

Early outcome after emergency gastrectomy for complicated peptic ulcer disease

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Objective To analyse outcomes of patients who underwent emergency gastrectomy for complicated peptic ulcer disease.

Design Prognostic study on a historical cohort.

Setting A regional hospital in Hong Kong.

Patients Patients who underwent emergency gastrectomy from 2000 to 2009 in our hospital.

Main outcome measures Primary outcome measures were in-hospital mortality and the predictors of such deaths. Secondary outcome measures were 7-day mortality, 30-day mortality, and morbidities.

Results In all, 112 patients had emergency gastrectomies performed for complicated peptic ulcer disease during the study period. In-hospital mortality was 30%. In the univariate analysis, old age, duodenal ulcer, failed primary surgery, gastrojejunostomy anastomosis for reconstruction, hand-sewn technique for duodenal stump closure, use of a sump drain, low haemoglobin level, preoperative blood transfusion, prolonged prothrombin time, and high creatinine or bilirubin levels were associated with an increased risk of in-hospital mortality. In the multivariate analysis, failed primary surgery, old age, and high creatinine level turned out to be independent risk factors.

Conclusions Emergency gastrectomy should be considered seriously as the primary treatment option in appropriately selected elderly patients, instead of salvage procedures to repair a perforation or control bleeding by plication.

New knowledge added by this study

- In patients who had emergency gastrectomies, complicated peptic ulcer disease, failed primary surgery, old age, and high creatinine levels are associated with mortality.

Implications for clinical practice or policy

- Instead of salvage procedures, emergency gastrectomy should be considered seriously as the primary treatment option in appropriately selected elderly patients.

Introduction

Emergency gastrectomy for complicated peptic ulcer disease (including bleeding, perforation, and obstruction) confers a high mortality rate of about 12 to 24%.¹⁻⁸ Since the advent of *Helicobacter pylori* eradication and endoscopic interventions for peptic ulcer disease, emergency gastrectomy is often regarded as salvage surgery after failure of primary interventions. Such surgery is often technically demanding. The purpose of this review was to analyse the outcome of patients who underwent emergency gastrectomy for complicated peptic ulcer disease in this era.

Factors associated with poor patient outcomes after emergency gastrectomy have been reported in the literature. They include advanced age, concurrent medical diseases, and high blood transfusion 'requirements'. However, debate still continues about other possible contributors, namely, the choice between definitive and non-definitive procedures, the method of duodenal stump closure, the use of decompressive duodenostomy, and the experience of surgeons.^{1,2,4,6,9-25} Thus, this review also set out to analyse these possible associated factors.

Methods

This was a single-institution, retrospective review of patients who underwent emergency

Key words

Duodenal ulcer; Emergencies;
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為患有相對複雜的胃潰瘍病人進行胃部切除術的早期結果

目的	分析為患有相對複雜的胃潰瘍病人進行胃部切除術後的治療結果。
設計	歷史性隊列的預後研究。
安排	香港一所分區醫院。
患者	2000至2009年期間在本院進行胃部切除術的病人。
主要結果測量	主要指標有院內死亡率及其預測因子。次要指標有七天死亡率、三十天死亡率和患病率。
結果	研究期間共112名患有相對複雜的胃潰瘍病人接受胃部切除術。院內死亡率為30%。單元回歸分析顯示以下因素均能增加院內死亡率的風險：年長的病人、十二指腸潰瘍、初次手術失敗、進行胃空腸吻合重建、因十二指腸殘端閉合術而進行人手縫製、使用深坑引流管、低血紅蛋白水平、術前輸血、凝血酶原時間延長、高肌酐水平及高膽紅素水平。多元回歸分析則顯示初次手術失敗、年長病人和高肌酐水平為獨立風險因素。
結論	應慎重考慮為經篩選的年長病人進行緊急胃部切除術來作為首個治療方法，而非作為一項二線的保留方法，這樣可以為病人修復穿孔或進行折疊術來控制出血的情況。

gastrectomy in Queen Elizabeth Hospital, Hong Kong, during the period from January 2000 to April 2009. The study design entailed a prognostic evaluation of a historical cohort. Queen Elizabeth Hospital is a tertiary referral centre in Kowloon. It is a major acute hospital with over 1800 beds and a staff of about 4800. Since its opening in 1963, it has provided a 24-hour accident and emergency service. It has a full complement of 16 medical specialties, and operates three specialist clinics and five general out-patient clinics.

