

Definition and Classification of Complications of Gastrectomy for Gastric Cancer Based on the Accordion Severity Grading System

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Abstract

Background Postoperative complications still comprise the marker used most frequently to assess the quality of gastrectomy. However, the definition and grading of morbidity is not standardized, hampering meaningful comparisons over time and among centers. This study proposes specific definitions and a reproducible classification of complications following gastrectomy using standardized grading tools.

Methods We defined each complication based on the literature, and adopted the Accordion Severity Grading System to stratify morbidity. The classification was applied to 890 patients with gastric cancer seen between January 2010 and April 2011. The correlation between the complication grades and the length of hospital stay (LOS) was analyzed, and risk factors for complications were examined with special reference to severity grade.

Results The overall morbidity rate was 18.1 %. Mild complications occurred in 31 patients (3.5 %), moderate in 77 patients (8.7 %), severe—invasive procedure/no general anesthesia (GA) in 27 patients (3.0 %), severe—invasive procedures/GA in 18 patients (2.0 %), and severe—organ failure in 3 patients (0.3 %). Five patients (0.6 %) died postoperatively. The grade of complications had a significant effect on the LOS ($p < 0.001$). Operating time and cardiovascular and pulmonary co-morbidities were

independent risk factors for severe complications [odds ratio (OR) 1.001, $p = 0.016$; OR 2.226, $p = 0.006$; OR = 2.896, $p = 0.003$, respectively].

Conclusions The complications after gastrectomy could be classified into different severity grades that had distinct clinical outcomes. The use of this classification provides more reliable, practical outcome data. Consequently, complications should be reported using a standardized classification tool such as the Accordion Severity Grading System, which requires consensus on the definition of specific complications.

Introduction

Surgical outcomes such as the length of hospital stay, operative mortality, and even quality of life can be monitored and reported easily. They are defined parameters, or generally accepted specific measurement tools are available [1]. Although complications are typically reported, it is impossible to compare centers or differences over time because of the lack of standardized criteria to define and/or grade the many complications associated with surgical procedures [2, 3].

In 1992, Clavien et al. proposed general principles for classifying surgical complications based on a therapy-oriented, four-level severity classification (T92) [4]. 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 [5]. Recently, however, Strasberg et al. [6] analyzed 127 published surgical studies that used T92 or its modifications and found many inconsistencies in the application of T92 (e.g., nonuniform grade contraction). As a result, in 2009

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they introduced an extensive modification of T92, called the Accordion Severity Grading System. 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 (<http://www.accordionclassification.wustl.edu/>).

Despite the advances in surgical techniques and perioperative care over the last decade, the surgical morbidity for gastric cancer is still high, ranging from 10.5 % to 40.1 % [7–11]. It has remained an important concern for patients, health care providers, and those paying for services. However, there is no consensus on the definition of specific complications related to gastrectomy: We have found one published article [12] and two articles in press [11, 13] that apply the standardized classification system (Clavien-Dindo classification) for reporting complications. Therefore, the wide range in the reported morbidity rates might be partly caused by the lack of uniform definitions and a system for grading severity.

In 2010, we adopted the Accordion Severity Grading System for a large cohort of patients who underwent gastrectomy for gastric cancer and were entered in a comprehensive database. We also defined each complication based on the literature. The primary aim of this study was to classify the complications after gastrectomy based on predefined specific definitions with special reference to severity by the Accordion system. A secondary aim was to analyze risk factors for complications according to the severity grade.

Methods

Definition and classification of complications

With the basic concept of a “complication” being any deviation from the ideal postoperative course that is not inherent to the procedure and does not comprise a failure to cure [2], the minimum criteria for each complication were defined based on the literature. Clinically nonsignificant changes after surgery that were normalized without treatment within a short time were not regarded as complications. Each complication recorded was then ranked by severity according to the Accordion Severity Grading System (see Appendix Table 4).

Postoperative bleeding was defined as a decrease in hemoglobin of >1 g/dl within 1 day in a patient who had one or more of the following signs: blood loss through abdominal drains or nasogastric tube, hematemesis, or melena. The diagnosis of postoperative bleeding may be confirmed by upper gastrointestinal endoscopy, angiography, computed tomography (CT), or reoperation [14].

Anastomotic leak was diagnosed when the luminal contents were detected in a drain or at the wound site or a leak was detected on imaging studies [15]. *Anastomotic stenosis* was defined as signs and symptoms of obstruction (dysphagia, postprandial regurgitation, vomiting) with inability to pass the anastomotic site using a 9.2-mm diagnostic endoscope [16, 17].

Wound infection included the presence of serous to purulent fluid at the incision site requiring drainage or wound revision [18, 19]. *Intraabdominal infection* was defined as the presence of septic fluid in the abdominal cavity on CT causing systemic inflammatory response syndrome (SIRS) [18].

Postoperative pancreatic fistula (POPF) was mainly diagnosed by sinister-appearing (e.g., dark brown) drainage fluid with an amylase content exceeding three times the upper normal serum value and draining from the peripancreatic area. For patients without drains, the diagnosis of POPF was established if clinical and radiologic examinations showed evidence of peripancreatic infection, [20, 21]. *Postoperative pancreatitis* was defined using the new Japanese diagnostic criteria for acute pancreatitis. Patients who presented with two of the following three manifestations were diagnosed with pancreatitis: characteristic upper abdominal pain, elevated levels of pancreatic enzymes (serum lipase level three times greater than the upper normal limit), and imaging findings suggesting acute pancreatitis [22].

