

D2 lymph node dissection has gradually become the standard surgery in gastric cancer to improve patient outcome^[9]. Skillful tumor removal corresponds with long-term survival, because the vast majority of patients, even those who have negative margins, eventually die from recurrent disease^[10,11], and postoperative complica-

Table 1 Case characteristics n (%)

Characteristic	Complication group				F/ χ^2	P value
	No (n = 446)	Grade I (n = 105)	Grade II (n = 106)	Grade III (n = 94)		
Age (yr)					24.064	< 0.001
≤ 65	239 (53.6)	74 (70.5)	39 (36.8)	50 (53.2)		
> 65	207 (46.4)	31 (29.5)	67 (63.2)	44 (46.8)		
Gender					10.265	0.016
Male	302 (67.7)	62 (59.0)	83 (78.3)	69 (73.4)		
Female	144 (32.3)	43 (41.0)	23 (21.7)	25 (26.6)		
Other diseases					34.383	< 0.001
No	358 (80.3)	87 (82.9)	70 (66.0)	52 (55.3)		
Yes	88 (19.7)	18 (17.1)	36 (34.0)	42 (44.7)		
BMI (kg/m ²)					14.640	0.002
Normal	348 (78.0)	83 (79.0)	72 (67.9)	58 (61.7)		
Abnormal	98 (22.0)	22 (21.0)	34 (32.1)	36 (38.3)		
Laboratory findings						
WBC (10 ³ /mm ³)	6.5 ± 2.1	6.4 ± 2.3	6.6 ± 2.3	6.4 ± 2.2	0.311	0.733
Serum albumin (mg/dL)	40.3 ± 5.7	40.1 ± 5.0	41.1 ± 5.6	40.2 ± 6.0	0.700	0.497
Tumor size (mm)					3.728	0.292
< 5 cm	178 (39.9)	46 (43.8)	36 (34.0)	31 (33.0)		
≥ 5 cm	268 (60.1)	59 (56.2)	70 (66.0)	63 (67.0)		
Intraoperative blood loss (mL)					9.875	0.020
< 200	211 (47.3)	55 (52.4)	39 (36.8)	33 (35.1)		
≥ 200	235 (52.7)	50 (47.6)	67 (63.2)	61 (64.9)		
Tumor location					23.550	0.005
Lower 1/3	204 (45.7)	11 (10.5)	40 (37.7)	27 (28.7)		
Middle 1/3	48 (10.8)	11 (10.5)	9 (8.5)	10 (10.6)		
Upper 1/3	111 (24.9)	57 (54.3)	39 (36.8)	36 (38.3)		
2/3 or more	83 (18.6)	26 (24.8)	18 (17.0)	21 (22.3)		
Histology					5.596	0.133
Differentiated	147 (33.0)	27 (25.7)	43 (40.6)	34 (36.2)		
Undifferentiated	299 (67.0)	78 (74.3)	63 (59.4)	60 (63.8)		
Extranodal metastasis					17.533	0.001
Positive	70 (15.7)	18 (17.1)	19 (17.9)	32 (34.0)		
Negative	376 (84.3)	87 (82.9)	87 (82.1)	62 (66.0)		
Serosal invasion					3.734	0.292
No	90 (20.2)	25 (23.8)	18 (17.0)	13 (13.8)		
Yes	356 (79.8)	80 (76.2)	88 (83.0)	81 (86.2)		
Lymph node metastasis					23.866	0.005
pN0	129 (28.9)	32 (30.5)	35 (33.0)	14 (14.9)		
pN1	57 (12.8)	17 (16.2)	14 (13.2)	28 (29.8)		
pN2	112 (25.1)	20 (19.0)	23 (21.7)	20 (21.3)		
pN3	148 (33.2)	36 (34.4)	34 (32.1)	32 (34.0)		
TNM stage					39.915	< 0.001
I	35 (7.8)	12 (11.4)	7 (6.6)	4 (4.3)		
II	101 (22.6)	28 (26.7)	23 (21.7)	22 (23.4)		
III	291 (65.2)	62 (59.0)	61 (57.5)	50 (53.2)		
IV	19 (4.3)	3 (2.9)	15 (14.2)	18 (19.1)		
Chemotherapy					19.76	< 0.001
Yes	261 (58.5)	72 (68.6)	45 (42.5)	43 (45.7)		
No	185 (41.5)	33 (31.4)	61 (57.5)	51 (54.3)		
Type of gastrectomy					1.004	0.800
Subtotal	315 (70.6)	71 (67.6)	74 (32.4)	62 (66.0)		
Total	131 (29.4)	34 (32.4)	32 (30.2)	32 (34.0)		

