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ORIGINAL ARTICLE

Analysis of the characteristics and management of perforated peptic ulcer from 2011 to 2022: A multicenter and retrospective descriptive study

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Abstract

Aim: Although perforated peptic ulcer is common in Japan, few large-scale studies have assessed its management, including surgical procedures and outcomes. This study aimed to survey the characteristics, management, and outcomes of perforated peptic ulcer.

Methods: A multicenter retrospective descriptive analysis was conducted across seven centers in Japan between 2011 and 2022. Perforated peptic ulcer was defined as gastric or duodenal ulcer perforation, excluding malignant or iatrogenic perforation.

Results: We enrolled 703 patients with perforated peptic ulcer. The overall in-hospital mortality rate was 35/703 (5.0%). Conservative treatment was performed as an initial treatment in 217/703 (30.9%) patients, among whom 52 (24.0%) eventually underwent surgery. The median age (interquartile range) of patients who successfully completed the conservative treatment was 60 (46–71) years. A total of 538/703 (76.5%) patients underwent surgery. The gastrectomy percentage increased with the perforation diameter. The anastomotic leakage rate for gastrectomy was high in 10/66 (15.2%) patients. Laparoscopy was performed in 115/538 (21.4%) patients, among whom 23 (20.0%) were converted to open surgery. Patients who underwent laparoscopy had a perforation diameter ≤ 20 mm. The use of laparoscopy varied among facilities, ranging from 1.8% to 61.2%.

Conclusion: The in-hospital mortality rate for perforated peptic ulcer in this study was 5.0%, and conservative treatment was safely performed even in elderly patients. As the perforation diameter increased, the rate of gastrectomy tended to rise, and the rate of anastomotic leakage in those patients was high. UMIN Clinical Trials Registry; UMIN000054391.

KEYWORDS
duodenal perforation, duodenal ulcer, gastric perforation, gastric ulcer, perforated peptic ulcer

1 | INTRODUCTION

Perforated peptic ulcer (PPU) is a surgical emergency, with short- and long-term mortality rates of 11%–30% and 25%, respectively.[1–5] Conservative and surgical treatment options are available for patients with PPU. Although conservative treatment for PPU is practiced worldwide, few randomized controlled trials (RCTs) exist on its efficacy and safety.[6,7] Surgery remains the standard treatment for PPU.[2] However, the difficulty in performing surgery is that the treatment and surgical technique vary significantly depending on the patient's situation, including the severity, perforation size, perforation site, and surgery timing; there is no consensus on the surgical technique. Despite several RCTs examining PPU treatment, all studies were small in scale, involving 43–121 patients.[6–13] Even in large observational studies that collected relatively detailed information, the number of patients was <600. Conversely, detailed information in nationwide database-based studies with many patients is lacking.[2,5,14–16]

To the best of our knowledge, few studies have provided an overview of PPU with detailed data from many patients. Therefore, this descriptive study aimed to analyze detailed data and describe the current management practices of PPU.

2 | METHODS

2.1 | Study design and settings

This multicenter, retrospective observational study, named PPU Analysis Project (PPAP), was conducted at seven centers in Japan between January 2011 and December 2022 to survey the characteristics, management, and outcomes of PPU. All centers were high-volume facilities with expertise in emergency surgery, conducting >1000 surgeries yearly.

2.2 | Ethics statement

The protocol for this research project has been approved by a suitably constituted ethics committee of the institution and it conforms to the provisions of the Declaration of Helsinki (Ethics Committee of Tsuchiura Kyodo General Hospital, approval no. 2023FY181). Ethical approval was also obtained from the ethics committees of all other participating institutions. As this was a retrospective study, the requirement for obtaining informed consent was waived, and an opt-out method was applied, allowing patients to refuse participation through the hospital's online disclosure of information. This study was conducted following the strengthening the reporting of cohort studies in surgery (STROCSS) guidelines.

2.3 | Study participants

This study included patients aged ≥18 years diagnosed with PPU between January 2011 and December 2022. During data collection, we excluded pregnant women, those who opted out of active treatment, patients with malignancy-related and iatrogenic perforations, and patients who were considered inappropriate by the research leaders at each facility.

2.4 | Measurements

We collected the following patient information from the PPAP database: age; sex; year of treatment; facilities for treatment; body mass index; data required to calculate the Charlson comorbidity index; Boey and peptic ulcer perforation (PULP) scores; history of abdominal surgery; risk factors for PPU (current smoking, alcohol consumption, *Helicobacter pylori* infection, use of nonsteroidal anti-inflammatory drugs [NSAIDs], and steroid use); history of prophylactics use for PPU (proton pump inhibitor, potassium competitive acid blocker, histamine H2 receptor antagonist, and gastric mucosal protective agent); time from onset to hospital visit; meal taken before hospital visit; history of the presence of sepsis, presence and extent of peritoneal irritation signs, and presence and extent of ascites on computed tomography (CT); body temperature; vital signs (systolic blood pressure [SBP] and heart rate [HR]); laboratory data (white blood cell count and C reactive protein, hemoglobin, albumin, and creatinine levels); American Society of Anesthesiologists Physical Status Classification (ASA-PS); treatment type (conservative treatment, conversion from conservative treatment to surgery, and surgery), perforation site; surgical findings (perforation diameter, volume of peritoneal lavage, surgical techniques, number of drains, and surgery duration); postoperative complications; time to start liquid intake; time to start diet intake; length of stay in intensive care unit (ICU); length of stay in hospital; and in-hospital mortality.