Gastric stasis (postsurgical gastroparesis) was defined as postprandial nausea, vomiting, and gastric atony in the absence of ileus, mechanical gastric outlet obstruction (stricture, stenosis), or adjacent inflammation (anastomotic leak, intraabdominal infection) [23]. *Postoperative ileus* (POI) was a temporary impairment of gastrointestinal motility following surgery (>72 h) without any precipitating complications (primary POI). It usually manifests as nausea, vomiting, abdominal pain, abdominal distension, and the delayed passage of flatus or stool [24, 25]. *Postoperative intestinal obstruction* was defined as mechanical obstruction with an air–fluid level and an obstructing point shown on imaging studies [18].

Chyle leak was diagnosed as the presence of milky fluid in a drain or on aspiration in excess of 200 ml/day, with a triglyceride level ≥ 110 mg/dl [26, 27]. *Postoperative ascites* (lymphorrhea) was defined as abdominal drainage exceeding 500 ml/day after 3rd postoperative day (POD3), the drainage not being bloody, and the amylase level normal. A diagnosis of ascites was also established if a patient complained of abdominal distension and needed diuretics or paracentesis to control it [28, 29].

The nonsurgical complications were grouped by organ system and were classified into six grades using the Accordion system based on the invasiveness of the therapy.

Data collection

This prospective observational study enrolled 890 consecutive patients undergoing gastrectomy for gastric cancer in our institution between January 2010 and April 2011. Every complication has been recorded in the cancer database in our institution since it was first adopted. Each complication was mentioned in the monthly morbidity and mortality conference, where all complicated cases were discussed in more detail. In this study, the time horizon for postoperative complications was 100 days after surgery. The postoperative in-hospital death and 100-day mortality rates were computed. We entered all complications that occurred in each patient, and a specific complication in each patient was entered at its highest level of severity. For patients in whom two or more complications developed serially, we recorded only the causative complication and the most severe grade when the other complications clearly occurred as consequence of the first, less severe complication.

Demographic data (age and sex), preoperative factors [co-morbidities, body mass index (BMI), serum hemoglobin and albumin levels], operation-related factors (type of operation, operating time, estimated blood loss), pathology data, and the clinical outcomes were also collected from the cancer database.

Statistical analyses

Means, standard deviations, and frequencies were used to describe the data. Correlations between the complication grades and length of hospital stay (LOS) were analyzed using one-way analysis of variance (ANOVA) with post hoc comparison (Games-Howell method; equal variances not assumed). Factors that might affect the postoperative complications were evaluated by univariate analysis using the two sample *t* test for continuous variables and the χ^2 test or Fisher's exact test for nominal variables. The independent contribution of various factors was assessed using multivariate binary logistic regression analysis. Risk factors with a univariate $p < 0.10$ were included in the multivariate analysis. The Statistical Package for the Social Sciences (version 17.0; SPSS, Chicago, IL, USA) was used for all analyses. The level of statistical significance was $p < 0.05$.

Results

Patient characteristics

The characteristics and operation data are outlined in Table 1. There were 606 men (68.1 %) and 284 women

(31.9 %), with a mean age of 61.5 ± 11.8 years. The mean BMI was 23.6 ± 3.2 kg/m². In total, 443 patients (49.8 %) had co-morbidities, and most of the patients had an American Society of Anesthesiologists (ASA) score of II (61.0 %). Preoperative anemia— <13 g/dl for men, <12 g/dl for women based on World Health Organization (WHO) criteria [30]—and hypoalbuminemia (<3.5 g/dl) were detected in 249 (28.0 %) and 35 (3.9 %) patients, respectively.

D2 lymphadenectomy was performed in 675 patients (75.8 %); 41 patients (4.6 %) underwent combined resection of adjacent involved organs. The mean operating time was 205.5 ± 72.2 min, and the estimated blood loss was 221.3 ± 215.3 ml. At pathology staging, 65.6 %, 13.6 %, 14.9 %, and 5.8 % of the patients were diagnosed as stages I, II, III, or IV, respectively.

Postoperative outcomes

The respective incidences of complications by diagnosis and severity are shown in Table 2. One or more complications occurred in 18.1 % of the patients. Mild complications occurred in 31 patients (3.5 %), moderate in 77 patients (8.7 %), severe—invasive procedure/no GA (general anesthesia) in 27 patients (3.0 %), severe—invasive procedures/GA in 18 patients (2.0 %), and severe—organ failure in three (0.3 %). Five (0.6 %) patients died postoperatively owing to sepsis with multiorgan failure (resulting from intraabdominal infection, anastomotic leak, remnant stomach necrosis, duodenal perforation, and aspiration pneumonia, respectively).

The most frequent surgical complication was bleeding (both luminal and abdominal, 4.2 %), followed by intraabdominal infection (2.5 %), duodenal stump leak (1.7 %), POPF (1.7 %), and anastomotic stenosis (1.3 %). Pneumonia was the most common nonsurgical complication (1.5 %). Moderate complications accounted for more than half of all complications (51.5 %). Complications of a severe grade requiring invasive procedures occurred in 58 patients (6.0 %) and constituted 28.4 % of all morbidity. The most common were bleeding (1.1 %) and duodenal stump leak (1.1 %), followed by anastomotic leak (0.7 %) and intraabdominal infection (0.7 %).

