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Risk factors affecting unplanned reoperation after laparoscopic gastrectomy for gastric cancer: experience from a high-volume center

Ping Li[1] · Chang-Ming Huang[1] · Ru-Hong Tu[1] · Jian-Xian Lin[1] · Jun Lu[1] · Chao-Hui Zheng[1] · Jian-Wei Xie[1] · Jia-Bin Wang[1] · Qi-Yue Chen[1] · Long-Long Cao[1] · Mi Lin[1]

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Abstract

Background To evaluate the risk factors affecting unplanned reoperation (URO) after laparoscopic gastrectomy (LAG) for gastric cancer (GC) and establish a model to predict URO preoperatively.

Study design Between May 2007 and December 2014, we prospectively collected and retrospectively analyzed the data of 2608 GC patients who underwent LAG. Among them, 2580 patients not requiring an URO were defined as the Non-URO group, and 28 patients requiring an URO were defined as the URO group. Univariate, multivariate, and bootstrap analyses were performed to determine the independent predictors for URO, and a nomogram was constructed to preoperatively predict the rate of URO after LAG.

Results Of the 2608 patients, the URO rate was 1.1% (28/2608) within the 30-day hospitalization. The mean URO time interval to first operation was 5.6 ± 5.5 (0.10–18.5) days. The main causes requiring URO were intraabdominal bleeding (57.1%), anastomotic bleeding (17.9%), anastomotic leakage (7.1%), and intraabdominal infection (7.1%). Compared to the Non-URO group, the URO group had a significantly longer hospital stay ($p < 0.001$) and significantly higher hospital fees ($p < 0.001$). The morbidity rate was 39.2% in the URO group and 14.5% in the non-URO group ($p = 0.001$), and mortality was 3.6% in the URO group and 0.2% in the non-URO group ($p = 0.063$). Multivariate analysis using bootstrap method revealed that age > 70 years (odds ratio (OR) = 2.232, 95% confidence interval (CI) = 1.023–4.491, $p = 0.028$), male gender (OR = 32.983, 95% CI 1.405–25.343 × 10^6, $p = 0.027$), and body mass index (BMI) > 25 kg/m^2 (OR = 2.550, 95% CI 1.017–5.398, $p = 0.012$) were independent risk factors for URO. A multivariable nomogram model for predicting URO exhibited a strong optimism-adjusted discrimination (concordance index, 0.687). No significant correlation was noted between the URO rate and operative period by Spearman analysis ($r = 0.012$, $p = 0.548$).

Conclusions Age > 70 years, Male, and BMI > 25 kg/m^2 were independent risk factors for URO. Based on the three risk factors, we developed a simple and practical nomogram to predict URO preoperatively, which might aid surgeons in reducing the URO rate when planning to perform LAG for GC.

Keywords Stomach neoplasms · Laparoscopy surgical procedures · Gastrectomy · Postoperative complications · Reoperation

Since laparoscopic gastrectomy (LAG) for gastric cancer (GC) was first reported by Kitano [1] in 1994, it has gained general acceptance and approval by an increasing number of surgeons for the treatment of GC due to its minimal invasiveness, superior recovery [2, 3], and comparable oncologic outcomes [4, 5] compared with open surgery. Clinically, guaranteeing the curative effect of laparoscopic surgery and simultaneously improving its safety to the greatest extent remain important issues for surgeons.

To date, the quality of surgical care is most often mirrored by the measurement of direct outcomes, such as patient postoperative morbidity and mortality [6, 7]. However, some scholars [8, 9] believe that the aforementioned

✉ Chang-Ming Huang
hcmlr2002@163.com

[1] Department of Gastric Surgery, Fujian Medical University Union Hospital, No.29 Xinquan Road, Fuzhou 350001, Fujian Province, China

indexes do not completely reflect operation safety and have put forward the concept of unplanned reoperation (URO) as a supplemental quality indicator of morbidity and mortality. As a severe adverse event after surgery for patients, URO markedly increases patient burden, directly affects rehabilitation, and potentially causes death [10, 11]. In recent years, the URO rate has been increasingly used by numerous medical centers as an important index to measure the quality of surgical care.

