Gastric Cancer
https://doi.org/10.1007/s10120-024-01538-x

ORIGINAL ARTICLE

# Importance of duodenal stump reinforcement to prevent stump leakage after gastrectomy: a large-scale multicenter retrospective study (KSCC DELICATE study)

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Received: 9 May 2024 / Accepted: 12 July 2024


## Abstract

**Background** The significance of reinforcement of the duodenal stump with seromuscular sutures and the effectiveness of reinforced staplers in preventing duodenal stump leakage remain unclear. We aimed to explore the importance of duodenal stump reinforcement and determine the optimal reinforcement method for preventing duodenal stump leakage.

**Methods** This retrospective cohort study was conducted between January 1, 2012 and December 31, 2021, with data analyzed between December 1, 2022 and September 30, 2023. This multicenter study across 57 institutes in Japan included 16,475 patients with gastric cancer who underwent radical gastrectomies. Elective open or minimally invasive (laparoscopic or robotic) gastrectomy was performed in patients with gastric cancer.

**Results** Duodenal stump leakage occurred in 153 (0.93%) of 16,475 patients. The proportions of males, patients aged ≥ 75 years, and ≥ pN1 were higher in patients with duodenal stump leakage than in those without duodenal stump leakage. The incidence of duodenal stump leakage was significantly lower in the group treated with reinforcement by seromuscular sutures or using reinforced stapler than in the group without reinforcement (0.72% vs. 1.19%, $p = 0.002$). Duodenal stump leakage incidence was also significantly lower in high-volume institutions than in low-volume institutions (0.70% vs. 1.65%, $p = 0.047$). The rate of duodenal stump leakage-related mortality was 7.8% (12/153). In the multivariate analysis, preoperative asthma and duodenal invasion were identified as independent preoperative risk factors for duodenal stump leakage-related mortality.

**Conclusions** The duodenal stump should be reinforced to prevent duodenal stump leakage after radical gastrectomy in patients with gastric cancer.

**Keywords** Gastric cancer · Duodenal stump leakage · Duodenal stump reinforcement · Seromuscular suture · Reinforced stapler

## Introduction

Distal and total gastrectomies are standard surgical procedures for resectable gastric cancer, with the choice of surgical technique depending on cancer location, depth of tumor invasion, and lymph node metastasis status. In recent years, these procedures have been increasingly performed using minimally invasive surgery (MIS), including laparoscopic or robot-assisted surgery, with MIS used in 53.8% of distal gastrectomies and 30.4% of total gastrectomies in Japan [1]. There are a variety of reconstruction techniques that can be applied after distal or total gastrectomy.

Duodenal stump leakage (DSL) is a postoperative complication specific to patients with the formation of a blind end of the duodenum, e.g., Roux-en-Y or Billroth-II reconstruction. The incidence of DSL after radical gastrectomy with a duodenal stump ranges between 1.8% and 7.7% [2, 3], with a

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mortality rate of 7–67% [4]. Several large-scale retrospective studies of DSL have been reported [5, 6]. The largest study to date of 8,268 gastrectomy patients from 16 centers in Italy showed that the laparoscopic approach is associated with a higher risk of developing DSL (odds ratio [OR] = 5.6, 95% confidence interval [CI] 2.7–10.6, $P < 0.001$) [5]. However, most patients underwent open surgery (7,987 and 281 by the laparotomic and laparoscopic approaches, respectively). The period covered by this study was from 1990 to 2011 when laparoscopic gastrectomy was initiated and developed. In a large-scale Japanese study of 965 patients who underwent laparoscopic gastrectomies [6], the incidence of DSL was 1.0% (10/965), which is quite low. However, this result was reported from a single high-volume institute and possibly did not reflect real-world data.