Validation of the accordion grading system

We examined the effect of the severity grades on the duration of hospitalization. For this analysis, the most severe complication was analyzed for patients with more than one complication. If a patient was readmitted with complications, the period of rehospitalization was added to the hospital stay.

The grade of complications was significantly related to the duration of hospital stay ($p < 0.001$) (Fig. 1). The mean length of hospitalization (LOS) in patients without complications was 8.1 ± 1.4 days. The LOS for patients with complications was 9.7 ± 2.4 days with mild complications only, 13.8 ± 5.8 days with moderate complications, 30.0 ± 25.2 days with severe—invasive procedure/no GA complications, 38.1 ± 31.2 days with severe—invasive procedure/GA, and 48.3 ± 21.1 days with severe—organ failure. The mean LOS for patients who died of a complication was 48.8 ± 46.5 days. There was a significant, progressive increase in the LOS from patients with no complications to those with severe grades ($p = 0.005$, $p < 0.001$, and $p < 0.001$, respectively). There was no significant prolongation of the LOS in patients with severe—invasive procedure/GA and severe—organ failure—compared with severe—invasive procedure/no GA complications ($p = 0.957$ and $p = 0.982$, respectively).

Risk factors for postoperative complications

We examined the preoperative and intraoperative risk factors associated with complications, with special reference to severity grade (Table 3). For all complications, male sex [$p = 0.016$, odds ratio (OR) 1.705, 95 % confidence interval (CI) 1.103–2.634], a higher ASA score ($p = 0.016$, OR 1.853, 95 % CI 1.201–2.858), preoperative hypoalbuminemia ($p = 0.003$, OR 3.124, 95 % CI 1.462–6.678), liver cirrhosis ($p < 0.001$, OR 4.597, 95 % CI 2.016–10.483), total gastrectomy ($p = 0.023$, OR 1.651, 95 % CI 1.072–2.541), and longer operating time ($p = 0.008$, OR 1.004, 95 % CI 1.001–1.006) were significant risk factors in the multivariate logistic regression.

Of those factors, only the operating time was found to be an independent risk factor for severe complications ($p = 0.016$, OR 1.004, 95 % CI 1.001–1.008). In addition, cardiovascular co-morbidity ($p = 0.006$, OR 2.226, 95 % CI 1.258–3.938) and pulmonary comorbidity ($p = 0.003$, OR 2.896, 95 % CI 1.424–5.890) were significant predictors of severe complications, although they were not significant for overall complications.

Discussion

The definition of surgical complications is a challenging task. Many surgeons would argue that the surgeon's intuition is an appropriate guide for defining a complication. However, the surgeon's intuition is unreliable in many situations because it lacks objective criteria and is strongly dependent on the experience of the individual clinician [31]. Dindo and Clavien [2] defined a complication as “any deviation from the ideal postoperative course that is not

Table 1 Characteristics of 890 patients who underwent gastrectomy for gastric cancer

| Demographics | Data |
|---|---------------|
| Age (years) | 61.5 ± 11.8 |
| Sex | |
| Male | 606 (68.1 %) |
| Female | 284 (31.9 %) |
| BMI (kg/m ²) | 23.6 ± 3.2 |
| ASA score | |
| 1 | 306 (34.4 %) |
| 2 | 543 (61.0 %) |
| 3 | 41 (4.6 %) |
| Preoperative anemia ^a | 249 (28.0 %) |
| Preoperative hypoalbuminemia ^b | 35 (3.9 %) |
| Co-morbidity | 443 (49.8 %) |
| Cardiovascular | 312 (35.1 %) |
| Diabetes mellitus | 153 (17.2 %) |
| Pulmonary | 88 (9.9 %) |
| Cerebrovascular | 23 (2.6 %) |
| Liver cirrhosis | 28 (3.1 %) |
| Renal failure | 12 (1.3 %) |
| Type of approach | |
| Open | 418 (47.0 %) |
| Laparoscopic | 472 (53.0 %) |
| Extent of resection | |
| Distal | 691 (77.6 %) |
| Total | 199 (22.4 %) |
| Combined resection | 41 (4.6 %) |
| Lymph node dissection ^c | |
| D1, D1+ | 215 (24.2 %) |
| D2, D2+ | 675 (75.8 %) |
| Operating time (min) | 205.5 ± 72.2 |
| Estimated blood loss (ml) | 221.3 ± 215.3 |
| TNM stage, AJCC 7th edition | |
| I | 584 (65.6 %) |
| II | 121 (13.6 %) |
| III | 133 (14.9 %) |
| IV | 52 (5.8 %) |

Results are given as the mean ± SD or the number

BMI: body mass index; ASA: American Society of Anesthesiologist; AJCC: American Joint Committee on Cancer

^a Preoperative anemia was defined according to World Health Organization (WHO) criteria [30]

^b Preoperative hypoalbuminemia was defined as the serum albumin level < 3.5 g/dl based on the normal cutoff value of our institution

^c Lymph node dissection was classified by Japanese gastric cancer treatment guidelines 2010 (version 3) [34]

inherent in the procedure and does not comprise a failure to cure.” This criterion might also permit clinician subjectivity to define the ideal postoperative course and deviation.

