Low Serum Albumin Level, Male Sex, and Total Gastrectomy Are Risk Factors of Severe Postoperative Complications in Elderly Gastric Cancer Patients

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Purpose: It is well known that old age is a risk factor for postoperative complications. Therefore, this study aimed to explore the risk factors for poor postoperative surgical outcomes in elderly gastric cancer patients.

Materials and Methods: Between January 2006 and December 2015, 247 elderly gastric cancer patients who underwent curative gastrectomy were reviewed. In this study, an elderly patient was defined as a patient aged ≥65 years. All possible variables were used to explore the risk factors for poor early surgical outcomes in elderly gastric cancer patients.

Results: Based on multivariate analyses of preoperative risk factors, preoperative low serum albumin level (<3.5 g/dl) and male sex showed statistical significance in predicting severe postoperative complications. Additionally, in an analysis of surgery-related risk factors, total gastrectomy was a risk factor for severe postoperative complications.

Conclusions: Our study findings suggest that low serum albumin level, male sex, and total gastrectomy could be risk factors of severe postoperative complications in elderly gastric cancer patients. Therefore, surgeons should work carefully in cases of elderly gastric cancer patients with low preoperative serum albumin level and male sex. We believe that efforts should be made to avoid total gastrectomy in elderly gastric cancer patients.

Key Words: Stomach neoplasms; Aged; Risk factors; Postoperative complications

Introduction

As the average life expectancy for elderly persons is increasing dramatically in many parts of the world,[1,2] many countries are expected to develop what is known as super-aged societies in the near future. This increase in the elderly population parallels the proportional increase in geriatric patients with cancer.[3] Therefore, the average age at cancer diagnosis is also expected to increase in most countries with aging populations. Following this trend, the results of geriatric assessments were introduced to provide information about risk evaluation in the surgical treatment of elderly cancer patients.[4,5]

The impact of old age on the early surgical outcomes of gastric cancer surgery is controversial. Several studies have suggested that old age is an independent risk factor of postoperative morbidity and mortality due to decreased reserve capacity.[6,7] Most elderly patients have multiple morbidities that may lead to severe postoperative complications and mortality. In particular, super-elderly patients (≥75 years of age) have increasing numbers of comorbidities and functional disorders.[8,9] Another study documented that having multiple morbidities increases the risk of postoperative complications in patients who undergo elective surgery.[10] Therefore, the risk assessment of elderly persons has become an important issue in the field of gastric cancer surgery.

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Several investigators recently suggested that old age is an important predictive risk factor of gastric cancer surgery.[11-13]

On the other hand, other studies suggested that open gastrectomy can also be safely performed in elderly patients because of improvements in surgical techniques and perioperative management.[14,15] Some recent studies in particular have shown that laparoscopic gastrectomy can be safely performed in elderly patients.[16,17]

Therefore, this study planned to explore the risk factors of minimal invasive surgeries such as laparoscopic gastrectomy.

Materials and Methods

1. Patients

We retrospectively reviewed data that were prospectively collected for 247 elderly gastric cancer patients who underwent curative gastrectomy with lymph node dissection between January 2006 and December 2015 at Hanyang University Guri Hospital. In this study, an elderly patient was defined as a patient aged 65 years or older according to World Health Organization guidelines.[18] According to this criterion, some studies showed that elderly patients had poor surgical outcomes including hospital stay length and days of inpatient care.[19]

2. Surgical techniques

Laparoscopic gastrectomy was performed in elderly gastric cancer patients with serosa-negative and perigastric lymph node metastasis according to preoperative clinical staging results. Clinical staging was determined by preoperative gastrofiberoscopy, computed tomography, and endoscopic ultrasonography. D1 plus beta lymphadenectomy was performed in all gastric cancer patients. In laparoscopic gastrectomy, total omentectomy was performed in patients with advanced gastric cancer. The extent of gastrectomy was dictated based on tumor location.