Although manual reinforcement of the duodenal stump is equally effective in preventing DSL development in both laparoscopic [6–8] and open [9] surgeries, it may not be routinely performed [10] because of its technical difficulty during laparoscopic gastrectomies. As an alternative to seromuscular suturing, the use of a linear stapler with a bioabsorbable polyglycolic acid (PGA) sheet for duodenal stump closure and reinforcement is simple and easy in laparoscopic surgery; the incidence of DSL with this method is 2% [11]. However, this was a single-arm study, and a comparison of safety and feasibility with seromuscular suture reinforcement has not been performed. As gastric cancer surgery has become less invasive in recent years, the real-world state of gastric cancer surgery needs to be updated. As DSL is a relatively rare complication, larger studies are needed to evaluate the technique's safety.

Thus, we aimed to explore the clinical impact of seromuscular suture reinforcement of the duodenal stump and assess whether using a stapler with a reinforcing material as an alternative method for seromuscular suturing prevents DSL following gastrectomies for gastric cancer (all-case survey). Furthermore, we investigated the effects of duodenal stump reinforcement on patients with DSL (DSL case-specific survey).

## Methods

### Study design

The protocol of this multicenter retrospective study was approved by the Institutional Ethics Committee of the Gunma University Hospital (protocol number: HS2021-258). Informed consent was obtained through an opt-out system on the website. The inclusion criteria for patients registered through a survey questionnaire were as follows: (a) pathologically diagnosed with resectable gastric cancer, (b) underwent elective gastrectomy with a duodenal stump, (c) aged > 20 years, and (d) treated between January 2012 and December 2021. Herein, DSL was diagnosed as the presence of duodenal juice in the surgical drainage or its leakage through the abdominal wall or confirmed based on computed tomography, fistulography, and/or surgical findings if performed [12].

### Data collection

Figure 1 shows a flowchart of the study population. A questionnaire was sent by e-mail to 95 institutions for a retrospective observational study by the Kyushu Study Group of Clinical Cancer (KSCC). Eighty-two institutions agreed to participate in the survey. Of those institutions, 25 were excluded because of incomplete data. Finally, 33,876 patients from 57 institutions were initially identified. Among them, 17,384 patients without duodenal stumps and 17 with incomplete data were excluded. Finally, 16,475 patients with duodenal stumps from 57 institutions (median [range] of 238 [3–970] patients per institute) were included in the analysis. This study was conducted in two stages (Fig. 1): first, a survey of all 16,475 patients (all-case survey) and second, a detailed survey of patients with DSL (DSL case-specific survey). In all cases surveyed, aggregated data for each facility were collected rather than data for each individual patient. Tumors were classified according to the 8th edition of the TNM classification of the International Union against Cancer. All patients underwent radical gastrectomies with lymphadenectomies in accordance with the guidelines of the Japanese Gastric Cancer Association [13]. Duodenal stump closure methods were classified into the following three categories: 1) using standard stapler (SS) without seromuscular sutures (SMS), 2) using SS with SMS, and 3) using reinforced stapler (RS). The relationship between duodenal stump closure method and the incidence of DSL was examined by comparing the patients with stump reinforcement (SS with SMS and RS) to those without stump reinforcement (SS without SMS). Institutions were divided into two groups, namely high volume (> median) and low volume (< median), on the basis of the total number of radical gastrectomies with duodenal stumps performed between 2012 and 2021. In the DSL case-specific survey, patients with DSLs were divided into two groups: those whose duodenal stumps were reinforced with SMS and others. Clinicopathological characteristics, perioperative data, and postoperative complications were investigated. The severity of postoperative complications was evaluated according to the Clavien–Dindo classification (C–D) [14], and adverse events were defined as C–D grade IIIa or higher.