A preoperative comprehensive understanding of the risk factors for an URO after LAG is beneficial for surgeons to reduce its incidence and improve surgical safety during the perioperative period. Previous studies [6, 7] have examined the morbidity and mortality following LAG for GC; however, at present, our knowledge of risk factors for URO is very limited. Furthermore, no studies on URO risk prediction for this type of surgery have been undertaken. Therefore, the purpose of the current study was to evaluate the risk factors that influence URO for GC patients undergoing LAG and for the first time to establish a simple and practical nomogram for preoperative prediction of URO.

Materials and methods

Materials

This study was a retrospective analysis of a prospectively collected database of GC patients treated with LAG in the Department of Gastric Surgery of Fujian Medical University Union Hospital from May 2007 to December 2014. All of the clinical-pathological and surgical data were recorded in a prospectively designed database for GC surgery. The clinical-pathological stages were established in accordance with the American Joint Committee on Cancer (AJCC) 7th Edition of Gastric Cancer TNM Staging [12].

The inclusion criteria were as follows: (1) patients with a preoperatively, histologically confirmed, primary adenocarcinoma; (2) patients without tumors invading the adjacent organs (liver, gallbladder, pancreas, spleen, and transverse colon), enlarged or integrated lymph nodes (LNs) around the stomach or evidence of distant metastasis demonstrated by preoperative abdominal endoscopic ultrasonography and spiral CT; and (3) patients with gastrectomy plus $D1+\alpha$, $D1+\beta$, or D2 lymphadenectomy and curative R0 resection based on the postoperative pathological diagnosis. The exclusion criteria were as follows: (1) patients with T4b tumors, (2) patients with enlargement or integration of LNs around the stomach, (3) patients with intraoperative evidence of peritoneum and pelvic implantation metastasis or distant metastasis, or (4) patients with insufficient clinical-pathological data. All patients were provided written informed consent prior to the operation, and the procedure was performed after approval by the Institutional Review Board. Lymphadenectomies were classified according to the 2nd and 3rd English edition of the Japanese Classification of Gastric Carcinoma [13, 14]. A total of 2608 patients were enrolled in this study. Among them, the 2580 patients who did not require URO were classified as the Non-URO group, and the 28 patients who required URO were classified as the URO group.

Variables and definitions

The definition of each complication was based on previous studies. In the current study, URO refers to that the patient must return to the operating room under general anesthesia and tracheal intubation to undergo reoperation inside the peritoneal cavity due to postoperative complications caused by the original LAG for GC within a 30-day hospitalization period. The URO rate is defined as the cases of reoperation divided by all cases. Parameters including the time to movement out of bed, first flatus, initiation of liquids, initiation of a semifluid diet, and the overall morbidity and mortality rates in the URO group refer to data recorded after the second operation. Hospital stay was defined as the time from the initial post-operation to discharge.

Morbidity was classified according to the revised version of the Clavien-Dindo classification system [15]. In cases with more than one complication, the most severe complication was noted. Complications higher than grade III were defined as "major" complications that are potentially life threatening. Briefly, grade 0 represented no complications, and grade I included complications requiring no intervention or minor interventions, such as basic monitoring, oral antibiotics, or bowel rest. Grade II complications were those requiring moderate interventions, such as intravenous medications (e.g., antibiotics or antiarrhythmic drugs), total parenteral nutrition, prolonged tube feeding, or chest tube insertion. Grade III complications were those requiring surgical intervention or radiological intervention (percutaneous drainage). Grade IV complications included those producing chronic disability, organ resection, or enteral diversion. Grade V complications were those resulting in death. Grade I–II complications were considered minor, and Grade IIIa or greater complications that required additional interventional or surgical treatment were considered major postoperative complications [7]. Hospital mortality was defined as any patient with postoperative death within 30 days or during the same hospitalization.