Table 2 Incidence of postoperative complications following gastrectomy, by diagnosis and severity

| Accordion severity grade [6] | Mild | Moderate | Severe: invasive procedure/no GA | Severe: invasive procedure/GA | Severe: organ failure | Death | Total (n = 890) |
|--|-------|----------------|----------------------------------|-------------------------------|-----------------------|----------------|-------------------------|
| Surgical complications (163 cases/144 patients) (16.2 %) | | | | | | | |
| Wound infection | 3 | 3 | 2 | – | – | – | 8 (0.9 %) |
| POPF | 3 | 11 | 1 | – | – | – | 15 (1.7 %) |
| Intraabdominal infection | – | 16 | 5 | – | – | 1 | 22 (2.5 %) |
| Duodenal stump leak | – | 4 | 2 | 5 | – | – | 11 (1.7 %) ^a |
| Anastomotic leak | – | 2 | 4 | 2 | – | – | 9 (0.9 %) |
| Anastomotic site stenosis | 4 | 3 | 5 | – | – | – | 12 (1.3 %) |
| Remnant stomach necrosis | – | – | – | 1 | 1 | 1 | 3 (0.4 %) ^b |
| Gastric stasis | 2 | 6 | – | – | – | – | 8 (1.2 %) ^b |
| Postoperative ileus | 4 | 5 | – | – | – | – | 9 (1.0 %) |
| Postoperative intestinal obstruction ^c | 2 | 2 | – | 5 | – | – | 9 (1.0 %) |
| Luminal bleeding | 6 | 14 | 7 | – | – | – | 27 (3.0 %) |
| Abdominal bleeding | 2 | 6 | 1 | 1 | 1 | – | 11 (1.2 %) |
| Ascites | 7 | 4 | – | – | – | – | 11 (1.2 %) |
| Chyle leak | – | 1 | 1 | 1 | – | – | 3 (0.3 %) |
| Others | – | – | – | 3 ^d | 1 ^e | 2 ^f | |
| No. of cases in each grade | 33 | 77 | 28 | 18 | 3 | 4 | |
| % in surgical Cx | 20.3 | 47.2 | 17.2 | 11.0 | 1.8 | 2.5 | |
| Nonsurgical complications (31 cases/31 patients) (3.5 %) | | | | | | | |
| Respiratory | | | | | | | 16 (1.8 %) |
| Pleural effusion | – | 3 | – | – | – | – | 3 |
| Pneumonia | – | 11 | 1 | – | – | 1 | 13 |
| Renal | | | | | | | 5 (0.6 %) |
| Transient elevated Cr | 4 | – | – | – | – | – | 4 |
| Urinary tract infection | – | 1 | – | – | – | – | 1 |
| Cerebrovascular | | | | | | | 3 (0.3 %) |
| TIA | – | 1 | – | – | – | – | 1 |
| Delerium | 2 | – | – | – | – | – | 2 |
| Others | – | 5 ^g | – | – | – | – | |
| No. of cases in each grade | 6 | 23 | 1 | 0 | 0 | 1 | |
| % in non-surgical Cx. | 19.4 | 74.2 | 3.2 | 0 | 0 | 3.2 | |
| No. of cases/no. of patients | 39/31 | 100/77 | 29/27 | 18/18 | 3/3 | 5/5 | 194/161 |
| % in total patients | 3.5 | 8.7 | 3.0 | 2.0 | 0.3 | 0.6 | 18.1 % |
| % in total Cx | 20.1 | 51.5 | 15.0 | 9.3 | 1.5 | 2.6 | – |

GA general anesthesia, POPF postoperative pancreatic fistula, Cx complication, Cr creatinine, TIA transient ischemic attack

^a The incidence was calculated for a total of 631 patients who underwent gastrectomy with the formation of duodenal stump

^b This rate was estimated for 691 patients who had a distal gastrectomy

^c Four cases of internal herniation and one case of herniation into a trocar site

^d One patient complained of dysphagia after total gastrectomy, which led to repeated aspiration pneumonia; he underwent feeding jejunostomy. Two patients with injury to the gallbladder and transverse colon anastomotic leak, respectively, were also treated surgically

^e Necrotizing pancreatitis occurred in one patient, who developed multiorgan failure