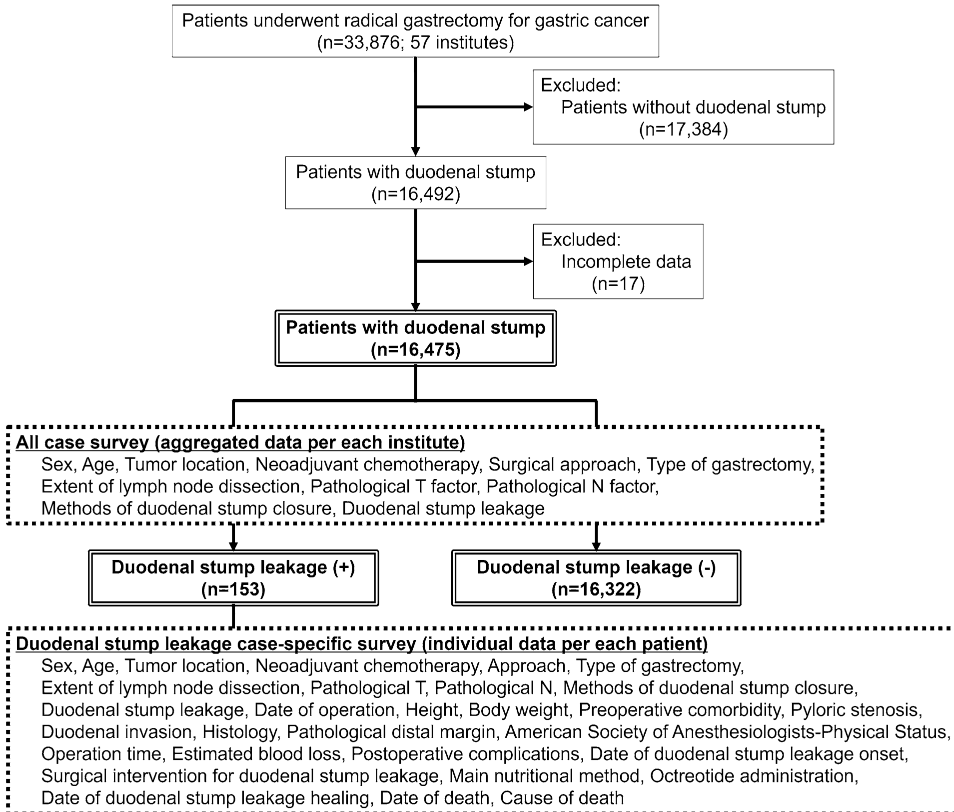


**Fig. 1** Flow chart of the study population

## Statistical analysis

Comparison analyses were conducted using Fisher's exact test for categorical variables and the Mann–Whitney U test for quantitative variables. The Bonferroni–Holm correction was used for comparisons among the three groups. Independent risk factors associated with DSL-related mortality were analyzed using logistic regression analysis, and ORs were estimated using 95% CIs. Differences were considered significant at $P$ values $< 0.05$. All data were analyzed using EZR version 1.64, a freely available, easy-to-use software for medical statistics [15].

## Results

### Patient characteristics with or without DSL in the entire cohort

The clinicopathological characteristics of patients with and without DSLs are summarized in Table 1. DSLs were observed in 153/16,475 (0.93%) patients. The proportions of males ($P < 0.001$), patients aged $\geq 75$ years ($P = 0.006$), and $\geq$ pN1 ($P = 0.018$) were higher in patients with DSLs than in those without DSLs. Table 2 shows the relationship between the DSL rate and methods of duodenal stump closure. The DSL rates when using SS with SMS, RS, and SS without SMS were 0.67%, 1.08%, and 1.19%, respectively. The incidence of DSLs was significantly lower in the groups treated with reinforcement by SMS and by RS than in the group without reinforcement (0.72% vs. 1.19%, $P = 0.002$). The incidence of DSLs was significantly lower in the SS with SMS group than in the SS without SMS group ($P = 0.003$). Meanwhile, the RS group showed no significant difference between both the SS without SMS group ($P = 0.885$) and the SS with SMS group ($P = 0.282$).

### Relationship between the DSL rate and hospital volume among patients who underwent gastrectomies

Figure 2 shows the relationship between the DSL rate and hospital volume among patients who underwent gastrectomies with duodenal stumps for resectable gastric cancer. The incidence of DSL was significantly lower in high-volume institutions than in low-volume institutions (0.70% vs. 1.65%, $P = 0.047$). While MIS was performed in 47.6% of all patients in the high-volume institutions, 50.2% and 9.2% underwent SMS reinforcement and received a RS at the duodenal stump, respectively, which was higher than the rate in the low-volume institutions (Table 3).