The potential risk factors for URO after LAG were extracted from the database. Clinical and pathological factors included gender, age, concomitant diseases, diabetes, autoimmune disorders, American Society of Anesthesiologist (ASA) score, smoking history, preoperative albumin(ALB), preoperative malnourishment or not (nutritional status), neoadjuvant treatment or not, a history of previous abdominal surgery, body mass index (BMI), tumor size, tumor location, pathological types, pT stage, pN stage, pTNM stage, type of surgical resection, type of reconstruction, D1+/D2 lymphadenectomy, operative time (recorded from skin incision to skin closure), intraoperative blood loss (measured by calculating the volume of blood in the suction container and weighing the gauze), numbers of resected LNs, and operative period (divided into 9 groups). In this study, four types of reconstruction are performed after gastrectomy: Roux-en-Y reconstruction following total gastrectomy, Billroth-I (B-I) or Billroth-II (B-II) reconstruction following distal gastrectomy, and Esophagogastrostomy following proximal gastrectomy. There are 71 patients undergoing neoadjuvant treatment, with all of them undergoing neoadjuvant chemotherapy and none of them undergoing neoadjuvant radiotherapy. We considered that the patients had concomitant diseases when they had a history of taking medical treatments for that disease [16]. A positive smoking history was defined as a documented lifetime use of more than 100 cigarettes based on WHO Guidelines [17]. Malnourishment was defined by meeting at least one of the four criteria listed below, based on the Guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN): weight loss >10–15% within 6 months, BMI < 18.5 kg/m2, Subjective Global Assessment Grade C, or serum albumin < 3.0 g/dl. However, patient with only BMI < 18.5 kg/m2 was considered to be lean but not malnourished [18, 19]. A BMI > 25 (kg/m^2) is defined as obesity by the WHO Asia Pacific guidelines [20], which is lower than the European and American standard. We classified patients into two groups, BMI ≤ 25 and BMI > 25, based on the Asia Pacific guidelines for obesity in this study.

Operative procedure

The operative procedure was referenced in our previously published monograph [21].

Statistical analysis

Continuous variables are expressed as means ± SD, and differences between groups were analyzed using Student's *t* test. Categorical data are presented as percentages and were analyzed with a χ^2 test or Fisher's exact test. Variables with $p < 0.05$ in the univariate analysis were subsequently included in a multivariate binary logistic regression model. Independent risk factors that influenced URO were identified by multivariate analysis using bootstrap method with random 1000 resamples. On the basis of the results of the bootstrap analysis, a nomogram was formulated by R 3.2.0 (http://www.r-project.org). Correlations between variables were analyzed using the Spearman correlation coefficient. Statistical analyses were performed with SPSS version 18.0 (SPSS, Chicago, IL, USA). A *p* value of <0.05 was considered statistically significant.

Results

Severe postoperative complications after LAG

Among 2608 patients with GC, 1950 (74.8%) were male, and 658 (25.2%) were female. The mean age was 60.8 ± 10.9 years (range 12–87 years), and the mean BMI was 22.2 ± 2.9 kg/m^2 (range 13.2–37.3 kg/m^2). Overall and severe postoperative complications within 30 days of hospitalization were observed in 374 cases (14.3%) and 98 cases (3.8%). Of the 98 cases of severe complications, 39 patients (1.5%) exhibited Grade IIIa complications, 22 (0.8%) had Grade IIIb complications, 29 (1.1%) had Grade IVa complications, 2 (0.1%) had Grade IIIb complications, and 6 (0.2%) had Grade V complications (Table 1). Six of 2608 patients (0.2%) died postoperatively within 30 days of hospitalization, with one patient dying from DIC and the others dying from sepsis.

Detailed clinical courses of the URO patients

Of the 2608 patients, 28 required URO, with a URO rate of 1.1% (28/2608). Clinical-pathological data, including gender, age, concomitant diseases, diabetes, autoimmune disorders, ASA score, smoking history, preoperative malnourishment or not, neoadjuvant treatment or not, and type of reconstruction, are presented in Table 2. The mean URO time interval from first operation to reoperation was 5.6 ± 5.5 (0.10–18.5) days. Among the 28 patients, the main causes of URO were intraabdominal bleeding 57.1% (16/28), anastomotic bleeding 17.9% (5/28), anastomotic leakage 7.1% (2/28), intraabdominal infection 7.1% (2/28), incision dehiscence 3.6% (1/28), intestinal obstruction 3.6% (1/28), and jejunal perforation 3.6% (1/28) (Fig. 1). There were 22 (78.6%) patients who underwent an open procedure and 6 (21.4%) patients who underwent a laparoscopic procedure. In total, 27 patients recovered after the second operation, and one required a third operation. One patient died due to sepsis after the second operation (within the 30-day hospitalization). Among all of the patients, the rate of anastomosis bleeding requiring URO is 0.2% (5/2608), with B-I reconstruction 0.1% (1/920) and Roux-en-Y reconstruction 0.3% (4/1411). The detailed clinical courses of patients with URO are presented in Table 3.