tions caused by D2 lymph node dissection also increase. Postoperative complications are associated with the prognosis of many malignant tumors such as breast cancer, hepatic carcinoma, and colorectal cancer^[12,13]. Kressner *et al*^[13] have reported that postoperative complications influence long-term survival of colon cancer, and postoperative complications are a risk factor for overall mortality in both univariate and multivariate analyses. Cho *et al*^[14] have suggested that postoperative complications affect prognosis and recurrence patterns in patients with periampullary cancer after pancreaticoduodenec-

tomy.

As to gastric cancer, few studies have focused on the grade of postoperative complications^[15]. In 1992, Clavien *et al*^[7] proposed general principles for classifying surgical complications based on a therapy-oriented, four-level severity classification. Twelve years later, they published the modified Clavien-Dindo classification, which added detail to the more serious complications. This system has been validated in a large cohort of patients and has universal applicability^[16]. Recently, however, Strasberg *et al*^[17] analyzed 127 published surgical studies that used

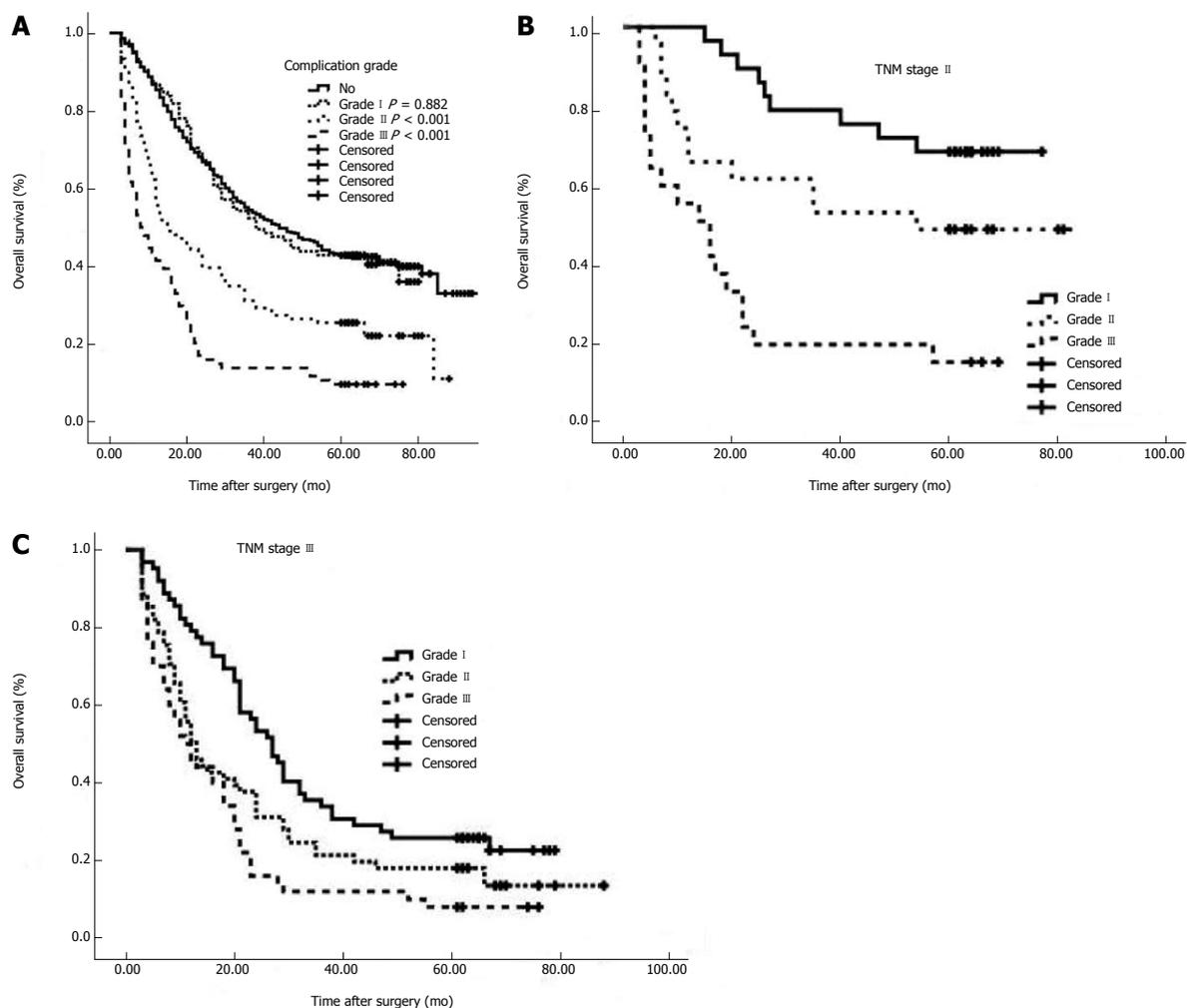


Figure 1 Overall survival curves. A: Overall survival (OS) curves for all patients grouped by complication grade. The 5-year OS rates were 43.0%, 42.5%, 25.5% and 9.6% for no complications, and Grade I, Grade II and Grade III complications, respectively. There was no difference between Grade I complications and no complications ($P = 0.882$); B: OS curves for patients with TNM Stage II cancer. There were significant differences in OS among the three grades of complications in patients with tumor-node-metastasis (TNM) Stage II cancer ($P < 0.001$); C: OS curves for patients with TNM Stage III cancer. There were significant differences in OS among the three grades of complications in patients with TNM Stage III cancer ($P = 0.001$).