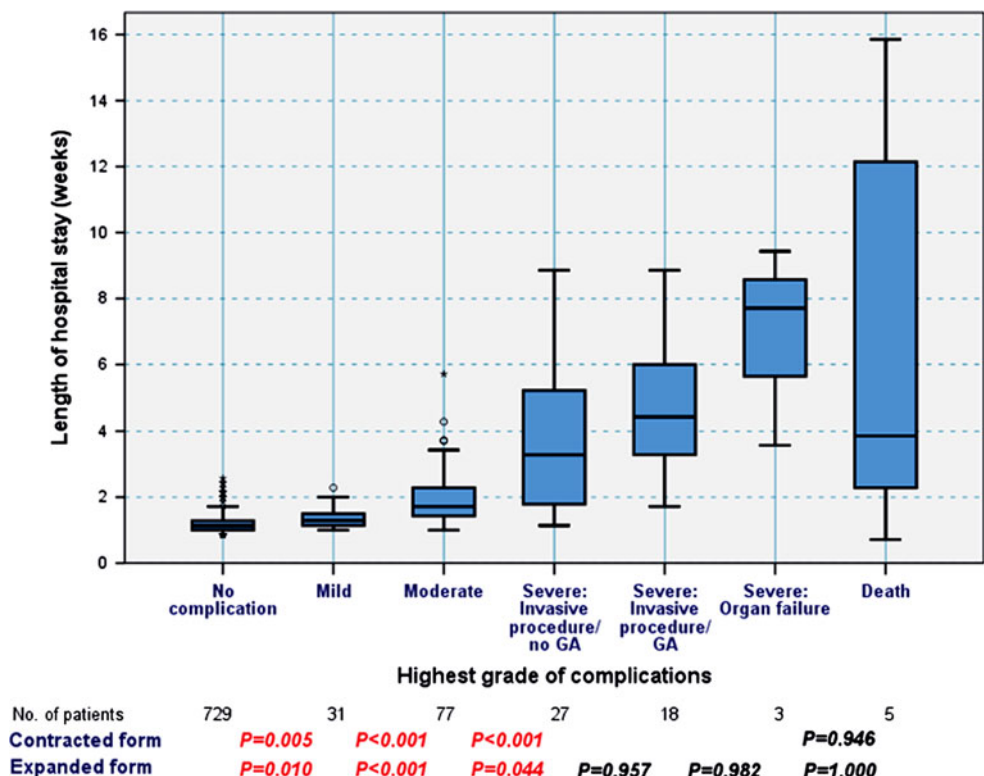
^f Two patients died because of duodenal perforation and nonocclusive mesenteric ischemia, respectively

^g Hepatic encephalopathy developed in two patients with liver cirrhosis. A patient with aplastic anemia developed neutropenic fever postoperatively. Deep vein thrombosis and phlebitis occurred in one patient each

To reduce this bias, it is first necessary to determine what constitutes a complication. We excluded clinically nonsignificant changes after surgery; that is, the patient's

condition normalized without treatment within a short time. This includes fever that developed just after the operation, transient postoperative abnormalities in

Fig. 1 Length of hospital stay (LOS) according to grade of severity of complications. Boxes represent the interquartile ranges, and the lines within the box show the median values. The whiskers represent the extreme values. There was a significant progressive increase in the LOS from patients with no complications to those with severe grades ($p < 0.001$, one-way analysis of variance with post hoc comparison using Games-Howell method). GA: general anesthesia



laboratory results, and asymptomatic atelectasis or a small pleural effusion that was identified only through imaging studies, and others. Then, we devised specific criteria for common complications after gastrectomy based on the literature. Although the definitions of many complications are held to be common knowledge, some specific complications remain controversial.

For example, the International Study Group on Pancreatic Fistula (ISGPF) defined POPF as drainage output of any measurable volume of fluid on or after POD 3, with an amylase content exceeding three times the upper normal serum value [20]. Unlike with pancreatic surgery, the likely source of amylase in drainage fluid after gastrectomy is minor traumatic leakage from the pancreatic surface or from the disrupted lymphatic vessels; and it subsides spontaneously without leading to clinical fistula formation [21]. Moreover, there are no data suggesting a reliable cutoff value of drain amylase activity after gastrectomy in regard to POPF. According to an analysis of 581 patients who had undergone gastrectomy in our institution, 83.3 % of the patients with elevated drain amylase did not need any treatment, but 90.9 % of the patients with a sinister appearance of the drainage fluid did need specific treatment (concordance rate 93.1 %; $\kappa = 0.759$) (unpublished data). Consequently, we introduced a stricter definition of POPF by adding drainage fluid with a sinister appearance to the criteria.

Postoperative ascites (lymphorrhea) is also controversial and is frequently omitted from complication reports; it is

discussed most often in patients with liver cirrhosis. Lin et al. [28] defined lymphorrhea as abdominal drainage exceeding 200 ml/day at least 3 days after the gastrectomy. Jang et al. [29] described the criteria for massive ascites after gastrectomy in patients with liver cirrhosis as drainage exceeding 500 ml/day or needing paracentesis for control. We used combined criteria of those two articles, as described earlier. To our knowledge, no other study has described specific criteria for each complication after gastrectomy based on the literature. In addition to the definition, the temporal horizon for complications is an important consideration. Although it is convenient to use a set number of days as the endpoint, this choice may not fully or accurately depict the outcome, as it relates principally to prolonged intensive care unit (ICU) stay or death beyond 30 days [3]. In addition, complications in the outpatient setting may be missed; for example, anastomotic stenosis sometimes occurs several months postoperatively. Therefore, we extended the time horizon to 100 days after surgery on the recommendation of the Accordion Severity Grading System [6].

Strasberg et al. [6] suggested a four-level contracted severity grading system called the Accordion Severity Grading System that used rigorously defined qualitative terms; this can be expanded to six levels for complex surgery with higher morbidity rates. In regard to grading, the main difference from the Clavien-Dino classification was that it eliminated grade IV complications (i.e., life-