2.5 | Definitions and outcomes

PPU was defined as gastric or duodenal ulcer perforation. Baseline patient data were obtained from the time of initial diagnosis. Regarding surgical techniques, "plugging" was defined as inserting the tissue into the perforation site, as seen in procedures such as the Cellan-Jones repair or Graham patch, while "patching" was defined as covering the perforation with tissue without insertion. "Plugging" included omental and ligamentum teres hepatis plugs. "Patching" included omental and small intestine patches. "Gastrectomy" included total or distal gastrectomies. Postoperative complications were defined according to the Clavien–Dindo classification. Leakage was defined as digestive fluid leakage from the perforation site when peritoneal lavage, simple closure, plugging, or patching was performed, and anastomotic leakage occurred when gastrectomy, duodenectomy, or pancreatoduodenectomy was performed. The Boey score was calculated based on the severity of the medical illness, presence of preoperative shock, and perforation duration >24 h.[17] The PULP score was calculated based on patients' age (>65 years), presence of active malignant disease or acquired immune deficiency

TABLE 1 Baseline characteristics of the patients with perforated peptic ulcers.

Variables	Overall ($n = 703$)	
	Registered data	Missing, *n* (%)
Age (years), median (IQR)	64 [52–75]	1 (0.1)
Sex, female, *n* (%)	217 (30.9)	1 (0.1)
Body mass index (kg/m^2), median (IQR)	20.7 [18.9–23.1]	66 (9.4)
History of abdominal surgery, *n* (%)	121 (17.2)	
Risk factors, *n* (%)		
Current smoker	353 (50.2)	36 (5.1)
Alcohol consumption	239 (34.0)	39 (5.5)
Helicobacter pylori infection	192 (27.3)	78 (11.1)
Nonsteroidal anti-inflammatory drug use	149 (21.2)	
Steroid use	24 (3.4)	
Prophylactic medicines, *n* (%)		11 (1.6)
Proton pump inhibitor	32 (4.6)	
Potassium competitive acid blocker	4 (0.6)	
Histamine H2 receptor antagonist	23 (3.3)	
Gastric mucosal protective agent	52 (7.4)	
Others	8 (1.1)	
Time from onset to hospital visit, *n* (%)		8 (1.1)
<6 h	321 (45.7)	
<12 h	134 (19.1)	
<24 h	82 (11.7)	
≥24 h	158 (22.5)	
Meals before hospital visit, *n* (%)	110 (15.6)	125 (17.8)
Sepsis		1 (0.1)
None	626 (89.0)	
Sepsis	40 (5.7)	
Septic shock	36 (5.1)	
Peritoneal irritation signs, *n* (%)		10 (1.4)
None	116 (16.5)	
Upper abdomen only	260 (37.0)	
Wider than upper abdomen	317 (45.1)	
Ascites on CT, *n* (%)		9 (1.3)
None	135 (19.2)	
Upper abdomen only	113 (16.1)	
Wider than upper abdomen	446 (63.4)	
Temperature (°C), median (IQR)	36.8 [36.3–37.3]	20 (2.8)
Systolic blood pressure (mmHg), median (IQR)	133 [114–150]	12 (1.7)
Heart rate (/min), median (IQR)	92 [80–107]	12 (1.7)
Laboratory data		
White blood cell (/μl), median (IQR)	10900 [7300–14950]	
C reactive protein (mg/dl), median (IQR)	1.1 [0.2–7.8]	2 (0.3)
Hemoglobin (g/dl), median (IQR)	13.5 [10.9–15.1]	1 (0.1)
Albumin (g/dl), median (IQR)	3.7 [3.0–4.2]	7 (1.0)
Creatinine (mg/dl), median (IQR)	0.8 [0.7–1.1]	2 (0.3)
ASA-PS, *n* (%)		
2	211 (30.0)	
3	377 (53.6)	
4	105 (14.9)	
5	10 (1.4)	
Boey score, median (IQR)	0 [0–1]	
Peptic ulcer perforation score, median (IQR)	4 [3–7]	
Charlson comorbidity index, median (IQR)	4 [3–6]	
Site of perforations, *n* (%)		48 (6.8)
Stomach	258 (36.7)	
Duodenum	397 (56.5)	
Time to start liquid intake (day), median (IQR)	4 [3–6]	55 (7.8)
Time to start diet intake (day), median (IQR)	6 [4–8]	51 (7.3)
ICU length of stay (day), median (IQR)	2 [0–3]	3 (0.4)
Hospital length of stay (day), median (IQR)	14 [10–22]	1 (0.1)
In hospital mortality, *n* (%)	35 (5.0)	1 (0.1)

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status Classification; CT, computed tomography; ICU, intensive care unit; IQR, interquartile range.

syndrome, presence of liver cirrhosis, steroid use, time from perforation to admission (>24 h), presence of preoperative shock, creatinine level (>1.47 mg/dL), and ASA-PS.[18] Preoperative shock was defined as SBP <100 mmHg and HR ≥100/min.[16] Current smoking was defined as smoking within 1 month before diagnosis. Alcohol consumption was classified as habitual rather than non-habitual or occasional. *Helicobacter pylori* infection was classified as current or no infection in patients previously infected and treated. Meals before the hospital visit were defined as meals consumed within 6 h of onset. Sepsis was defined according to the 2021 international guidelines for managing sepsis and septic shock.[19] ASA-PS was defined as ≥2 for all patients because of the PPU.