3. Clinical analysis

Clinical data obtained from medical records included patient age, sex, body mass index (BMI; kg/m^2), American Society of Anesthesiologist (ASA) score, and others (Table 1). The operative characteristics and early surgical outcomes reviewed included operation method (laparoscopic vs. open surgery), extent of gastrectomy (total vs. subtotal gastrectomy), omentectomy (total vs. partial), combined resection of other organs, operation time, postoperative complications, postoperative mortality, and length of postoperative hospital stay. Pathologic results were analyzed for tumor size, number of retrieved lymph nodes, and 7th American Joint Committee on Cancer staging system score.[20]

The classification of underweight was defined as a BMI < 18.5 kg/m^2. The ASA classification was determined by anesthesiologists 1 day before the surgery. The preoperative serum albumin and hemoglobin levels were measured when the patient was admitted to the hospital. Hypoalbuminemia was defined as serum albumin levels below the normal range (< 3.5 g/dl). The Prognostic Nutrition Index (PNI) was used as risk factor of post-

Table 1. Clinical characteristics of elderly patients who underwent gastrectomy

Variable	Value
Age (yr)	72.8±4.9
≥75	83 (33.6)
≥65, <75	164 (66.4)
Sex	
Male	162 (65.6)
Female	85 (34.4)
BMI (kg/m^2)	23.0±3.4
<18.5	18 (7.3)
≥18.5	229 (92.7)
ASA score	
ASA 1	6 (2.4)
ASA 2	143 (57.9)
Over ASA 3	98 (39.7)
Presence of comorbidities	178 (78.4)
No. of comorbidities	
≥3	51 (20.6)
<3	196 (79.4)
History of major abdominal surgery	32 (13.0)
Hemoglobin level (g/dl)	
<12.0 (female), 13.0 (male)	148 (59.9)
≥12.0 (female), 13.0 (male)	99 (40.1)
Albumin level (g/dl)	
<3.5	55 (22.3)
≥3.5	192 (77.7)
PNI score	
<46	87 (35.2)
≥46	160 (64.8)

Values are presented as mean±standard deviation or number (%). BMI = body mass index; ASA = American Society of Anesthesiologists; PNI = Prognostic Nutritional Index.

operative complication.[21,22] Anemia was defined as a decreased hemoglobin level (female < 12.0; male < 13.0 g/dl).

Postoperative complications were defined as any condition requiring conservative or surgical treatment. Severe postoperative complications were defined as those that required management by an endoscopic or interventional procedure or re-operation (expanded classification > level 3).[23] Thirty-day mortality was used for postoperative mortality and defined as death within 30 days of surgery.

In this study, a soft diet was started when patients felt comfortable enough to consume a liquid diet twice at consecutive meal times. Patients were discharged if they had no problems eating a soft diet, showed an absence of inflammatory conditions including leukocytosis, unstable vital signs, or abrupt-onset abdominal pain, and if they were generally comfortable. The final decision regarding discharge was left up to each patient.

4. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics ver. 21 (IBM Co., Armonk, NY, USA). All values are expressed as means±standard deviation. Categorical variables were analyzed using the chi-square test and all continuous variables were analyzed with Student's t-test depending on the data. A multivariate analysis was performed to identify risk factors associated with early surgical outcomes. Factors with relatively small P-values (P < 0.1) on univariate analysis were selected as variables for multivariate analysis. A multivariate analysis was performed using multiple logistic regression analysis. Hazard ratios with 95% confidence intervals were estimated for each variable in the multivariate analysis. A P-value < 0.05 was considered statistically significant.

Results

1. Clinical characteristics

The clinical characteristics of the 247 patients are shown in Table 1. The mean patient age was 72.8 years. Eighty-three patients (33.6%) were 75 years of age or older. Men outnumbered women in this study population. The majority of patients (78.4%) had one or more comorbid conditions, while 51 patients had three or more comorbidities. Anemia was seen in 148 patients (59.9%). A low serum albumin level was measured in 55 patients (22.3%). A low PNI score was seen in 87 patients.