All patients who underwent emergency gastrectomy for complicated benign peptic ulcer disease during the study period were included. Each patient's socio-demographic history, and clinical and laboratory information were retrieved from the hospital's computerised medical record system. We retrieved all the medical records with the procedure "emergency gastrectomy" entered in the system, and then reviewed them to exclude those with histopathological results showing presence of tumour. Primary outcome measures included in-hospital mortality and the predictors of such deaths. Secondary outcome measures included 7-day mortality, 30-day mortality, and morbidities (including the following medical complications: pneumonia, stroke, acute renal failure, sepsis, myocardial infarction and heart failure, surgical

leakage, anastomotic or intra-peritoneal bleeding, intra-abdominal abscess or collections, wound infection, and burst abdomen).

In this study, gastrectomy was defined as any form of gastric resection. Complicated benign peptic ulcer disease was defined as the presence of gastric or duodenal ulcer complicated by bleeding, perforation or obstruction, and with histopathological examination to exclude tumour. The definition of in-hospital mortality was death after gastrectomy within the same hospitalisation. The definition of 7-day mortality was death within 7 days of a gastrectomy. Similarly, the definition of 30-day mortality was death within 30 days after gastrectomy. Shock was defined as a persistent hypotension (systolic blood pressure <90 mm Hg, mean arterial pressure <60 mm Hg, or a reduction in systolic blood pressure >40 mm Hg from the baseline). Duration of symptoms was defined as the time interval between the onset of presenting symptoms (eg, abdominal pain in cases of perforation, presence of melena or per-rectal bleeding in cases of bleeding, repeated vomiting in cases of obstruction) and time of diagnosis of complicated peptic ulcer disease.

Statistical analysis

For continuous variables, group means were compared using the unpaired Student's *t* test. Categorical variables were compared using Pearson's Chi squared or Fisher's exact probability tests. For binomial data, 95% confidence intervals and odds ratios were also calculated. Significant variables identified by univariate analysis were further analysed by logistic regression using the forward stepwise (likelihood ratio) method. Any P value of <0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US).

Results

During the 9-year study period, 208 patients underwent emergency gastrectomy in Queen Elizabeth Hospital, of which 112 were for complicated peptic ulcer disease. The remaining 96 patients had the operations for gastric or duodenal tumour complications (including perforation, bleeding, and obstruction), and were therefore excluded from our study.

The mean and median ages of the study patients were 68 and 70 years, respectively (range, 37-94 years), and the male-to-female ratio was 89:23. Among the 112 patients included in our study, 110 had Polya gastrectomies, 1 had a total gastrectomy, and 1 had a partial gastrectomy; 67 (60%) and 45 (40%) had complications from duodenal and gastric

ulcers, respectively. The most common site for a complicated peptic ulcer was the anterior wall of first part of duodenum (22 patients, 20%), followed by the incisura of the stomach (19 patients, 17%), and co-existing anterior and posterior (“kissing”) ulcers at the duodenum (18 patients, 16%). The diameters of the perforations ranged from 1 to 5 cm. The median size of these benign ulcers was 2 cm. The most common indication was perforation (61 patients, 54%), followed by uncontrolled bleeding (49 patients, 44%) and obstruction (2 patients, 2%). For bleeding, the most common indication for gastrectomy was rebleeding after initial endoscopic haemostasis (25 patients, 22%), followed by uncontrolled bleeding during endoscopy (19 patients, 17%), failure to plicate the ulcer (3 patients, 3%), and development of shock during endoscopy (1 patient, 1%). Gastrectomy was performed in 13 patients as salvage surgery for failed primary surgery, seven of whom died during the same hospitalisation. Gastrojejunostomy anastomoses were performed by hand-sewing in 110 (98%) of the patients and by stapling in two (2%). Duodenal stump closure was performed by hand-sewing in 67 (60%) of the patients and by stapling in 45 (40%). The median duration of these operations was 217 (range, 125-325) minutes. The mean hospital stay was 25 (range, 5-140) days. Regarding experience of the surgeons, 71 (63%) emergency gastrectomies were performed by resident specialists or resident trainees, while 41

(37%) were performed by consultants. There was no association between the experience of the surgeons and postoperative mortality or morbidity (P=0.507).