Table 3 Risk factors for postoperative complications after gastrectomy with reference to the accordion severity grade [6]

| Factors | Any complication (<i>n</i> = 161/890, 18.1 %) | | | At least one severe complication (<i>n</i> = 53/890, 6.0 %) | | |
|---|--|---------------------------|----------|--|---------------------------|----------|
| | Univariate | Multivariate [‡] | | Univariate | Multivariate [‡] | |
| | <i>p</i> | OR (95 % CI) | <i>p</i> | <i>p</i> | OR (95 % CI) | <i>p</i> |
| Age (years) | 0.009* | 1.001 (0.981–1.022) | 0.892 | 0.010* | 1.019 (0.990–1.050) | 0.196 |
| Sex | 0.001** | | 0.016 | 0.016** | | 0.059 |
| Female | | 1 | | | 1 | |
| Male | | 1.705 (1.103–2.634) | | | 2.048 (0.972–4.316) | |
| BMI (kg/m ²) | 0.601** | – | – | 0.854** | – | – |
| <25 | | | | | | |
| ≥25 | | | | | | |
| ASA score | <0.001** | | 0.016 | 0.004** | | 0.572 |
| I | | 1 | | | 1 | |
| II | | 1.853 (1.201–2.858) | 0.005 | | 1.647 (0.623–4.352) | 0.315 |
| III | | 2.12 (0.917–4.907) | 0.079 | | 1.901 (0.471–7.663) | 0.367 |
| Preoperative anemia ^a | <0.001** | 1.110 (0.715–1.723) | 0.643 | 0.317** | – | – |
| Preoperative hypoalbuminemia ^b | <0.001** | 3.124 (1.462–6.678) | 0.003 | 0.051 [†] | 2.687 (0.970–7.445) | 0.057 |
| Co-morbidity | | | | | | |
| Cardiovascular | 0.081** | 1.076 (0.704–1.646) | 0.735 | 0.005** | 2.226 (1.258–3.938) | 0.006 |
| DM | 0.870** | – | – | 0.964** | – | – |
| Pulmonary | 0.018** | 1.248 (0.700–2.225) | 0.452 | 0.001** | 2.896 (1.424–5.890) | 0.003 |
| Cerebrovascular | 0.283 [†] | – | – | 1.000 [†] | – | – |
| Liver cirrhosis | <0.001** | 4.597 (2.016–10.483) | <0.001 | 0.681 [†] | – | – |
| Renal failure | 0.246 [†] | – | – | 0.157 [†] | – | – |
| Type of approach | <0.001** | | 0.060 | 0.753** | – | – |
| Laparoscopic | | 1 | | | | |
| Open | | 1.510 (0.983–2.320) | | | | |
| Extent of resection | <0.001** | | 0.023 | 0.006** | | 0.144 |
| Distal | | 1 | | | 1 | |
| Total | | 1.651 (1.072–2.541) | 0.023 | | 1.595 (0.853–2.982) | |
| Combined resection | <0.001** | 1.519 (0.685–3.366) | 0.303 | 0.030 [†] | 1.565 (0.461–5.309) | 0.473 |
| Lymph node dissection ^c | | | | | | |
| D1, D1+ | 0.983** | – | – | 0.467** | – | – |
| D2, D2+ | | | | | | |
| Operating time (min) | 0.001* | 1.004 (1.001–1.006) | 0.008 | 0.016* | 1.004 (1.001–1.008) | 0.016 |
| Estimated blood loss (ml) | <0.001* | 1.001 (1.000–1.001) | 0.213 | 0.037* | 1.000 (0.999–1.001) | 0.943 |
| TNM stage, AJCC 7th edition | <0.001** | | 0.352 | 0.037** | | 0.207 |
| I | | 1 | | | 1 | |
| II | | 0.828 (0.450–1.525) | 0.545 | | 0.356 (0.104–1.218) | 0.100 |
| III | | 1.075 (0.590–1.959) | 0.813 | | 0.694 (0.273–1.764) | 0.442 |
| IV | | 1.794 (0.810–3.973) | 0.150 | | 1.535 (0.564–4.179) | 0.402 |

OR (95 % CI) odds ratio (95 % confidence interval), BMI body mass index, DM diabetes mellitus, ASA American Society of Anesthesiologist, AJCC American Joint Committee on Cancer

^a Preoperative anemia was defined according to WHO criteria [30]

^b Preoperative hypoalbuminemia was defined as a serum albumin level < 3.5 g/dl based on the normal cutoff value of our institution

^c Lymph node dissection was classified by Japanese Gastric Cancer Treatment Guidelines 2010 (version 3) [34]

* Two-sample *t* test

** χ^2 test

[†] Fisher's exact test

[‡] Binary logistic regression analysis. Risk factors with a univariate *p* < 0.10 were included in the multivariate analysis

threatening complications requiring IC/ICU management), and organ dysfunction was classified as a severe complication because an ICU admission may occur simply to monitor a patient, irrespective of organ failure, and reported grade IV complications made up a very small portion of all complications. Our institution adopted this novel severity grading system in 2010. In addition, to rule out surgeon intuition, we specified the treatment modalities for each complication according to the basic concepts of that system (see Appendix). For example, maintenance of a drainage tube that was inserted intraoperatively is a treatment method for several complications, including anastomotic or duodenal stump leakage, intraabdominal infection, POPF, and abdominal bleeding. Although a noninvasive procedure in itself, it often results in prolongation of the hospital stay. Therefore, removal of the drain after what was found to be the mean hospital stay was regarded as moderate grade. Thoracentesis and paracentesis were also included in moderate grade because they can usually be done at the bedside but are more invasive than procedures deemed to have a mild grade. In addition, listed drugs, prokinetics, laxatives, antispasmodics, and hemostatics were considered mild complications as they are used commonly in patients without specific complications after gastrectomy, and the use of these drugs is often dependent on the surgeon's preference. Both an antiprotease and somatostatin analogs are used frequently to treat or prevent pancreas-related complications. Although somatostatin is described as one of the optional treatment for grade B POPF by ISGPF [20], the antiprotease does not improve the clinical outcomes in the meta-analysis, and its routine use is not recommended for pancreatitis [32]. Therefore, we regarded the empiric use of antiprotease as mild grade.