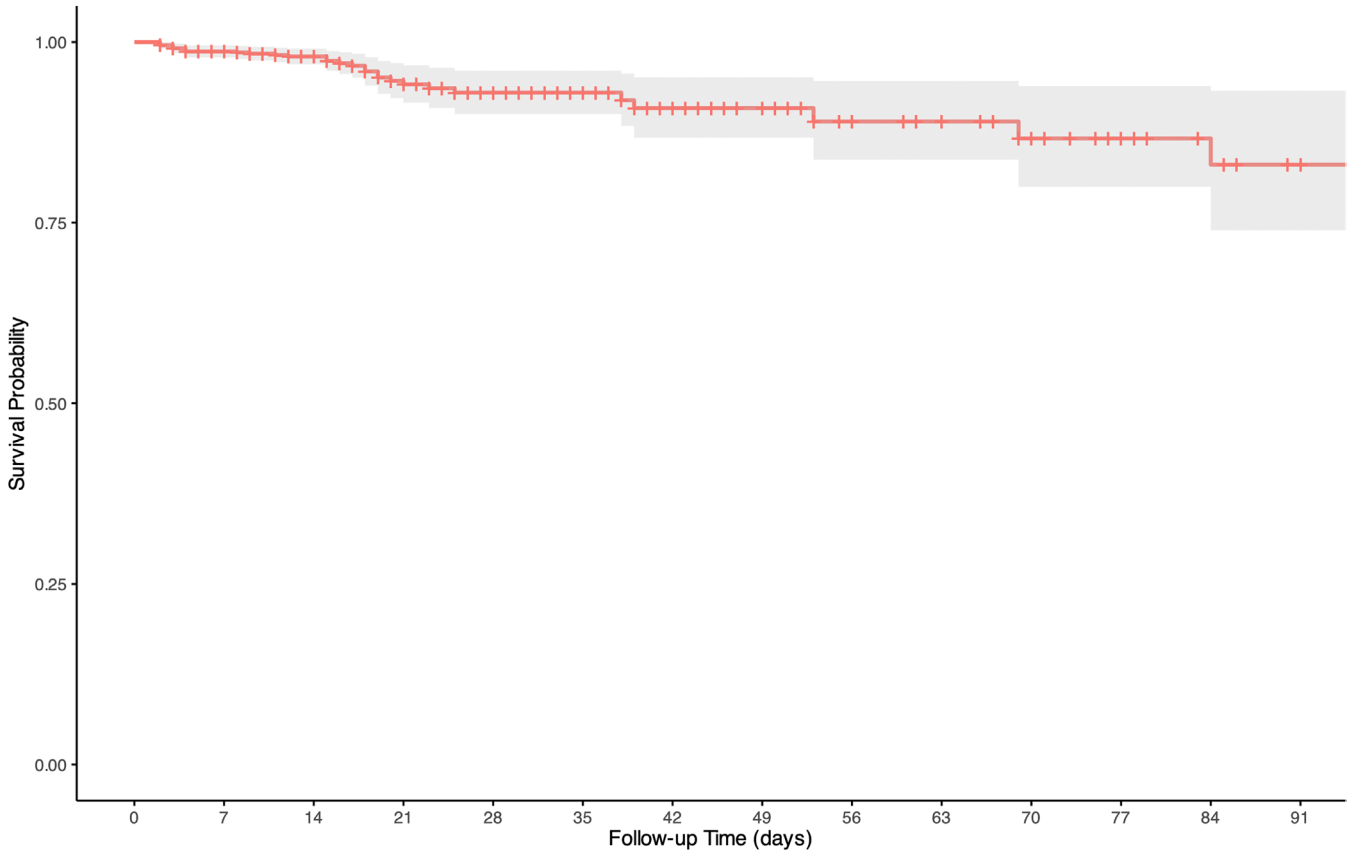

FIGURE 1 Kaplan–Meier survival curve for the patient cohort. The red line represents cumulative survival probabilities over time, while the shaded gray area indicates the 95% confidence intervals.

The primary outcome was in-hospital mortality. The secondary outcomes were postoperative complications, time to start liquid intake, time to start oral diet intake, and length of ICU and hospital stays.

2.6 | Statistical analysis

Patient characteristics are described using median and interquartile range (IQR) for continuous variables and number and percentage (%) for categorical variables. Continuous variables were compared using Mann–Whitney *U*-tests or Kruskal–Wallis tests. Categorical variables were compared using Pearson's chi-square tests. We considered two-sided $p < 0.05$ to be significant. We performed survival analysis using the Kaplan–Meier method, and the survival curves were plotted to visualize the cumulative survival rates over time, with 95% confidence intervals. All statistical analyses were performed using R software, version 4.3.2 (R Foundation for Statistical Computing).

3 | RESULTS

3.1 | Patient characteristics

This study included 703 patients, and 217 (30.9%) were females (Table 1). The median age (IQR) was 64 (52–75) years. Among the patients, 353/703 (50.2%) were current smokers, 192/703 (27.3%) had *H. pylori* infection, and 149/703 (21.2%) used NSAIDs. Overall, 119/703 (16.9%) patients took some form of peptic ulcer disease prophylactic medicines. The perforation sites included the stomach in 258/703 (36.7%) and duodenum in 397/703 (56.5%) patients. The in-hospital mortality rate was 35/703 (5.0%). Kaplan–Meier survival curves were generated to estimate the cumulative survival probabilities. The 30-day survival rate was 93.0%, as shown in Figure 1.

3.2 | Conservative treatment

Table 2 presents the patient characteristics for each treatment type (conservative treatment [C group], conversion from conservative treatment to surgery [CS group], and surgery [S group]). In the C group, the median age (IQR) was 60 (46–71) years. Conservative treatment was performed as an initial treatment in 217/703 (30.9%) patients, among whom 52 (24.0%) eventually underwent surgery. The most common reason for converting to surgery was exacerbation of imaging findings (Table S1). The C group had the highest proportion of patients with no peritoneal irritation signs (30.3% [50/165]) and the lowest proportion of patients with the extent of ascites wider than the upper abdomen (17.0% [28/165]). The extent of ascites observed in the CT findings was similar between the C and CS groups. More detailed characteristics are provided in Table S2.

TABLE 2 Characteristics of patients according to treatment type: Conservative treatment, conservative treatment to surgery, and surgery.