Table 1 Types and cases of postoperative severe complications (%)

Type	No	%
Grade IIIa	39	1.5
Anastomotic bleeding	1	
Duodenal stump fistula	1	
Anastomotic leakage	13	
Wound infection	4	
Ileus or obstruction	1	
Intraabdominal infection	8	
Pneumonia	15	
Chylous leak	2	
Grade IIIb	22	0.8
Intraabdominal bleeding	15	
Anastomotic bleeding	5	
Ileus or obstruction	1	
Wound infection	1	
Grade IVa	29	1.1
Intraabdominal bleeding	1	
Duodenal stump fistula	1	
Anastomotic leakage	2	
Ileus or obstruction	1	
Intraabdominal infection	1	
Cardiac event	2	
Pneumonia	21	
Grade IVb	2	0.1
Pneumonia + Cardiac event	2	
Grade V	6	0.2
Intraabdominal bleeding	4	
Anastomotic leakage	2	
Pancreatic fistula	1	
Intrabdominal infection	1	
Cardiac event	1	
Reoperation	28	1.1
In-hospital mortality	6	0.2

Table 2 Clinicopathological characteristics of URO

Items	No
Gender (male/female)	26/2
Mean age (years)	64.07 ± 10.37
Concomitant diseases (no/yes)	20/8
Diabetes (no/yes)	26/2
Autoimmune disorders (no/yes)	28/0
ASA classification (≤2/>2)	26/2
Smoking history (no/yes)	21/7
Malnourishment (no/yes)	27/1
Neoadjuvant treatment (no/yes)	28/0
Mean BMI (kg/m^2)	23.27 ± 3.84
Histories of abdomen surgery (no/yes)	24/4
Tumor diameter, (cm) (≤5.0/>5.0)	17/11
Tumor location (upper/middle/lower/≥2 areas)	9/7/9/3
Reconstruction (B-I/B-II/ Roux-en-Y)	7/2/19
Surgical resection (total/distal/proximate)	19/9/0
pT stage (T1/T2/T3/T4a)	6/2/12/8
pN stage (N0/N1/N2/N3)	8/5/4/11
pTNM stage (I/II/III)	7/9/12

The influence of URO on early surgical outcomes

Compared to the Non-URO group, the URO group had significantly longer hospital stays (26.9 vs.13.0 days, $p < 0.001$) and increased hospital fees (16082 vs. 9542 USD, $p < 0.001$). The morbidity rate was 39.2% in the URO group and 14.5% in the non-URO group ($p = 0.001$), and mortality was 3.6% in the URO group and 0.2% in the non-URO group ($p = 0.063$). In addition, no statistically significant differences were noted regarding the time to movement out of bed, first flatus, initiation of liquids, and initiation of a semifluid diet between the two groups ($p > 0.05$) (Table 4).

Univariate, multivariate, and bootstrap analysis of risk factors for URO

As shown in Table 5, the univariate analysis indicated that concomitant diseases ($p = 0.829$), diabetes ($p = 0.905$), autoimmune disorders ($p = 1.000$), smoking history ($p = 0.730$), preoperative malnourishment or not ($p = 1.000$), neoadjuvant treatment or not ($p = 1.000$), reconstruction type ($p = 0.568$), etc. have no statistical relation with URO. However, three factors including age ($p = 0.023$), gender ($p = 0.027$), and BMI ($p = 0.021$) were significantly associated with URO. Age > 70 years, male gender, and BMI > 25 kg/m^2 were closely related to URO. As shown in Table 6, multivariate analysis using bootstrap method demonstrated that older age [>70 years, odds ratio (OR) = 2.232, 95% confidence interval (CI) = 1.023–4.491, $p = 0.028$], male gender (OR = 32.983, 95% CI = 1.405–25.343 × 10^6, $p = 0.027$), and BMI > 25 kg/m^2 (OR = 2.550, 95% CI = 1.017–5.398, $p = 0.012$) were independent risk factors for URO.