Table 2. Surgery-related characteristics of elderly patients who underwent gastrectomy

Variable	Value
Conversion of cases to open surgery	0 (0)
Operation time (min)	194.4±59.8
≥180	130 (52.6)
<180	117 (47.4)
Surgical method	
Laparoscopic gastrectomy	117 (47.4)
Open gastrectomy	130 (52.6)
Extent of gastrectomy	
Total gastrectomy	61 (24.7)
Subtotal gastrectomy	186 (75.3)
Total omentectomy	180 (72.9)
Combined resection of other organs	41 (16.6)
Overall postoperative complications	50 (20.2)
Severe postoperative complications	20 (8.1)
Postoperative mortality (within 30 days)	6 (2.4)
Commencement of soft diet (d)	8.5±5.5
Postoperative hospital stay (d)	17.1±12.5
≥21	57 (23.1)
<21	190 (76.9)
T classification (7th AJCC)	
T1	111 (44.9)
T2	26 (10.5)
T3	21 (8.5)
T4	89 (36.0)
N classification (7th AJCC)	
N0	121 (49.0)
N1	36 (14.6)
N2	24 (9.7)
N3	64 (25.9)
TNM stage	
Stage I	124 (50.2)
Stage II	20 (8.1)
Stage III	103 (41.7)
Tumor size (cm)	4.9±3.3
≥7	58 (23.5)
<7	189 (76.5)

Values are presented as number (%) or mean±standard deviation. AJCC = American Joint Committee on Cancer; TNM = tumor, node, metastasis.

2. Surgery-related characteristics

Table 2 shows the early surgical outcomes and pathologic results of elderly gastric cancer patients. None of these patients required conversion to open surgery. The mean operation time was 194.4 minutes. A little more than half of the operations (52.6%) lasted longer than 3 hours. Laparoscopic gastrectomy was performed in 117 patients (47.4%). The percentage of patients who underwent total gastrectomy was 24.7%. Forty-one patients (16.6%) underwent combined resection of another organ. Postoperative complications occurred in 50 patients (20.2%). A total of 20 patients (8.1%) experienced severe postoperative complications. Postoperative mortality occurred in six patients (2.4%). The mean postoperative hospital stay was 17.1 days. Fifty-seven patients (23.1%) were hospitalized for >3 weeks after their operations. One hundred and eleven patients had early gastric cancer. Negative lymph node metastasis occurred in 121 patients. Fifty-eight patients had large tumors (≥7 cm).

3. Univariate analyses of risk factors for early surgical outcomes

Table 3 and 4 list the risk factors for early surgical outcomes. More patients who developed overall postoperative complications were found in the anemia, low serum albumin level, long operation time, total omentectomy, and large size tumor groups. Severe

Table 3. Univariate analysis of preoperative risk factors for early surgical outcomes

Variable	Overall complication	P-value	Severe complication	P-value
Age (yr)		0.947		0.890
≥75 (n=83)	17 (20.5)		7 (8.4)	
<75 (n=164)	33 (20.1)		13 (7.9)	
Sex		0.462		0.017
Male (n=162)	35 (21.6)		18 (11.1)	
Female (n=85)	15 (17.6)		2 (2.4)	
No. of comorbidities		0.193		0.773
≥3 (n=51)	7 (13.7)		3 (5.9)	
<3 (n=196)	43 (21.9)		17 (8.7)	
History of abdominal surgery		0.486		0.730
Yes (n=32)	5 (15.6)		3 (9.4)	
No (n=215)	45 (20.9)		17 (7.9)	
BMI (kg/m^2)		0.766		1.000
<18.5 (n=18)	4 (22.2)		1 (5.6)	
≥18.5 (n=229)	46 (20.1)		19 (8.3)	
ASA score		0.707		0.975
ASA 1, 2 (n=149)	29 (19.5)		12 (8.1)	
Over ASA 3 and E (n=98)	21 (21.4)		8 (8.2)	
Hemoglobin level (g/dl)		0.023		0.056
<12.0 (female), 13.0 (male) (n=148)	37 (25.0)		16 (10.8)	
≥12.0 (female), 13.0 (male) (n=99)	13 (13.1)		4 (4.0)	
Serum albumin level (g/dl)		0.009		0.004
<3.5 (n=55)	18 (32.7)		10 (18.2)	
≥3.5 (n=192)	32 (16.7)		10 (5.2)	
PNI score		0.074		0.004
<46 (n=87)	23 (26.4)		13 (14.9)	
≥46 (n=160)	27 (16.9)		7 (4.4)	