Clavien-Dindo classification or its modifications and found many inconsistencies. As a result, they introduced an extensive modification of the classification, called the Accordion Severity Grading System^[5]. Specifically, the Accordion System added flexibility by introducing an expandable classification, and clarity was improved by introducing rigorously defined qualitative terms. It also provides a web-based method for compiling complication data in a standard tabular form. However, to date, the value of all complication severity grading systems, including the Accordion Modification, still need to be elucidated and the traditional classifications are too complicated. Hence, the aim of this study was to reclassify the complications and investigate whether the grade of complications in patients received curative gastrectomy could be a prognostic factor.

The prognosis of patients after surgical resection depends on various tumor-specific factors (primary tumor location, TNM stage classification, tumor differentiation, and the presence or absence of lymph node metastasis), surgery-related factors (status of resection margins and blood loss), and treatment-related factors (systemic disease treatment with either adjuvant or neoadjuvant therapy)^[18,19].

Although there has been recent progress in the early detection of tumors, the development of effective adjuvant therapy continues to be unsatisfactory. Therefore, the ability to determine potentially controllable prognostic factors to improve the dismal long-term outcomes of gastric cancer is a goal of surgeons. Previous studies have reported that postoperative complications are potentially serious, life-threatening events that may prolong hospital stay and increase costs^[20]. Li *et al*^[21] have reported that the occurrence of in-hospital postoperative complications was an independent predictor of a worse 5-year OS rate after radical resection of gastric cancer. In the present study, we divided patients into four groups according to the complication grade, as defined by T92 (Toronto 1992 or Clavien), Accordion Classification and Revised Accordion Classification. We evaluated the potential prognostic factors and found that