Variables	Conservative treatment $n=165$	Conversion from conservative treatment to surgery $n=52$	Surgery $n=486$	p
Age (years), median (IQR)	60 [46–71]	67 [54–77]	65 [54–75]	<0.01
Sex, female, *n* (%)	62 (37.6)	9 (17.3)	146 (30.0)	0.07
Body mass index (kg/m2), median (IQR)	21.0 [19.1–23.6]	20.8 [19.8–23.4]	20.6 [18.8–22.8]	0.22
Sepsis				<0.01
None	161 (97.6)	50 (96.2)	415 (85.4)	
Sepsis	3 (1.8)	1 (1.9)	36 (7.4)	
Septic shock	0 (0)	1 (1.9)	35 (7.2)	
Peritoneal irritation signs, *n* (%)				<0.01
None	50 (30.3)	4 (7.7)	62 (12.8)	
Upper abdomen only	86 (52.1)	26 (50.0)	148 (30.5)	
Wider than upper abdomen	28 (17.0)	22 (42.3)	267 (54.9)	
Ascites on CT, *n* (%)				<0.01
None	58 (35.2)	17 (32.7)	60 (12.3)	
Upper abdomen only	31 (18.8)	10 (19.2)	72 (14.8)	
Wider than upper abdomen	74 (44.8)	25 (48.1)	347 (71.4)	
ASA-PS, *n* (%)				<0.01
2	72 (43.6)	17 (32.7)	122 (25.1)	
3	87 (52.7)	32 (61.5)	258 (53.1)	
4	6 (3.6)	3 (5.8)	96 (19.8)	
5	0 (0)	0 (0)	10 (2.1)	
Boey score, median (IQR)	0 [0–1]	0 [0–1]	0 [0–1]	0.88
Peptic ulcer perforation score, median (IQR)	3 [2–6]	4 [3–6]	5 [3–8]	<0.01
Charlson comorbidity index, median (IQR)	4 [2–6]	5 [3–6]	4 [3–6]	0.03
Site of perforations, *n* (%)				<0.01
Stomach	42 (25.5)	16 (30.8)	200 (41.2)	
Duodenum	78 (47.3)	35 (67.3)	284 (58.4)	
Time to start liquid intake (day), median (IQR)	5 [4–7]	4 [2–6]	4 [2–6]	<0.01
Time to start diet intake (day), median (IQR)	7 [5–10]	6 [4–8]	6 [4–8]	<0.01
ICU length of stay (day), median (IQR)	0 [0–1]	2 [0–4]	2 [2–4]	<0.01
Hospital length of stay (day), median (IQR)	13 [10–18]	16 [12–27]	14 [10–24]	<0.01
In hospital mortality, *n* (%)	4 (2.4)	1 (1.9)	30 (6.2)	0.26

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status Classification; CT, computed tomography; ICU, intensive care unit; IQR, interquartile range.

3.3 | Perforation sites

Table 3 presents the characteristics of patients based on the perforation site (anterior [A group] and posterior walls [P group]). The P group had a higher proportion of patients with time from onset to hospital visit ≥24 h (34.8% [23/66]) and no peritoneal irritation signs (28.8% [19/66]) than that of the A group. The proportion of patients who received conservative treatment was higher in the P group (28.8% [19/66]) than in the A group (14.6% [83/570]). The proportion of patients who underwent gastrectomy was higher in the P group (28.8% [19/66]) than in the A group (8.2% [47/570]). The median perforation diameter (IQR) was 15 [7–29] mm in the P group, which was larger than the 8 [5–15] mm of the A group.

3.4 | Surgical techniques

The complications and outcomes according to surgical techniques are presented in Table 4. The most common surgical technique, plugging, was performed in 244/538 (45.4%) patients. In patients undergoing pancreaticoduodenectomy, the Boey score, PULP score, and CCI were the highest among all surgical procedure

TABLE 3 Characteristics of patients according to the perforation site: Anterior and posterior walls.

Variables	Anterior wall $n = 570$	Posterior wall $n = 66$	p
Age (years), median (IQR)	64 [52–75]	63 [61–74]	0.07
Sex, female, *n* (%)	169 (29.6)	27 (40.9)	0.17
Body mass index (kg/m^2), median (IQR)	20.6 [18.9–22.9]	21.5 [19.5–24.4]	0.07
Time from onset to hospital visit, *n* (%)			0.15
<6 h	258 (45.3)	23 (34.8)	
<12 h	113 (19.8)	10 (15.2)	
<24 h	68 (11.9)	9 (13.6)	
≥24 h	127 (22.3)	23 (34.8)	
Sepsis			0.08
None	507 (88.9)	53 (80.3)	
Sepsis	32 (5.6)	8 (12.1)	
Septic shock	31 (5.4)	5 (7.6)	
Peritoneal irritation signs, *n* (%)			0.01
None	76 (13.3)	19 (28.8)	
Upper abdomen only	207 (36.3)	24 (36.4)	
Wider than upper abdomen	278 (48.8)	22 (33.3)	
Ascites on CT, *n* (%)			0.08
None	96 (16.8)	18 (27.3)	
Upper abdomen only	95 (16.7)	6 (9.1)	
Wider than upper abdomen	371 (65.1)	42 (63.6)	
Temperature (°C), median (IQR)	36.8 [36.3–37.3]	36.6 [36.3–37.0]	0.18
Systolic blood pressure (mmHg), median (IQR)	133 [113–150]	129 [108–145]	0.19
Heart rate (/min), median (IQR)	92 [80–108]	97 [85–110]	0.16
Laboratory data			
White blood cell (/μL), median (IQR)	10 900 [7370–14 853]	11 320 [6925–15 250]	0.71
C reactive protein (mg/dL), median (IQR)	1.0 [0.2–8.3]	4.2 [1.1–12.4]	<0.01
Hemoglobin (g/dL), median (IQR)	13.5 [11.0–15.1]	10.9 [8.8–14.1]	<0.01
Albumin (g/dL), median (IQR)	3.7 [3.0–4.2]	3.0 [2.4–3.7]	<0.01
Creatinine (mg/dL), median (IQR)	0.8 [0.7–1.2]	1.0 [0.7–2.1]	0.01
ASA-PS, *n* (%)			0.04
2	174 (30.5)	17 (25.8)	
3	304 (53.3)	31 (47.0)	
4	82 (14.4)	18 (27.3)	
5	10 (1.8)	0 (0)	
Boey score, median (IQR)	0 [0–1]	1 [0–1]	0.02
Peptic ulcer perforation score, median (IQR)	4 [3–7]	6 [3–8]	0.01
Charlson comorbidity index, median (IQR)	4 [3–6]	5 [4–6]	0.01
Perforated organ, *n* (%)			<0.01
Stomach	216 (37.9)	41 (62.1)	
Duodenum	354 (62.1)	25 (37.9)	
Treatment, *n* (%)			<0.01
Conservative treatment	83 (14.6)	19 (28.8)	
Conversion from conservative treatment to surgery	45 (7.9)	6 (9.1)	
Surgery	442 (77.5)	41 (62.1)	