To date, only three published articles have applied a standardized classification system in gastric cancer; all used the Clavien–Dindo classification system, and no study adopted the Accordion Severity Grading System. Jiang et al. [12] reported the complication rate after laparoscopy-assisted pylorus-preserving gastrectomy (all complications 17.3 %, major complications 1.3 %). Lee et al. [11] compared the morbidity rates between laparoscopy-assisted distal gastrectomy (LADG) and open distal gastrectomy (all complications 25.3 % vs. 40.1 %, major complications 2.1 % vs. 5.4 %). Kumagai et al. [13] described the incidence of severe complications with Billroth I and Roux-en-Y reconstruction after LADG (13.7 % vs. 5.2 %). In our analysis, the rates of all complications and severe complications following gastrectomy were 18.1 % and 6.0 %, respectively. The complication rate in Lee et al. is somewhat higher than the others because they classified all deviations during the postoperative course as complications; as a result, grade I complications accounted for 70.8 % (358 of 506 events) of all reported complications

[11]. Therefore, consensus on what is a complication after gastrectomy is critical. Interestingly, all of the above-mentioned studies used qualitative terms (i.e., major or severe) for complications higher than grade III (requiring intervention) to contract the classifications. In addition, as mentioned above, the portion of grade IV complications was very small: 0.9 % in Lee et al. [11] and zero in Jiang et al. [12] and Kumagai et al. [13]. In our series, severe—organ failure constituted only 1.5 % of all morbidity (Table 2). These results suggest that the Accordion Severity Grading System is more suitable for reporting complications after gastrectomy for gastric cancer.

The LOS, although an unreliable outcome criterion among centers, is a useful parameter of the severity of a complication within a single center [5]. Therefore, we evaluated the correlations between the complication grades and the LOS to validate the Accordion Severity Grading System in gastric cancer. To see more practical effects, the rehospitalization period was added to the hospital stay. In our series, the severity of complications had a highly significant effect on the LOS ($p < 0.001$, one-way ANOVA) (Fig. 1). The hospital stay increased with the grade, although the differences were not significant among the severe grades, which is probably due to the relatively small number of cases with those three grades. In summary, classifying complications by severity allowed a better comparison of the quality of surgery.

Previous studies assessing risk factors in patients undergoing gastrectomy have used only mortality or specific complications as endpoints, irrespective of the severity. 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, male sex, a high ASA score, preoperative hypoalbuminemia, underlying liver cirrhosis, total gastrectomy, and longer operating time were significant. However, All of these factors, however, except operating time (OR = 1.004, $p = 0.016$), lost significance in the analysis of severe complications. Instead, we found that underlying cardiovascular or pulmonary disease was a significant predictor of severe complications (OR = 2.226, $p = 0.006$; OR = 2.896, $p = 0.003$) (Table 3). Co-morbidity was a major concern related to complications, but the effects were inconsistent [11–13, 33]. In our analysis, co-morbidity was not significantly related to overall complications; but specific co-morbidities (e.g., cardiovascular and pulmonary disease) were significantly related to more serious complications. Therefore, patients with those co-morbidities would be considered for one of the limited surgeries, and the perioperative management should involve particular care to prevent postoperative complications.

Our study has several shortcomings. To our knowledge, this is the first report using the Accordion Severity Grading System in gastric cancer based on definitions of complications

derived from the literature. Accordingly, the suggested definitions of complications and the classification of treatment modalities were somewhat arbitrary. The classification of severity was based on the treatment used in response to complications, which could lead to variability in the classification of severity. For example, an intraabdominal abscess after bowel resection may be treated with antibiotics, percutaneous drainage, or repeat laparotomy, often depending on somewhat subjective appraisals [5]. In addition, the use of this system for intraoperative complications is possible, but it has a different type of threshold problem [6].

In this study, we reported the complications after gastrectomy based on predefined specific definitions for each complication with special reference to severity by the Accordion Severity Grading System. Most of the complications were mild to moderate; only 27.4 % of the complications were classified as severe and required invasive procedures. The LOS significantly increased with the grade; that is, complications of different grades have distinguishable clinical outcomes. Therefore, this grading system enables us to report complications after gastrectomy more practically. The classification system also allowed us to analyze risk factors related to different

degrees of severity. According to our findings, a longer operating time and cardiovascular and pulmonary comorbidities were significantly related to severe complications. As co-morbidity was not a significant risk factor for overall complications, this might be overlooked.

Conclusions

Surgeons should be encouraged to report complications using a standardized classification tool for better comparison of surgery among centers, therapies, and within a center over time. To achieve this practice, it is necessary to have general agreement on what is considered a complication. A standardized way of grading severity is also necessary for better care of patients undergoing gastrectomy for gastric cancer.

Conflict of interest The authors declare no conflict of interest.

Appendix

See Table 4.