Values are presented as number (%). BMI = body mass index; ASA = American Society of Anesthesiologists; E = emergency; PNI = Prognostic Nutritional Index.

Table 4. Univariate analysis of surgery-related risk factors for early surgical outcomes

Variable	Overall complication	P-value	Severe complication	P-value
Operation time (min)		<0.001		0.011
≥180 (n=130)	39 (30.0)		16 (12.3)	
<180 (n=117)	11 (9.4)		4 (3.4)	
Type of surgery		0.243		0.037
Laparoscopy (n=117)	20 (17.1)		5 (4.3)	
Open (n=130)	30 (23.1)		15 (11.5)	
Extent of gastrectomy		0.088		0.002
Total (n=61)	17 (27.9)		11 (18.0)	
Subtotal (n=186)	33 (17.7)		9 (4.8)	
Total omentectomy		0.048		0.455
Yes (n=180)	42 (23.3)		16 (8.9)	
No (n=67)	8 (11.9)		4 (6.0)	
Other organ resection		0.899		0.292
Yes (n=41)	8 (19.5)		5 (12.2)	
No (n=206)	42 (20.4)		15 (7.3)	
Tumor depth (7th AJCC)		0.100		0.065
T1, 2, 3 (n=158)	27 (17.1)		9 (5.7)	
T4 (n=89)	23 (25.8)		11 (12.4)	
Nodal status (7th AJCC)		0.762		0.048
N0, 1, 2 (n=182)	36 (19.8)		11 (6.0)	
N3 (n=65)	14 (21.5)	0.098	9 (13.8)	0.083
TNM Stage (7th AJCC)				
Stage I and II (n=144)	24 (16.7)		8 (5.6)	
Stage III (n=103)	26 (25.2)		12 (11.7)	
Tumor size (cm)		0.019		0.026
≥7 (n=58)	18 (31.0)		9 (15.5)	
<7 (n=189)	32 (16.9)		11 (5.8)	
Retrieved lymph nodes		0.458		0.083
≥30 (n=167)	36 (21.6)		17 (10.2)	
<30 (n=80)	14 (17.5)		3 (3.8)	

Values are presented as number (%). AJCC = American Joint Committee on Cancer; TNM = tumor, node, metastasis.

postoperative complications were significantly different in the male sex, low serum albumin level, low PNI score, long operation time, total gastrectomy, N3 stage, and large size tumor groups.

4. Multivariate analyses of risk factors for early surgical outcomes

Table 5 shows the preoperative risk factors. Low serum albumin level was an overall risk factor (odds ratio [OR], 7.451; 95% confidence interval [CI], 1.327~41.831; P=0.023) and severe postoperative complications (OR, 5.543; 95% CI, 2.076~14.797; P=0.001) of elderly gastric cancer patients.

In surgery-related risk factors, large tumor size (>7 cm; OR, 2.111; 95% CI, 1.022~4.359; P=0.044) and long operation time (>3 hours; OR, 4.317; 95% CI, 2.012~9.265; P<0.001) were risk factors of overall postoperative complications, while total gastrectomy (OR, 3.062; 95% CI, 1.146~8.177; P=0.026) was a risk factor of severe postoperative complications (Table 6).

Table 5. Multivariate analysis of preoperative risk factors for early surgical outcomes

Variable	Overall complications			Severe complications		
	RR	95% CI	P-value	RR	95% CI	P-value
Serum albumin level (<3.5 g/dl)	7.451	1.327~41.831	0.023	5.543	2.076~14.797	0.001
Male sex				7.406	1.605~34.175	0.010

RR = relative risk; CI = confidence interval.