Construction of the nomogram for URO

Based on the above three independent risk factors, a simple and practical nomogram was established to predict URO after LAG (Fig. 2). A discrimination concordance index of 0.687 indicated a 68.7% correct ordering of risk across pairs of patients and a good calibration of observed versus predicted outcomes. The efficiency of this model to differentiate between low-risk and high-risk patients is illustrated

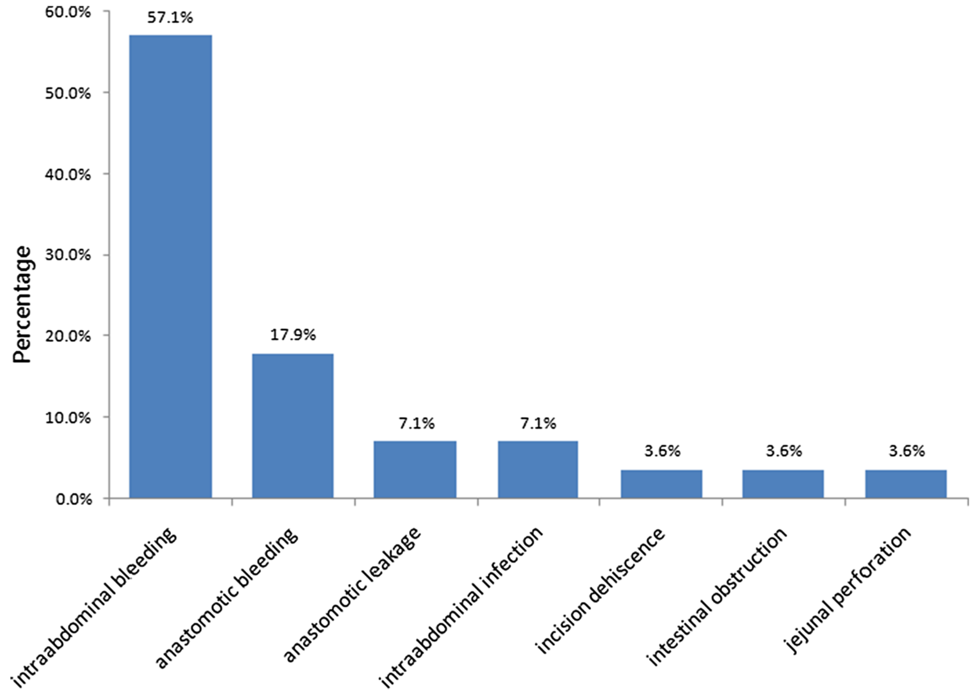

Fig. 1 Cause and proportion for URO

by two hypothetical individuals. Patient A is a 60-year-old female with a BMI of 23 kg/m^2, whereas Patient B is a 75-year-old male with a BMI of 26 kg/m^2. Our model predicted that Patient A has a 0.2% chance of URO, whereas Patient B has a 5.0% chance of URO. The risk of URO for Patient B was predicted to be 25-fold greater than that of Patient A.

Correlations between URO rate and operative period

The 2608 patients were divided into nine operative period groups based on a cutoff of 300 in surgical cases. The URO rates in the operative period groups were 0.3% (1/300), 0.7% (2/300), 1.3% (4/300), 1.3% (4/300), 1.3% (4/300), 1.7% (5/300), 1.3% (4/300), 1.0% (3/300), and 0.5% (1/208) (Table 7). No correlation between the URO rate and operative period was observed based on the Spearman rank correlation analysis ($r=0.012$, $p=0.548$).

Discussion

In recent years, with the great advance in laparoscopic techniques and the continuous improvement in surgical instruments, the application of laparoscopic radical gastrectomy for the treatment of GC has made encouraging curative progress in patients with cancer from early lesions to advanced stages [2–5]. However, the safety of the laparoscopic surgery remains the main focus of surgeons' concern. Clinically, URO usually aims to manage some severe or life-threatening postoperative complications, and the URO rate has attracted more attention from surgeons and become widely recognized as an important evaluation index of the medical quality [8, 9]. Sah [11] et al. reported the URO rate after open gastrectomy (OG) for GC was 2.2%, and the leading causes for URO were intraabdominal bleeding and anastomotic leakage. In Kim's laparoscopic surgery [22], the URO rate after LAG was reportedly 1.6%, with intraabdominal bleeding, duodenal stump, and intestinal obstruction being the major causes for URO. In the current study, the results showed that the URO rate was 1.1%, and intraabdominal bleeding and anastomotic bleeding were the main causes of URO. Compared to the Non-URO group, a significantly prolonged hospital stay, increased medical expenses, and higher morbidity and mortality rates were noted in the URO group, which is in line with Sah' study [11]. We believed the URO after GC surgery seriously affects patient's postoperative recovery, obviously increases patient's economic burden and even leads to early death in some patients. Therefore, it is very important for surgeons to assess the potential risk factors of URO before surgery, which might assist surgeons in preventing or reducing the incidence of URO.