Table 2 Survival analysis of all patients with gastric cancer

Characteristic	S	5-yr OS	Univariate analysis		Multivariate analysis	
			χ^2	P value	HR (95%CI)	P value
Age (yr)			15.816	< 0.001	1.378 (1.147-1.654)	0.001
≤ 65	402	42.8				
> 65	349	28.7				
Gender			1.842	0.175		
Male	516	34.3				
Female	235	40.9				
Other diseases			2.457	0.117		
No	567	37.2				
Yes	184	33.7				
BMI			1.675	0.196		
Normal	561	37.6				
Abnormal	190	32.6				
Tumor size			57.692	< 0.001	1.296 (1.049-1.600)	0.016
< 5 cm	291	52.9				
≥ 5 cm	460	25.9				
Intraoperative blood loss (mL)			22.678	< 0.001	1.259 (1.038-1.526)	0.019
< 200	338	45.3				
≥ 200	413	29.1				
Tumor location			29.940	< 0.001	1.078 (0.99-01.173)	0.086
Upper 1/3	189	31.2				
Middle 1/3	78	37.2				
Lower 1/3	336	44.6				
2/3 or more	148	23.0				
Histology			0.895	0.344		
Differentiated	251	37.8				
Undifferentiated	500	35.6				
Extranodal metastasis			42.214	< 0.001	1.190 (0.956-1.482)	0.120
Positive	139	18.7				
Negative	612	40.5				
Serosal invasion			44.226	< 0.001	1.185 (0.878-1.600)	0.266
No	146	61.0				
Yes	605	30.4				
Lymph node metastasis			159.593	< 0.001	1.342 (1.211-1.487)	< 0.001
pN0	210	66.2				
pN1	116	38.8				
pN2	175	28.0				
pN3	250	15.6				
TNM stage			182.016	< 0.001	1.525 (1.238-1.879)	< 0.001
I	58	79.3				
II	174	59.2				
III	464	25.9				
IV	55	5.6				
Chemotherapy			0.420	0.517		
Yes	421	35.2				
No	330	37.6				
Type of gastrectomy			13.241	< 0.001	1.073 (0.881-1.307)	0.485
Subtotal	522	40.2				
Total	229	27.5				
Complication grade			131.080	< 0.001	1.456 (1.343-1.579)	< 0.001
None	446	43.0				
Grade I	105	42.5				
Grade II	106	25.5				
Grade III	94	9.6				

grade of postoperative complications was significantly associated with long-term survival of patients who underwent radical surgery. The 5-year OS rates were 42.5%, 25.5% and 9.6% for Grade I, Grade II and Grade III complications, respectively ($P < 0.001$). Our multivariate analysis demonstrated that, in addition to these conventional factors, the postoperative complication grade was an independent predictor for OS (HR = 1.456, 95%CI: 1.343-1.579; $P < 0.001$). The small number of patients

with UICC Stage I cancer might explain why cancer stage is not correlated with OS, because only 12, seven and four UICC Stage I patients had Grade I, II and III complications, respectively. Postoperative complications included anastomotic leakage, gastric motility disorders, anastomotic block, wound infections, intra-abdominal abscesses, infectious diarrhea, bleeding, bowel obstructions, arrhythmia, angina pectoris, pneumonia, atelectasis, thrombosis, unexplained fever, delirium, ocular fun-

Table 3 Risk factors associated with all levels of complication grade

Characteristic	Grade I		Grade II		Grade III	
	Multivariate analysis		Multivariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value
Lymph node metastasis	1.947 (1.506-2.517)	< 0.001	1.577 (1.208-2.058)	0.001		
Age			1.751 (1.044-2.939)	0.034		
Tumor size	1.913 (1.059-3.453)	0.031				
Intraoperative blood loss	1.850 (1.063-3.222)	0.030			2.099 (1.288-3.421)	0.003
TNM stage					1.607 (1.158-2.228)	0.005
Chemotherapy					2.354 (1.451-3.819)	< 0.001

TNM: Tumor-node-metastasis.

Table 4 Tumor-node-metastasis-stratified analysis of the overall survival

	Grade I	Grade II	Grade III	χ^2	P value
	5-yr OS	5-yr OS	5-yr OS		
TNM					
I	83.3	57.1	50.0	3.094	0.213
II	67.9	47.8	13.6	24.908	< 0.001
III	25.8	18.0	8.0	15.121	0.001
IV	0	5.3	0	2.387	0.303

OS: Overall survival; TNM: Tumor-node-metastasis.

gal infection, and multiple organ failure, which affected the prognosis of gastric cancer patients.

The classification of complications allowed us to study the risk factors related to different severities of morbidity. When we analyzed the risk factors for all complications, age, tumor size, intraoperative blood loss, lymph node metastasis, TNM stage, and chemotherapy were significant. With regard to age, Wydra *et al.*^[22] demonstrated that age itself is not a risk factor for postoperative complications in colorectal cancer in spite of the higher rate of accompanying diseases in elderly patients, whereas Yamada *et al.*^[23] reported that patients aged > 85 years are more likely to suffer postoperative pneumonia after gastrectomy than younger patients, and preoperative risk assessment is essential for the older patients. In our study, age was a risk factor for Grade II postoperative complications ($P = 0.034$). Patients aged > 65 years often have underlying diseases such as hypertension and chronic obstructive pulmonary disease. And in patients with the underlying diseases, the prognosis is correspondingly worse. In previous studies, increased intraoperative blood loss is associated with an elevated risk of complications^[24]. Dhar *et al.*^[25] have reported that intraoperative blood loss > 500 mL was an independent prognostic factor. Kamei *et al.*^[26] have demonstrated that the cumulative survival rate was significantly lower in patients with intraoperative blood loss ≥ 475 mL compared with < 475 mL ($P = 0.0038$), and intraoperative blood loss was a critical risk factor for peritoneal recurrence after curative resection of advanced gastric cancer. In our study, intraoperative blood loss was a risk factor for Grade I and III postoperative complications. More blood loss can cause immunity, resistance and other aspects of decline, thus increasing the