(Continues)

TABLE 3 (Continued)

Variables	Anterior wall $n = 570$	Posterior wall $n = 66$	p
Surgical findings			
Major surgical techniques, *n* (%)			<0.01
Peritoneal lavage only	5 (0.9)	2 (3.0)	
Simple closure	12 (2.1)	5 (7.6)	
Plugging[a]	234 (41.1)	10 (15.2)	
Patching[b]	186 (32.6)	6 (9.1)	
Gastrectomy[c]	47 (8.2)	19 (28.8)	
Duodenectomy	0 (0)	3 (4.5)	
Pancreatoduodenectomy	2 (0.4)	0 (0)	
Perforation diameter (mm), median (IQR)	8 [5–15]	15 [7–29]	<0.01
Operation time (min), (median IQR)	100 [75–132]	203 [150–259]	<0.01
Time to start liquid intake (day), median (IQR)	4 [2–6]	5 [3–8]	0.01
Time to start diet intake (day), median (IQR)	6 [4–8]	7 [5–11]	0.03
ICU length of stay (day), median (IQR)	2 [0–3]	3 [0–8]	0.02
Hospital length of stay (day), median (IQR)	14 [10–22]	19 [14–33]	<0.01
In hospital mortality, *n* (%)	28 (4.9)	6 (9.1)	0.34

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status Classification; CT, computed tomography; ICU, intensive care unit; IQR, interquartile range.

[a]Including the omental plug and the ligamentum teres hepatis plug.

[b]Including the omental patch and a small intestine patch.

[c]Including total gastrectomy and distal gastrectomy.

groups. The leakage rate was high for patients who underwent pancreatoduodenectomy (50.0% [1/2]), followed by that of those who underwent peritoneal lavage only (30.0% [3/10]), and simple closure (17.6% [3/17]). The in-hospital mortality rate was also high for patients who underwent pancreatoduodenectomy (100% [2/2]), followed by that of those who underwent peritoneal lavage only (20.0% [2/10]), and simple closure (17.6% [3/17]). As the perforation diameter increased, the proportion of invasive surgical procedures such as gastrectomy, duodenectomy, and pancreaticoduodenectomy increased (Figure 2).

3.5 | Laparoscopic surgery

Table 5 presents the characteristics of patients based on each treatment (open surgery [O group], laparoscopy [L group], and conversion from laparoscopy to open surgery [LO group]). Laparoscopy was performed as the initial treatment in 115/538 (21.4%) patients, among whom 23 (20.0%) eventually underwent surgery. The most common reason for converting from laparoscopy to open surgery was "difficulty in securing the visual field owing to a large amount of ascites" (Table S3). In the L group, gastrectomy, duodenectomy, or pancreatoduodenectomy were not performed, and the perforation diameter was ≤20 mm. The use of laparoscopy varied among facilities, ranging from 1.8% to 61.2% (Figure S1). More detailed information is provided in Table S4.

4 | DISCUSSION

We conducted a multicenter descriptive study where we collected the data of 703 patients with PPU and evaluated their characteristics in detail, including treatment strategy, perforation sites, perforation diameter, and surgical techniques. To the best of our knowledge, this study includes a larger sample size than most previous PPU studies and provides an overview of the characteristics and current treatments for PPU.

The overall mortality rate in this study was 5.0% (35/703), which is much lower than the 11%–30% reported in previous studies.[1–5] A nationwide analysis of a Japanese database showed an even lower mortality rate of 2.4%,[20] indicating that mortality rates for PPU in Japan tend to be lower compared to other regions. Although risk factors for mortality in PPU are not fully established, older age, presence of comorbidities, and delayed surgery have been identified as possible factors.[3] In this study, the median age was high at 64 years, and the ASA-PS, CCI, Boey, and PULP scores were comparable to those in other studies.[1–5] The mortality rate in the CS group was not particularly high. While the overall health of the Japanese elderly population is often cited as a reason for positive outcomes,[21] it may not completely explain the observed differences in mortality rates. Studies on peptic ulcer disease have shown significant variations in mortality rates between countries, with findings suggesting that regions such as the high-income Asia Pacific, including Japan, tend to have particularly low mortality rates.[22] Differences in national

TABLE 4 Complications and outcomes according to major surgical techniques.