Currently, the risk factors for URO after GC surgery reported in the literatures are not coincident [22–24]. In open surgery for GC, Yi [23] et al. reported that the URO rate was closely related to tumor size and type of operation. In Oh's study [24], the results revealed more males and an increased mean age in the URO group than in the Non-URO group, which is consistent with results of the

Table 3 Clinical courses from gastrectomy to treatment of URO

No	Gastrectomy	Reconstruction	Interval (d)	Cause	Treatment
1	LATG	Roux-en-Y	0.8	Esophagojejunal anastomosis bleeding	Suture
2	LATG	Roux-en-Y	0.9	Esophagojejunal anastomosis bleeding	Suture
3	LATG	Roux-en-Y	12.7	Transverse mesocolon vascular bleeding	Suture
4	LADG	B-I	0.3	Wall of duodenum vascular bleeding	Suture
5	LADG	B-I	0.3	Wall of remnant stomach vascular bleeding	Suture
6	LATG	Roux-en-Y	9.7	Adhesive intestinal obstruction	Enterolysis plus intestine anastomosis
7	LATG	Roux-en-Y	3.9	Pancreatic vascular bleeding	Suture
8	LADG	B-I	0.6	Gastroduodenal anastomosis bleeding	Suture
9	LATG	Roux-en-Y	3.1	Intraabdominal bleeding (unexplained)	Exploratory
10	LADG	B-II	2.3	Wall of remnant stomach vascular bleeding	Suture
11	LATG	Roux-en-Y	10.2	Intraabdominal bleeding (unexplained)	Exploratory
12	LATG	Roux-en-Y	0.2	Esophagojejunal anastomosis bleeding	Suture
13	LATG	Roux-en-Y	0.8	Esophagojejunal anastomosis bleeding	Suture
14	LADG	B-I	15.9	Gastroduodenal anastomosis leakage	Debridement
15	LATG	Roux-en-Y	0.8	Right gastric artery bleeding	Suture
16	LADG	B-I	0.5	Transverse mesocolon vascular bleeding	Suture
17	LADG	B-I	0.1	Transverse mesocolon vascular bleeding	Suture
18	LATG	Roux-en-Y	11.8	Jejunal perforation	Repair
19	LATG	Roux-en-Y	18.5	Intraabdominal infection	Splenectomy
20	LATG	Roux-en-Y	12.9	Intraabdominal infection	Debridement
21	LATG	Roux-en-Y	2.0	Splenocolic ligament vascular bleeding	Suture
22	LATG	Roux-en-Y	8.4	Intraabdominal bleeding (unexplained)	Exploratory
23	LADG	B-I	0.5	Pancreatic vascular bleeding	Suture
24	LATG	Roux-en-Y	10.9	Crura of diaphragm bleeding	Suture
25	LATG	Roux-en-Y	7.6	Esophagojejunal anastomosis leakage	Reanastomosis
26	LATG	Roux-en-Y	8.2	Splenic lobar artery bleeding	Splenectomy
27	LATG	Roux-en-Y	5.1	Left gastric artery bleeding	Suture
28	LADG	B- II	8	Abdominal incision dehiscence	Return and relaxation suture

current study. Elderly patients are generally more likely to have concurrent medical conditions like hypertension and cardiovascular diseases and have decreased functional reserves and poor wound healing. Males frequently tend to have more bad habits than females, such as smoking, overdrinking, or overeating. Therefore, elderly and male patients are more prone to postoperative bleeding, anastomotic leakage, and surgical site-related infection [16, 22, 25, 26], which would increase the incidence of URO accordingly. In LAG for GC, Kim [22] et al. suggested that comorbidities, type of reconstruction, and operation time affected the postoperative URO rate. However, some studies [6, 7] showed that comorbidities and type of reconstruction had no relation with the complications after LADG for GC. In the current study, we found that the concomitant diseases, diabetes, autoimmune