risk of complications.

Some studies have confirmed that chemotherapy increases the incidence of postoperative complications^[27,28]. As a result of the toxicity of chemotherapeutic drugs, the prognosis of patients with severe postoperative complications will vary. Therefore, the choice of chemotherapeutic drugs is important, especially for patients with underlying diseases. In the present study, chemotherapy was an independent prognostic factor only for Grade III complications (HR = 2.354, 95%CI: 1.451-3.819; $P < 0.001$). As a result of its relatively rapid disease progression, surgery plus chemotherapy for patients with gastric cancer may have a good prognosis in patients with severe complications.

Lymph node metastasis and TNM stage are independent prognostic factors that have long been associated with gastric cancer^[29,30]. According to the results of the present study, TNM stage was an independent prognostic factor for Grade III complications, and lymph node metastasis was an independent prognostic factor for Grade I and II complications. Intraoperative blood loss (HR = 2.099) and chemotherapy (HR = 2.354) had a significantly higher effect on Grade III complications than TNM stage (HR = 1.607). This may have been because chemotherapy and intraoperative blood loss had more recent effects than other factors, and were more suitable for identifying patients with higher grade complications.

The limitations of the present study were its retrospective nature, a relatively small sample population and the presence of several confounding factors. There was a lack of standardized postoperative chemotherapy regimens during that period, which may have affected patient survival. Despite these limitations, we believe that the grade of complications in gastric cancer is an important and adverse prognostic indicator. Further investigations should be performed with a larger, multicenter, randomized prospective cohort to evaluate the prognostic effect of complication grade and identify the underlying mechanism.

In conclusion, the complication grade may be an independent prognostic factor for gastric cancer patients after curative resection. It can be used to stratify the prognostic risk of gastric cancer. Meticulous surgery is needed and new methods should be considered to decrease the amount of intraoperative blood loss.

COMMENTS

Background

Many studies have indicated that, in gastric cancer, the presence or absence of complications is an important prognostic factor following curative gastrectomy. The traditional classification of complications was too complicated and the methods for classification were not uniform. Hence, the aim of this study was to reclassify the complications and investigate whether the grade of complications could provide a new prognostic factor in patients undergoing curative gastrectomy.

Research frontiers

Gastrectomy with D2 lymph node dissection has been increasingly regarded as the standard surgical procedure for most patients with operable gastric cancer, but it also brings a simultaneous increase in surgical complications. In the present study, the authors demonstrated that the complication grade was an independent prognostic factor for gastric cancer patients after curative resection.

Innovations and breakthroughs

Few studies have reported the value of all complication severity grading systems, including the Accordion Modification, in assessing the long-term survival of gastric cancer following curative gastrectomy. In this study, the authors reclassified the grade of complications and demonstrated that the grade was an independent prognostic factor for gastric cancer patients after curative resection.

Applications

By understanding the characteristics and prognostic factors for gastric cancer patients with different complication grades, this study may provide evidence for treatment planning for gastric cancer patients with different complication grades in China.

Terminology

Extranodal metastasis is defined as the presence of tumor cells in extramural soft tissues that is discontinuous with either the primary lesion or locoregional lymph nodes.

Peer review

The authors revealed that the new classification may be an independent prognostic factor for patients with gastric cancer after gastrectomy. Lymph node metastasis, tumor size, and intraoperative blood loss were independent prognostic factors for Grade I complications; age and lymph node metastasis were independent prognostic factors for overall survival (OS) of patients with Grade II complications; and intraoperative blood loss, tumor-node-metastasis stage, and chemotherapy were independent prognostic factors for OS in patients with Grade III complications. The conclusions of the study are of potential significance for clinicians.

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