Variables	Peritoneal lavage only $n=10$	Simple closure $n=17$	Plugging[a] $n=244$	Patching[b] $n=193$	Gastrectomy[c] $n=66$	Duodenectomy $n=3$	Pancreatoduodenectomy $n=2$	p
Boey score, median (IQR)	1 [0–1]	1 [0–1]	0 [0–1]	0 [0–1]	1 [0–1]	0 [0–1]	2 [1–2]	0.02
Peptic ulcer perforation score, median (IQR)	7 [3–9]	6 [3–8]	6 [3–8]	4 [3–6]	6 [4–8]	4 [3–6]	11 [10–11]	<0.01
Charlson comorbidity index, median (IQR)	5 [4–7]	4 [2–7]	4 [3–6]	4 [3–6]	5 [4–6]	4 [4–5]	12 [12–12]	0.06
Operation time (min), median (IQR)	99 [89–154]	100 [74–188]	98 [75–122]	96 [72–123]	230 [192–302]	216 [173–313]	514 [493–535]	<0.01
Perforation diameter (mm), median (IQR)	6 [3–8]	5 [3–13]	8 [5–10]	7 [5–10]	20 [10–33]	6 [3–8]	35 [28–43]	<0.01
Perforation diameter, *n* (%)								<0.01
≤10 mm	2 (20.0)	11 (64.7)	177 (72.5)	149 (77.2)	17 (25.8)	2 (66.7)	0 (0)	
11–20 mm	0 (0)	3 (17.6)	44 (18.0)	33 (17.1)	14 (21.2)	0 (0)	1 (50.0)	
21–30 mm	0 (0)	0 (0)	6 (2.5)	5 (2.6)	13 (19.7)	0 (0)	0 (0)	
≥31 mm	0 (0)	1 (5.9)	6 (2.5)	1 (0.5)	15 (22.7)	0 (0)	1 (50.0)	
Unknown	8 (80.0)	2 (11.8)	11 (4.5)	5 (2.6)	7 (10.6)	1 (33.3)	0 (0)	
Leakage, *n* (%)								<0.01
None	7 (70.0)	14 (82.4)	234 (95.9)	185 (95.9)	56 (84.8)	3 (100)	1 (50.0)	
Grade 1–2	1 (10.0)	0 (0)	5 (2.0)	1 (0.5)	0 (0)	0 (0)	0 (0)	
Grade 3a ≤	2 (20.0)	3 (17.6)	5 (2.0)	7 (3.6)	10 (15.2)	0 (0)	1 (50.0)	
Superficial + deep incisional surgical site infection, *n* (%)								<0.01
None	10 (100)	15 (88.2)	208 (85.2)	171 (88.6)	47 (71.2)	3 (100)	0 (0)	
Grade 1–2	0 (0)	2 (11.8)	31 (12.7)	19 (9.8)	14 (22.7)	0 (0)	2 (100)	
Grade 3a ≤	0 (0)	0 (0)	5 (2.0)	3 (1.6)	4 (6.1)	0 (0)	0 (0)	
Organ/space surgical site infection, *n* (%)								<0.01
None	5 (50.0)	13 (76.5)	227 (93.0)	174 (90.2)	53 (80.3)	2 (66.7)	1 (50)	
Grade 1–2	3 (30.0)	1 (5.9)	5 (2.0)	6 (3.1)	3 (4.5)	0 (0)	0 (0)	
Grade 3a ≤	2 (20.0)	3 (17.6)	12 (4.9)	8 (6.7)	10 (15.2)	1 (33.3)	1 (50.0)	
Ileus, *n* (%)								0.64
None	9 (90.0)	17 (100)	228 (93.4)	185 (95.9)	63 (95.5)	2 (66.7)	2 (100)	
Grade 1–2	1 (10)	0 (0)	14 (5.7)	6 (3.1)	3 (4.5)	1 (33.3)	0 (0)	
Grade 3a ≤	0 (0)	0 (0)	2 (0.8)	2 (1.0)	0 (0)	0 (0)	0 (0)	
Time to start liquid intake (day), median (IQR)	3 [2–11]	3 [2–3]	4 [3–7]	3 [2–5]	3.5 [2–6]	11 [7–16]	Could not start	<0.01
Time to start diet intake (day), median (IQR)	10 [6–14]	5 [4–8]	6 [5–8]	5 [4–7]	6 [4–8]	3 [3–12]	Could not start	<0.01
ICU length of stay (day), median (IQR)	1 [0–9]	2 [0–10]	3 [2–4]	2 [0–3]	3 [2–6]	3 [2–5]	52 [34, 70]	<0.01
Hospital length of stay (day), median (IQR)	27 [17–39]	18 [9–25]	14 [10–23]	13 [10–22]	19 [14–32]	9 [9–18]	90 [53–127]	<0.01
In hospital mortality, *n* (%)	2 (20.0)	3 (17.6)	11 (4.5)	8 (4.1)	5 (7.6)	0 (0)	2 (100)	<0.01

Abbreviations: ICU, intensive care unit; QR, interquartile range.

[a]Including the omental plug and the ligamentum teres hepatis plug.

[b]Including the omental patch and a small intestine patch.

[c]Including total gastrectomy and distal gastrectomy.