Table 4 Surgical outcome between URO group and Non-URO group

Parameters	Reoperation group (n = 28)	No-reoperation group (n = 2580)	p
Time to movement (d)[a]	2.29 ± 1.33	2.14 ± 0.94	0.418
Time to first flatus (d)[a]	3.38 ± 1.54	3.69 ± 1.28	0.210
Initiation of liquid (d)[a]	5.11 ± 1.93	4.98 ± 1.65	0.695
Initiation of semifluid (d)[a]	7.70 ± 1.56	7.84 ± 1.65	0.638
Hospital stay(d)	26.86 ± 14.26	13.03 ± 6.89	0.000
Total hospital fee (USD)	16082.43 ± 8567.59	9542.43 ± 2182.17	0.000
Morbidity rate[a]	11 (39.2)	374 (14.5)	0.001
Mortality rate[a]	1 (3.6)	5 (0.2)	0.063

[a]The parameters in reoperation group refer to data after the second operation

Table 5 Univariate analysis of potential influencing factors for URO

Parameters	Reoperation group ($n=28$)	No-reoperation group ($n=2580$)	p
Age (years)			0.023
≤70	18	2095	
>70	10	485	
Gender			0.027
Male	26	1924	
Female	2	656	
Concomitant diseases			0.829
No	20	1794	
Yes	8	786	
Diabetes			0.905
No	26	2332	
Yes	2	248	
Autoimmune disorders			1.000
No	28	2554	
Yes	0	26	
ASA score			0.328
≤2	26	2486	
>2	2	94	
Smoking History			0.730
No	21	1859	
Yes	7	721	
Malnourishment			1.000
No	27	2445	
Yes	1	135	
Neoadjuvant treatment			1.000
No	28	2509	
Yes	0	71	
BMI (kg/m^2)			0.021
≤25	19	2200	
>25	9	380	
Abdominal surgery			1.000
No	24	2205	
Yes	4	375	
Tumor size (cm)			0.379
≤5.0	17	1767	
>5.0	11	813	
Tumor location			0.766
Upper	9	661	
Middle	7	557	
Lower	9	1049	
≥2 areas	3	313	
Reconstruction type			0.568
Roux-en-Y	19	1392	
B-I	7	913	
B-II	2	215	
Esophagogastrostomy	0	60	
Surgical resection			0.182
Total	19	1392	
Subtotal	9	1188	
T stage			0.425
T1	6	625	
T2	2	310	
T3	12	747	
T4a	8	898	
N stage			0.707
N0	8	968	
N1	5	367	
N2	4	422	
N3	11	823	
TNM stage			0.384
I	7	755	
II	9	551	
III	12	1274	0.309
Operative time, min			
≤180	16	1710	
>180	12	870	
Blood loss(ml)			0.130
≤100	23	2370	
>100	5	210	
No. of resected LNs			
≤30	13	1063	0.576
>30	15	1517	

disorders, smoking history, preoperative malnourishment or not, neoadjuvant treatment or not, and reconstruction type were not associated with URO. In clinical practice, we suggested that the suitable application of anastomotic approach and technique, tension-free and well-vascularized anastomosis, proper inspection and precise hemostasis after anastomosis, and the procedure performed by experienced surgeons might effectively reduce the incidence of postoperative complications [27–29] and URO. Early anastomotic bleeding after surgery could be controlled by the use of conservative or endoscopic management in some patients [25, 30]. However, if conservative or endoscopic management did not work, the patient should be treated by emergent reoperation. Additionally, BMI > 25 kg/m2 was also an independent risk factor for URO in the current study. In patients with high BMI, more fat and connective tissues need to be separated, which results in higher operating difficulty, longer operation time, and increased blood loss [6, 31, 32]. Moreover, high BMI patients are susceptible to some comorbidities like hypertension, diabetes, and heart disease [33]. Therefore, the surgery-related complications, including postoperative bleeding, anastomotic leakage, and intraabdominal infection, occurred more frequently in patients with

Table 6 Multivariate logistic regression analysis of risk factors for URO

Variables	Multivariate analysis[a]			Bootstrap analysis[b]		
	OR	95% CI	*p*	OR	95% CI[c]	*p*
Age (>70)	2.287	1.046–4.998	0.038	2.232	1.023–4.491	0.028
Gender (male)	4.214	0.996–17.831	0.051	32.983	$1.405–25.343 \times 10^6$	0.027
BMI (>25 Kg/m^2)	2.652	1.188–5.920	0.017	2.550	1.017–5.398	0.012