The respective values for 7-day mortality, 30-day mortality, and in-hospital mortality were 10%, 23%, and 30%. Medical complications occurred in 21% of the patients; pneumonia was the most common and accounted for 19 (17%) of them. Other medical complications included stroke, acute renal failure, sepsis, myocardial infarction, and heart failure. Surgical complications occurred in 22% of the patients; leakage was the most frequent of these (16 patients, 14%) and most commonly at the duodenal stump (9 patients, 8%). In all, 20 (18%) of the patients underwent re-operation, 16 for leakage, 2 for burst abdomen, 1 for intra-abdominal abscess, and 1 for bleeding at a valve requiring gastrotomy and plication of a bleeder. Other surgical complications included wound infection, intra-abdominal collections, anastomotic and intra-peritoneal bleeding.

According to the univariate analysis, old age, duodenal ulcer, failed primary surgery, gastrojejunostomy anastomosis (“Omega sling”) for reconstruction, hand-sewn technique for duodenal stump closure, use of a sump drain, low haemoglobin level, preoperative blood transfusion, prolonged prothrombin time, high creatinine level, and high bilirubin level were associated with an increased risk of in-hospital mortality (Tables 1 and 2). In the

TABLE 1. Univariate analysis of putative predictors (continuous variables)

Predictor	Mean (SD)* of survivors	Mean (SD) of those who were dead	P value
Age (years)	65.8 (13.1)	73.3 (10.4)	0.004
Duration of symptoms (hours)	47.5 (44.1)	59.8 (66.1)	0.126
Preoperative blood transfusion (units)	3.2 (5.1)	6.2 (5.9)	0.008
Intra-operative blood transfusion (units)	1.4 (1.6)	1.7 (1.6)	0.284
Total blood transfusion (units)	5.3 (6.3)	12.3 (12.6)	0.001
Intra-operative blood loss (mL)	641.4 (561.2)	820.6 (756.2)	0.167
Duration of operation (mins)	211.7 (50.5)	229.4 (47.0)	0.084
Size of perforation (cm)	1.4 (1.4)	1.3 (1.2)	0.380
Lowest haemoglobin level (g/L)	86.5 (27.6)	71.8 (19.9)	0.006
Haemoglobin level on admission (g/L)	106.9 (34.8)	106.5 (30.5)	0.948
Preoperative haemoglobin level (g/L)	105.4 (30.2)	95.3 (29.8)	0.106
White cell count on admission (x 10 ⁹ /L)	12.4 (4.9)	13.6 (5.2)	0.242
Platelet count on admission (x 10 ⁹ /L)	282.8 (149.0)	232.2 (115.7)	0.085
Creatinine level on admission (µmol/L)	123.3 (65.1)	214.3 (120.7)	0.001
Albumin level on admission (g/L)	29.9 (8.1)	24.2 (7.7)	0.739
Prothrombin ratio	1.2 (0.2)	1.4 (0.3)	0.011
Bilirubin level on admission (µmol/L)	12.7 (11.4)	22.8 (32.1)	0.005
Duration from admission to gastrectomy (days)	3.2 (5.7)	3.9 (6.6)	0.574
Duration from gastrectomy to discharge (days)	20.9 (18.8)	21.3 (22.6)	0.930

* SD denotes standard deviation

TABLE 2. Univariate analysis of the predictors (categorical variables)