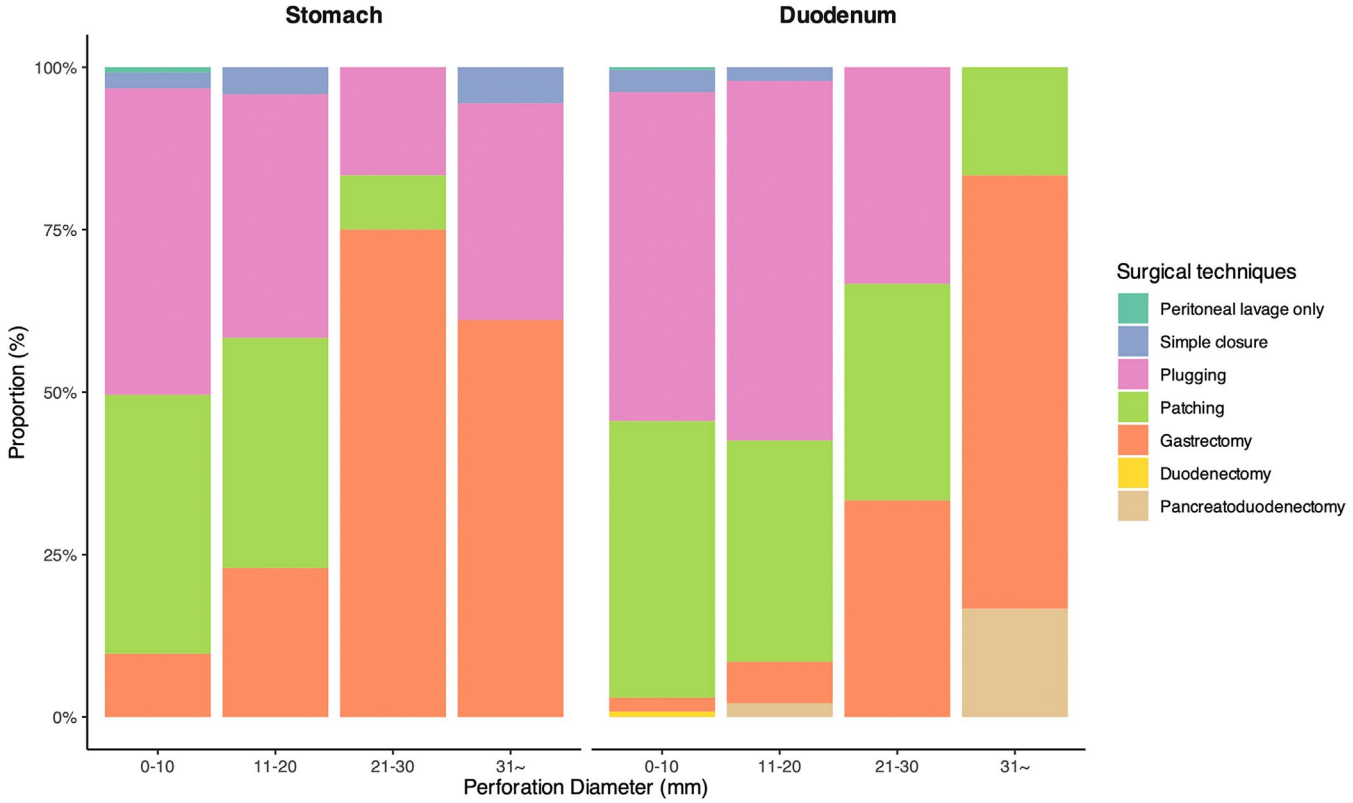

FIGURE 2 Distribution of surgical techniques according to perforation diameter. "Plugging" includes omental and ligamentum teres hepatis plugs. "Patching" includes omental and small intestine patches. "Gastrectomy" includes total and distal gastrectomy. As the perforation diameter increased, the proportion of invasive surgical procedures such as gastrectomy, duodenectomy, and pancreaticoduodenectomy increased.

healthcare systems and population characteristics may contribute to these variations in mortality.

There is no established consensus on the indications for conservative treatment of PPU. The suggested indications for conservative treatment include factors such as age < 70 years, stable vital signs, absence of sepsis, absence of peritonitis, and confirmation that the ulcer itself is sealed by a water-soluble contrast examination.[6,23] In our study, one-quarter of the patients who successfully completed conservative treatment were over 70 years old. This suggests that conservative treatment may be safely performed in older patients who are generally healthy. However, it is important to consider that the mortality rates increase with delayed surgery,[16] indicating that the decision for conservative treatment should be made cautiously. Our study found no significant differences in initial diagnostic findings between patients who completed conservative treatment and those who eventually required surgery, making it challenging to predict the success of conservative management at the initial presentation. Close monitoring of physical and diagnostic findings is crucial, and the decision for surgery should be made as early as possible to improve patient outcomes.

While the site of perforation is also important in determining the treatment strategy, few studies have analyzed patient characteristics based on the perforation site. Posterior wall perforation was associated with a slower and delayed onset of abdominal pain and higher mortality,[24] which was similar to the findings of this study. Laboratory data, various scores, and outcomes were worse in the patients with posterior wall perforation, suggesting that these patients likely had a more severe general condition at diagnosis than those with anterior perforation. This is probably due to the fact that patients became more severely ill as a result of delays in seeking medical attention due to the gradual worsening of symptoms. Patients with posterior wall perforation also had a larger perforation diameter and a higher rate of gastrectomy. The most standard surgical procedures for PPU are omental patching or plugging.[8,25] However, as the size of the perforation increases, these surgical techniques are prone to leakage, and the probability of an underlying malignancy increases, making it challenging to avoid resection.[11,26–28] Our study also found that the rate of gastrectomy increased with the diameter of the perforation. Since Japan has a high incidence of gastric cancer, gastrectomy is a relatively common procedure for most surgeons, explaining why they do not hesitate to perform gastrectomy when the perforation diameter is large. However, gastrectomy for PPU is associated with a high leakage rate compared to elective gastrectomy performed for gastric cancer.[29–31] Because post-gastrectomy leakage often necessitates reoperation,[32] when performing gastrectomy for PPU, it is crucial to recognize that the leakage rate is higher than that of elective surgeries.

TABLE 5 Characteristics of patients according to the treatment type: Open surgery, laparoscopy, laparoscopy to open surgery.