Table 6. Multivariate analysis of surgery-related risk factors for early surgical outcomes

Variable	Overall complications			Severe complications		
	RR	95% CI	P-value	RR	95% CI	P-value
Tumor size (>7 cm)	2.111	1.022~4.359	0.044			
Operation time (>3 h)	4.317	2.012~9.265	<0.001			
Total gastrectomy (vs. subtotal)				3.062	1.146~8.177	0.026

RR = relative risk; CI = confidence interval.

Discussion

Biological age is a key factor in determining surgical success. Consequently, a comprehensive geriatric assessment was recently instituted to assess the components of an elderly person's physical, mental, and social status.[4,5] However, determining how this overarching method should be applied in practice for surgical patients remains challenging.[24] Furthermore, there has been no consensus with respect to the best tool for predicting postoperative outcomes.[25,26]

Our multivariate analyses showed that three variables (serum albumin level, sex, and extent of gastrectomy) can be risk factors for poor early surgical outcomes in elderly gastric cancer patients. In particular, our study showed that elderly age ($\geq$75 years) is not a significant risk factor for early surgical outcomes of conventional gastric cancer surgery.

Several authors have reported that postoperative mortality rates are higher in elderly patients because of pre-existing comorbidities.[14,27] Meanwhile, recent studies have suggested that elderly gastric cancer patients can be safely operated on using improved surgical techniques and perioperative management.[14–17] Our study also obtained a similar result in that we found no difference in early surgical outcomes between elderly patients aged $\geq$65 years and those $\geq$75 years. Despite this, we are not arguing that old age is not a risk factor for early surgical outcomes of gastric cancer. We previously reported that early surgical outcomes of totally laparoscopic distal gastrectomy were also affected by old age.[28]

It is well known that low preoperative serum albumin is a strong predictor of postoperative morbidity and mortality.[29,30] Our study also showed that hypoalbuminemia can be an independent risk factor of postoperative complications. The important thing to note is that initial hypoalbuminemia can affect early surgical outcomes irrespective of the replacement of albumin. It is assumed that initial hypoalbuminemia reflects a state of malnutrition. Therefore, this serum albumin test could be a reasonably simple and cost-effective method for identifying at-risk patients. On the other hand, our study did not show the significance of PNI as a predictive risk factor for early surgical outcomes.

Several recent studies have suggested that male sex is a risk factor of postoperative complication in bowel surgery.[31–33] In particular, our results showed that male sex is an independent risk factor for severe postoperative complications in multivariate analysis.

Total gastrectomy is a known risk factor of postoperative complications.[33,34] One report stated that total gastrectomy should be performed in patients >80 years of age only if absolutely necessary.[35] Our multivariate analysis also showed that total gastrectomy is an independent risk factor of severe postoperative complication in elderly gastric cancer patients.

This study had several limitations. First, it was a retrospective study with possible selection bias. Second, only a small number of patients had severe postoperative complications. Therefore, fur-

ther large randomized controlled trials are needed to evaluate the risk factors.

In clinical practice, most surgeons believe that, based on their experience, they can predict the physiological reserve of an elderly person who plans to undergo cancer surgery. On the other hand, most surgeons are aware that their methods for determining this status are fairly subjective. As a result, some elderly persons miss the opportunity to undergo surgery. In contrast, the overestimation of patient reserve can also lead to postoperative death. Therefore, despite the study limitations, we believe that our identification of poor risk factors will help physicians predict postoperative surgical outcomes in elderly gastric cancer patients.

In summary, we found that the poor risk factors for early surgical outcomes of gastric cancer surgery in elderly patients included low serum albumin level, male sex, and total gastrectomy. In particular, we suggest that surgeons should operate carefully in elderly male patients with gastric cancer as well as in those with low serum albumin levels to decrease severe postoperative complications. We believe that efforts should be made to avoid total gastrectomy in elderly gastric cancer patients.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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