Predictor	Survival	In-hospital death	P value	Odds ratio	95% Confidence interval
Sex			0.605	0.774 (female=1)	0.293-2.046
Female	15	8			
Male	63	26			
Pathology			0.010	3.352 (gastric ulcer=1)	1.302-8.629
Gastric ulcer	37	8			
Duodenal ulcer	41	26			
Co-morbidities			0.068	-	-
Good past health	35	5			
1 Co-morbidity	21	13			
>1 Co-morbidities	22	16			
History of previous laparotomy			0.975	1.019 (no=1)	0.327-3.170
No	65	29			
Yes	12	6			
Fever on admission			0.574	0.629 (no=1)	0.123-3.207
No	66	31			
Yes	12	3			
Shock on admission			0.070	2.254 (no=1)	0.925-5.489
No	58	22			
Yes	18	14			
Indication for operation			0.459	-	-
Bleeding	34	15			
Perforation	42	19			
Obstruction	2	0			
Gastrectomy as a salvage operation			0.046	3.111 (no=1)	1.959-4.940
No	72	27			
Yes	6	7			
Type of operation			0.255	-	-
Polya gastrectomy	77	33			
Total gastrectomy	1	0			
Partial gastrectomy	0	1			
Rank of surgeon			0.507	1.322 (resident=1)	0.578-3.023
Resident level	51	20			
Consultant level	27	14			
Site of ulcer*			0.289	-	-
Body of stomach	4	0			
Antrum of stomach	10	3			
Pylorus of stomach	3	2			
Incisura of stomach	16	2			
Lesser curve of stomach	2	2			
D1	22	17			
Junction between D1 and D2	4	3			
Kissing ulcers at duodenum	14	4			
Degree of soiling			0.652	-	-
No soiling	33	13			
Soiling present	17	6			
Heavy soiling	27	15			

* D1 denotes first part of duodenum, and D2 second part of duodenum

TABLE 2. (Cont'd)

Predictor	Survival	In-hospital death	P value	Odds ratio	95% Confidence interval
Stump closure			0.036	2.625 (staple=1)	1.046-6.586
Staple	36	9			
Hand-sewn	41	26			
Type of anastomosis			0.025	1.523 (Roux-en-Y=1)	1.321- 1.756
Roux-en-Y	11	0			
Gastrojejunostomy	66	35			
Duodenostomy			0.233	2.367 (absent=1)	0.555-10.091
Absent	73	31			
Present	4	4			
Use of a sump drain			0.018	6.293 (no=1)	1.155-34.287
No	73	29			
Yes	2	5			
Admitting specialty			0.130	2.009 (surgical=1)	0.806-5.005
Surgical	63	23			
Medical	15	11			
Presence of <i>Helicobacter pylori</i>			0.432	0.710 (no=1)	0.301-1.673
No	44	22			
Yes	31	11			
Leaking site			0.136	-	-
No	66	27			
Gastrojejunostomy	0	1			
Duodenum	3	6			
Others	2	2			
Gastrojejunostomy and duodenum	0	2			

multivariate analysis, failed primary surgery, old age, and high creatinine level were independent risk factors (Table 3).

Discussion

The first gastric resection was performed by Theodor Billroth in 1881 for an antral carcinoma.²⁶ In the same year, Rydiger performed a partial gastrectomy for a patient with a gastric ulcer.²⁷ Nowadays, the operative mortality for elective gastrectomy has decreased to less than 5%.^{1,28} In this era of advanced medical therapy, after the discovery of *H pylori*'s role in the pathogenesis of peptic ulcer and endoscopic intervention for peptic ulcers, the numbers of elective gastric resections performed by general surgeons have declined dramatically.²⁹⁻³¹ Surgical demand is still high, however, as complications of peptic ulcer disease (including perforation, bleeding, and obstruction) have remained fairly constant^{29,32,33} or increased.^{30,31} Emergency gastrectomy for complicated peptic ulcer disease is now often regarded as salvage surgery,³⁴ or is reserved for giant ulcers when it is not safe to attempt simple closure

alone.^{1,2} However, such surgery is often technically challenging due to the friability of tissues, and is also associated with significant risks of mortality and morbidity.

In the series of over 3000 patients with bleeding peptic ulcers reported by Lau et al,³ salvage surgery carried a 30-day mortality rate of around 18%. In the series by So et al⁴ of 82 patients who underwent emergency gastrectomy for complicated peptic and gastric cancer diseases, the overall 30-day mortality rate was about 17%. Lanng et al⁵ reported a mortality risk of 24% in 41 patients with perforated benign gastric ulcers who underwent gastrectomy. In the series by Hodnett et al,² the overall mortality rate

TABLE 3. Multivariate analysis by logistic regression with forward stepwise (likelihood ratio) method