Variables	Open surgery $n=422$	Laparoscopy $n=92$	Conversion from laparoscopy to open surgery $n=23$	p
Age (years), median (IQR)	65 [54–75]	63 [51–76]	73 [65–79]	0.06
Sex, female, *n* (%)	122 (28.9)	29 (31.5)	4 (17.4)	0.15
Body mass index (kg/m^2), median (IQR)	20.6 [18.8–23.0]	21.2 [18.6–22.6]	20.0 [19.5–20.9]	0.96
Peritoneal irritation signs, *n* (%)				<0.01
None	57 (13.5)	8 (8.7)	1 (4.3)	
Upper abdomen only	140 (33.2)	27 (29.3)	6 (26.1)	
Wider than upper abdomen	217 (51.4)	56 (60.9)	16 (69.6)	
Ascites on CT, *n* (%)				<0.01
None	67 (15.9)	9 (9.8)	1 (4.3)	
Upper abdomen only	54 (12.8)	21 (22.8)	7 (30.4)	
Wider than upper abdomen	295 (69.9)	61 (66.3)	15 (65.2)	
Surgical findings				
Perforation diameter (mm), median (IQR)	10 [5–15]	7 [3–10]	9 [5–20]	0.30
Perforation diameter, *n* (%)				0.04
≤10 mm	277 (65.6)	68 (73.9)	12 (52.2)	
11–20 mm	77 (18.2)	15 (16.3)	4 (17.4)	
21–30 mm	23 (5.5)	1 (1.1)	1 (4.3)	
≥31 mm	21 (5.0)	0 (0)	3 (13.0)	
Volume of peritoneal lavage (l), median (IQR)	7 [5–10]	5 [3–7]	10 [6–10]	0.06
Operation time (min), (median IQR)	101 [75–144]	117 [84–152]	109 [88–183]	0.01
Complications				
Leakage, *n* (%)				0.47
None	394 (93.4)	87 (94.6)	20 (87.0)	
Grade 1–2	7 (1.7)	1 (1.1)	0 (0)	
Grade 3a ≤	21 (6.6)	4 (4.3)	3 (13.0)	
Superficial + deep incisional surgical site infection, *n* (%)				0.01
None	348 (82.5)	89 (96.7)	19 (82.6)	
Grade 1–2	63 (14.9)	3 (3.3)	3 (13.0)	
Grade 3a ≤	11 (2.6)	0 (0)	1 (4.3)	
Time to start liquid intake (day), median (IQR)	4 [3–6]	3 [2–4]	3 [2–5]	<0.01
Time to start diet intake (day), median (IQR)	6 [4–8]	5 [4–6]	6 [4–8]	<0.01
ICU length of stay (day), median (IQR)	3 [2–4]	2 [0–2]	1 [0–3]	<0.01
Hospital length of stay (day), median (IQR)	15 [11–25]	12 [9–21]	16 [13–28]	<0.01
In hospital mortality, *n* (%)	29 (6.9)	2 (2.2)	0 (0)	0.26

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status Classification; CT, computed tomography; ICU, intensive care unit; IQR, interquartile range.

Laparoscopic surgery for PPU is one of the most actively researched areas in the field. Many RCTs on PPU have reported the advantages of laparoscopic surgery over open surgery, including less postoperative pain, shorter hospital stays, and faster recovery times.[9,10,12,13,15,33] However, protocols vary and there is no consensus on the indications for laparoscopic surgery for PPU. The results of our study showed that a higher proportion of patients who completed laparoscopic surgery had stable hemodynamics, narrower ascites, and a perforation diameter of ≤20 mm, and these findings are generally consistent with those of previous studies.[23,34] There were no mortalities among those who converted from laparoscopy to open surgery, suggesting that laparoscopic surgery is a safe initial approach. In our study, the rate of laparoscopic surgery varied significantly across facilities, ranging from 1.8% to 61.2%. Nationwide data from Japan indicated that, on average, around 60% of PPU cases were treated using a laparoscopic approach.[20] In practice, the indications for laparoscopic surgery may be more strongly influenced by institutional practice than by patient factors.

Our study had some limitations. Determining the exact time of onset was difficult, as many patients had prior peptic ulcer pain exacerbated by PPU onset. Details on conservative treatment and perioperative management other than the collected data, such as the duration of nasogastric tube use, type and duration of use of proton pump inhibitors and antibiotics, and other non-surgical procedures, were unclear. In addition, the reconstruction technique in cases of perforation site resection was unknown, potentially affecting the complications and outcomes. Finally, due to the limited number of cases despite the multicenter study, we were unable to test causal inference using multivariable analysis.

5 | CONCLUSIONS

In summary, the in-hospital mortality rate for PPU in this study was 5.0%, and conservative treatment was safely performed even in elderly patients. As the perforation diameter increased, the rate of gastrectomy tended to rise, while the rate of anastomotic leakage in those patients was high. The results provide an overview of the current management of PPU, which would contribute to further research based on these data.

AUTHOR CONTRIBUTIONS

Hiromasa Hoshi: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; writing – original draft; writing – review and editing. **Akira Endo:** Conceptualization; formal analysis; project administration; supervision; validation; writing – review and editing. **Koji Ito:** Investigation; project administration; writing – review and editing. **Tomohiro Akutsu:** Investigation; project administration; writing – review and editing. **Hikaru Odera:** Investigation; project administration; writing – review and editing. **Hideto Shiraki:** Investigation; project administration; writing – review and editing. **Kei Ito:** Investigation; project administration; writing – review and editing. **Takeshi Yokoyama:** Investigation; project administration; writing – review and editing. **Yasukazu Narita:** Investigation; project administration; writing – review and editing. **Taro Masuda:** Investigation; project administration; writing – review and editing. **Akira Suekane:** Investigation; project administration; writing – review and editing. **Koji Morishita:** Project administration; supervision; validation; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

Authors declare no conflicts of interest for this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Approval of the research protocol by an Institutional Reviewer Board: This study was approved by the Ethics Committee of the lead institution, Tsuchiura Kyodo General Hospital (approval number: 2023FY181) and subsequently by the ethics committees of all participating institutions.

Informed Consent: As this was a retrospective study, the requirement for obtaining informed consent was waived, and an opt-out method was applied, allowing patients to refuse participation through the hospital's online disclosure of information.

Registry and the registration no. of the study/trial: Our study was retrospectively registered at the University Hospital Medical Information Network Clinical Trials Registry on May 14, 2024 (registration ID, UMIN000054391).

Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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