Table 4 Practical grading of complications after gastrectomy for gastric cancer according to accordion severity classification [6] at CNUHH

| Grade ^a | Mild | Moderate | Severe—invasive procedure/no GA | Severe—invasive procedure/GA |
|----------------------------|--|---|---|------------------------------------|
| Required management | Minor invasive procedures that can be done at the bedside ^b Physiotherapy and following drugs are allowed: antiemetics, antipyretics, analgesics, diuretics, electrolytes | Pharmacologic treatment with drugs other than those allowed for minor complications Blood transfusions and TPN are also included | Endoscopy, interventional procedure, or reoperation without general anesthesia | Operation under general anesthesia |
| Surgical complications | | | | |
| Wound infection | Drainage at bedside | Antibiotics | Revision under LA | Revision under GA |
| Intraabdominal infection | Delayed removal of drain (\leq POD 7) | Antibiotics Delayed removal of drain ($>$ POD 7) ^d | Percutaneous aspiration/drainage | Operation under GA |
| POPF | Antiproteases ^c Delayed removal of drain (\leq POD 7) | Antibiotics, somatostatin analogs NPO and TPN Delayed removal of drain ($>$ POD 7) ^d | Percutaneous drainage | Operation under GA |
| Postoperative pancreatitis | Antiproteases ^c | Antibiotics, somatostatin analogues NPO and TPN | Radiologic/endoscopic necrosectomy and drainage | Operation under GA |
| Leak | Insertion of nasogastric tube Delayed removal of drain (\leq POD 7) | Antibiotics NPO and TPN Delayed removal of drain ($>$ POD 7) ^d | Endoscopic clipping/stent insertion Insertion of feeding tube Percutaneous drainage | Operation under GA |

Table 4 continued

| Grade ^a | Mild | Moderate | Severe—invasive procedure/no GA | Severe—invasive procedure/GA |
|--------------------------------------|--|---|--|---|
| Anastomotic stenosis | Changes in the form of meals (regular diet → soft diet → liquid diet) | NPO and TPN | Endoscopic balloon dilatation/stent insertion | Operation under GA |
| Gastric stasis | Insertion of nasogastric tube Prokinetics ^c | NPO and TPN | Insertion of feeding tube Venting gastrostomy | Operation under GA |
| Postoperative ileus | Insertion of nasogastric tube Prokinetics, ^c laxatives ^{c2} | NPO and TPN | – | – |
| Postoperative intestinal obstruction | Insertion of nasogastric tube Antispasmodics ^c | Antibiotics NPO and TPN | – | Operation under GA |
| Postoperative bleeding | Hemostatics ^c Delayed removal of drain (\leq POD 7) | Blood transfusion Delayed removal of drain ($>$ POD 7) ^d | Endoscopic hemostasis Angioembolization | Operation under GA |
| Ascites | Low-salt diet Diuretics | NPO and TPN Antibiotics, paracentesis ^e Delayed removal of drain ($>$ POD 7) ^d | Percutaneous drainage Percutaneous drainage | Operation under GA |
| Chyle leak | Delayed removal of drain (\leq POD 7) High-protein/low-lipid diet Diuretics | Antibiotics Paracentesis ^e NPO and TPN | Percutaneous drainage | Operation under GA |
| Nonsurgical complications | | | | |
| Respiratory | Atelectasis requires physiotherapy | Pleural effusion treated with thoracentesis ^c at the bedside | Pleural effusion/empyema requires insertion of drainage tube | Pleuroenteric fistula requires surgical closure |
| | Pleural effusion treated with diuretics | Pneumonia treated with antibiotics | Pneumonia treated with bronchoscopic aspiration | |
| Cardiovascular | Atrial fibrillation treated with correction of imbalanced electrolytes/acidosis | Tachyarrhythmia requires β -receptor antagonists | Bradyarrhythmia requires pacemaker implantation under LA | Ischemic heart disease requires surgery |
| | | Ischemic heart disease treated with vasodilators/anticoagulants | Ischemic heart disease requires PCI | VTE requires surgery |
| | | VTE treated with anticoagulants | VTE requires intervention | |
| Cerebrovascular | Transient confusion not requiring specific therapy | Transient ischemic attack requiring treatment with anticoagulants | Ischemic stroke/brain hemorrhage require intervention | Ischemic stroke/brain hemorrhage require surgery |
| Renal | Transient elevation of serum creatinine | Urinary tract infection treated with antibiotics | – | – |
| Others | | Infectious colitis/cholecystitis treated with antibiotics | – | Infectious colitis/cholecystitis requires surgery |

Table 4 continued

CNUHH Chonnam National University Hwasun Hospital, GA general anesthesia, LA local anesthesia, POPF postoperative pancreatic fistula, POD postoperative day, NPO nothing per oral, TPN total parenteral nutrition, VTE venous thromboembolism, PCI percutaneous coronary intervention

^a Severe: Organ failure grade was classified according to “definitions of organ failure for accordion classification of postoperative” [6]. Postoperative deaths included postoperative in-hospital deaths and postoperative deaths within 100 days

^b Minor invasive procedures included insertion of intravenous lines, urinary catheters, and nasogastric tubes; and drainage of wound infections

^c These drugs were considered mild complications because they are used commonly in patients without specific complications after gastrectomy, and use of the drugs is often dependent on the surgeon’s preference

^d Our institution applied a clinical pathway system wherein patients without complications were discharged usually at POD 7 or 8. Removal of a drain after POD 7 often results in prolongation of the hospital stay; therefore it was regarded as moderate grade

^e Paracentesis and thoracentesis were also included in moderate grade because they can usually be done at the bedside but are more invasive than procedures said to have a mild grade

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