[a]Multivariate analysis using binary logistic regression method

[b]Multivariate analysis using bootstrap method with the bootstrap results based on 1000 bootstrap samples

[c]95% bootstrap confidence interval (CI) was calculated using BCa method

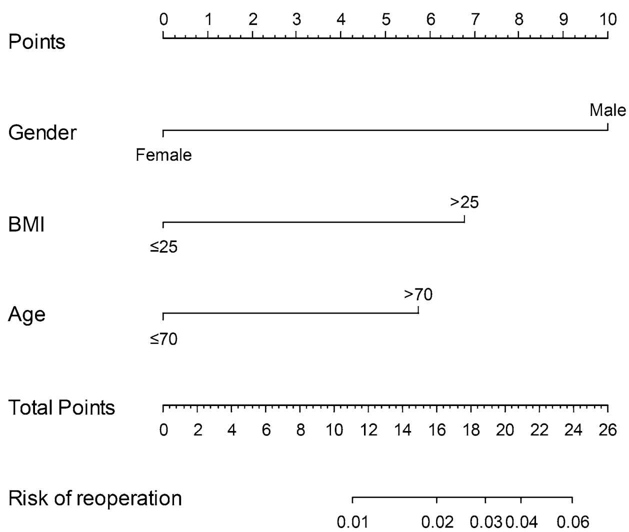

Fig. 2 Nomogram for URO after LAG

high BMI [31, 32, 34, 35], which might result in a corresponding increase incidence of URO. Based on three independent risk factors, including age, gender, and BMI, we constructed a simple and practical nomogram to predict the risk of occurrence of URO for GC patients undergoing LAG. The nomogram model could help surgeons to distinguish between low-risk and high-risk patients with a discrimination concordance index of 0.685. The three parameters needed for our model are easily available after patient's admission to hospital. Therefore, it is easy for surgeons to obtain a total risk score for the patient and preliminarily estimate the incidence of URO in individual patient before surgery. Based on this model, surgeons could identify subgroups of patients who are in need of a specific treatment strategy, and subsequently take corresponding preoperative and intraoperative intervention measures in order to reduce the rate of URO and improve the short-term outcomes in some patients.

To date, no final conclusion has yet been reached on whether surgeon's experience, which was represented as each individual surgeon's case sequence number, affects URO for GC patients undergoing LAG. In a previous study, Kim [31] et al. concluded that patients whose surgeons had performed fewer than 50 LAGs had a risk of URO 3.008-fold higher than that of patients with surgeons who had treated more than 50 cases. The authors believed that surgeons with limited experience in LAG should carefully choose their cases. In the current study, there were no patients requiring URO before the surgeon performed less than 50 LAGs. Based on a cutoff of 300 in surgical cases, we divided all the cases into nine operative periods. The result revealed that there was no correlation between the URO rate and operative period. Therefore, we suggested that surgeons should pay high attention to the independent risk factors for URO during different operative periods, even after the surgeons have gone through a learning curve. In addition, surgeons should take effective measures, including comprehensive evaluation and adequate preparation before the operation, standard performance and reliable hemostasis during the operation, and close observation and strict management after the operation, to reduce the incidence of URO and improve the safety of the operation.

However, our study has certain limitations. For example, despite the large case series in single-center retrospective analysis, the small number of patients with unplanned gastric reoperation (primary outcome) limits the statistical approach to modeling with logistic regression. The use of bootstrap analysis improves the deficiency and instability of the logistic regression to some extent. Moreover, it is different in the definition of obesity in the East and the West and the nomogram lacks external validation. Therefore, the predictive effect of

Table 7 Relation between URO rate and operative period

Period	First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth
Cases	0–300	301–600	601–900	901–1200	1201–1500	1501–1800	1801–2100	2101–2400	2401–2608
URO case	1	2	4	4	4	5	4	3	1
URO rate (%)	0.3	0.7	1.3	1.3	1.3	1.7	1.3	1.0	0.5

the model in different populations, such as Eastern and Western, requires prospective, multicenter, large sample studies to further validate.

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Compliance with ethical standards

Disclosures Drs. Ping Li, Chang-Ming Huang, Ru-Hong Tu, Jian-Xian Lin, Jun Lu, Chao-Hui Zheng, Jian-Wei Xie, Jia-Bin Wang, Qi-Yue Chen, Long–Long Cao, and Mi Lin have no conflicts of interest or financial ties to disclose.

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