Predictor	P value	Exp (B)	95% Confidence interval
Age	0.014	1.206	1.039-1.400
Gastrectomy as a salvage operation	0.042	1.136	1.014-1.273
Creatinine level	0.015	1.030	1.006-1.054

for emergency gastrectomy was 12%. Other series reported that emergency gastrectomies for bleeding peptic ulcers carried a mortality risk of 12 to 23%.^{1,6-8} In our series, the mortality of emergency gastrectomy was higher than that of other series. The 7-day, 30-day, and in-hospital mortality rates were: 10%, 23% and 30%, respectively. A possible explanation was that these operations were for protracted and scarred ulcers that were not amendable to simple closure for perforation or plication for bleeding. By contrast, past series were gastrectomies performed as definitive surgery in the era of less-potent anti-ulcer medications. Another reason was the long duration from admission to gastrectomy, which was on average 3 days (in both groups). This was because 37 (33%) of the gastrectomies were performed as salvage surgery for failed primary treatment in cases of perforation (12 patients, 12%) or rebleeding after initial endoscopic haemostasis (25 patients, 22%). This is in contrast to the series by So et al⁴ in which the majority of patients (67%) had their emergency gastrectomies within 24 hours of admission.

There were numerous studies that assessed the association of clinical predictors of mortality in patients with perforated peptic ulcers. However, a large series of emergency gastrectomies assessing this association in recent years is lacking. We therefore undertook this analysis of outcomes in patients who underwent emergency gastrectomy for complicated peptic ulcer disease, to determine what factors predict operative mortality.

This series has identified old age to be one of the independent predictors of high mortality from emergency gastrectomy, which is consistent with the literature. So et al⁴ also reported that age of >65 years was associated with poor outcomes after emergency gastrectomy. Moreover, evidence in the literature suggests that early surgery is preferable, especially in the elderly.⁹ Kum et al¹⁰ reported that for perforated peptic ulcers, elderly as opposed to young patients had a much higher risk when undergoing gastrectomy. A study by Hewitt et al¹¹ also found that mortality and morbidity rates of gastric resection for perforated peptic ulcers were significantly increased in elderly patients. In a study by Branicki et al,¹² an age of >60 years was related to poor outcomes after emergency operations for bleeding peptic ulcers; such findings also concurred with other studies.¹³⁻¹⁷ Kocer et al¹⁸ also reported older age to be an independent predictor of mortality.

A high creatinine level was another independent predictor identified in this study, whereas a high bilirubin level was a significant predictor according to the univariate analysis only. In our study, co-morbidities were not found to be associated with mortality, which was not consistent with the results of previous studies. In patients with perforated

peptic ulcers, Boey et al^{6,19} identified a poor prognosis associated with the presence of medical diseases, preoperative shock, and perforation for more than 24 hours. These three independent risk factors constitute the Boey scoring system. None of them were identified as significant in our study, however. In a prospective cohort study by Sharma et al,²⁰ presence of concomitant medical illness was a clinical predictor of the risk and number of postoperative complications in patients with perforated peptic ulcer. This lack of concordance with previous reports may be a limitation of our study, whereas our results suggest that renal impairment and deranged liver function are more important prognostic indicators than other co-morbidities.

Failed primary surgery is also an independent predictor. In our study, gastrectomy was performed in 13 patients as a salvage surgery due to failed primary surgery. Among them, seven (54%) died after the procedure within the same hospitalisation. The in-hospital mortality of salvage gastrectomy is high. This is in agreement with some previous studies, in which the authors suggested that definitive surgery (vagotomy and antrectomy, vagotomy and pyloroplasty, or subtotal gastrectomy and gastroenterostomy) could decrease the recurrence rate without increasing operative mortality and morbidity.^{2,6,21} Some studies, however, showed no difference in mortality between the non-definitive (simple closure with postoperative medical treatment) and definitive procedures.^{1,14,16,22,23} As mentioned previously, Kocer et al¹⁸ even reported definitive surgery as an independent predictor of mortality. Moreover, the choice of surgical procedure in an emergency is still debated.

High preoperative blood transfusion requirement was a significant predictor identified in the univariate analysis. Patients who survived only received 3 units of blood transfusion on average, whereas those who succumbed received an average of 6 units. This finding also concurs with the literature. In a study by Branicki et al,¹² blood transfusions of more than 5 units were related to poor outcomes after emergency operations for bleeding peptic ulcer. In Sharma et al's study,²⁰ the risk of developing postoperative complications was significantly influenced by receipt of blood transfusions. In So et al's study,⁴ low haemoglobin level was an independent predictor of complications after emergency gastrectomy. In Lau et al's study³ of patients having definitive surgery for rebleeding after initial endoscopic haemostasis, a median of 5 units of blood was transfused, suggesting significant haemorrhage associated with the procedure. According to current practice in our institution, if anticipated blood transfusion requirements exceed 5 units, early definitive surgery would be recommended.

Although retrospective, the results of our study are clear and show that old age, high creatinine level, and failed primary surgery are independent predictors of in-hospital mortality after emergency gastrectomy for complicated benign peptic ulcer disease. We therefore propose that gastrectomy be considered early and seriously as the primary treatment option in elderly patients with renal impairment and deranged liver function, especially when significant preoperative blood transfusion requirements are anticipated. Such patients may also need more intensive postoperative management.

Regarding limitations of this study, data retrieval and review were performed without blinding as to the vital status of the patients, which could well have biased the analysis. Furthermore, many of the 95% confidence intervals shown in Table 2 were wide, suggesting a lack of statistical power. External validity or generalisation may be limited in a single institution study, thus a high-quality systematic review is required to further validate the derived set of predictors.

Leakage is another issue worth noting, and was the most common surgical complication in our study. All corresponding patients had re-operations. The most common site for leakage was at the duodenal stump. The majority (67%) of patients with such a leak did not survive the operation, as many of them were already in a moribund state. Moreover, surgical closure of a duodenal stump inflamed or extensively scarred from chronic ulcer disease is often difficult and challenging. Resorting to hand-sewn Connell's stitches is particularly difficult when applying the last few stitches, and thus these few stitches should not be tightened before all stitches have been applied. In addition, for the stitches to be applied around the stump, the duodenal wall needs to be completely mobilised around the stump, particularly the medial wall. Usually, a plane between the healthy medial duodenal wall and a posterior wall ulcer over the pancreas needs to be dissected out with care, before the stump can be closed safely. However, the papilla must be identified by palpation through the stump to avoid damage. In cases where the ulcer is too close to the papilla, resorting to Nissen's closure is advisable. In our study, eight patients had duodenostomies, the majority (88%) of whom did not have leakage. Although not having a duodenostomy was not shown to be a predictor of mortality, it may still have a role in preventing leakage. Previous reports have stressed the value of duodenostomy to reduce the early postoperative intraluminal duodenal pressures, an important contributory factor of duodenal leaks.¹ However, duodenostomy can also delay closure of drainage tracts after removal of

duodenostomy catheters, and thus prolong hospital stays. Selective use of decompressive duodenostomy seems reasonable. We would emphasise that despite duodenostomy, it is prudent to close the stump as safely as possible, before resorting to another more distal decompressive duodenostomy in a more healthy part.

Some studies advocate that these operations should be managed by surgeons with a special interest in this area, as lack of surgical experience is a predictor of complications due to upper gastrointestinal surgery.^{24,25} We could not replicate this finding, however. The association between rank of the operating surgeons and patient outcome may nevertheless require further validation in larger studies.

Nowadays, omental patch repair, ulcer plication, ulcerectomy, and simple perforation closure are the usual primary treatment options for complicated peptic ulcers. Emergency gastrectomy for complicated peptic ulcer disease is often regarded as a salvage surgery, or is reserved for giant ulcers when it is not safe to carry out simple closure alone. We appreciate that emergency gastrectomy is associated with a significant risk of mortality and morbidity. However, our study found that failed primary surgery is an independent predictor for in-hospital mortality. For 13 patients in our study, gastrectomy was performed as a salvage surgery due to failed primary surgery, among whom seven (54%) of the patients died during the same hospital stay. Thus, in-hospital mortality of salvage gastrectomy is high.

Conclusions

Although there are limitations with any retrospective study, our study clearly showed that failed primary surgery, old age, and a high creatinine level were independent predictors of in-hospital mortality after emergency gastrectomy for complicated benign peptic ulcer disease. Therefore, we propose that gastrectomy should be considered early and seriously as the primary treatment option, especially in elderly patients with renal impairment, and not resorted to only as a salvage procedure for failure to repair a perforation or plicate bleeding. This patient group may also need a more intensive postoperative management. Safe duodenal stump closure seems prudent, as leak from this site is the commonest surgical complication warranting emergency gastrectomy. A high-quality systematic review and prognostic study is necessary to validate the set of predictors we derived as well as our recommendations.

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