**Table 1** Clinicopathologic characteristics of patients with or without duodenal stump leakage

| Variables | All patients (n = 16,475) | Duodenal stump leakage | | *P*-value |
|---|---|---|---|---|
| | | Yes (n = 153) | No (n = 16,322) | |
| Sex | | | | |
| Male | 11,729 (71.2%) | 128 (83.7%) | 11,601 (71.1%) | < 0.001 |
| Female | 4,746 (28.8%) | 25 (16.4%) | 4,721 (28.9%) | |
| Age (years) | | | | |
| < 75 | 10,727 (65.1%) | 83 (54.2%) | 10,644 (65.2%) | 0.006 |
| ≥ 75 | 5,748 (34.9%) | 70 (45.8%) | 5,678 (34.8%) | |
| Tumor location | | | | |
| Lower | 4,488 (27.2%) | 52 (34.0%) | 4,436 (27.2%) | 0.179 |
| Middle | 6,905 (41.9%) | 59 (38.6%) | 6,846 (41.9%) | |
| Upper | 5,082 (30.9%) | 42 (27.4%) | 5,040 (30.9%) | |
| Neoadjuvant chemotherapy | | | | |
| Yes | 1,538 (9.3%) | 12 (7.8%) | 1,526 (9.3%) | 0.674 |
| No | 14,937 (90.7%) | 141 (92.2%) | 14,796 (90.7%) | |
| Approach | | | | |
| Open | 9,046 (54.9%) | 93 (60.8%) | 8,953 (54.9%) | 0.279 |
| Laparoscopic | 6,556 (39.8%) | 55 (35.9%) | 6,501 (39.8%) | |
| Robot assisted | 873 (5.3%) | 5 (3.3%) | 868 (5.3%) | |
| Type of gastrectomy | | | | |
| DG/R-Y | 6,525 (39.6%) | 62 (40.5%) | 6,463 (39.6%) | 0.136 |
| DG/B-II | 1,359 (8.3%) | 19 (12.4%) | 1,340 (8.2%) | |
| TG/R-Y | 8,591 (52.1%) | 72 (47.1%) | 8,519 (52.2%) | |
| Lymph node dissection | | | | |
| < D2 | 7,518 (45.6%) | 65 (42.5%) | 7,453 (45.7%) | 0.463 |
| ≥ D2 | 8,957 (54.4%) | 88 (57.5%) | 8,869 (54.3%) | |
| pT | | | | |
| ≤ pT1 | 6,247 (37.9%) | 45 (29.4%) | 6,202 (38.0%) | 0.060 |
| pT2 | 1,759 (10.7%) | 24 (15.7%) | 1,735 (10.6%) | |
| pT3 | 4,213 (25.6%) | 39 (25.5%) | 4,174 (25.6%) | |
| pT4 | 4,256 (25.8%) | 45 (29.4%) | 4,211 (25.8%) | |
| pN | | | | |
| pN0 | 8,362 (50.8%) | 63 (41.2%) | 8,299 (50.8%) | 0.018 |
| ≥ pN1 | 8,113 (49.2%) | 90 (58.8%) | 8,023 (49.2%) | |

*DG* distal gastrectomy; *TG* total gastrectomy; *R-Y* Roux-en-Y reconstruction; *B-II* Billroth-II reconstruction

**Table 2** Relationship between the methods of duodenal stump closure and duodenal stump leakage

| Duodenal stump reinforcement | Duodenal stump leakage | | Rate of DSL development |
|---|---|---|---|
| | Yes (n = 153) | No (n = 16,322) | |
| Yes (n = 9,269) | 67 | 9,202 | 0.72% a) |
| SS with SMS (n = 8,065) | 54 | 8,011 | 0.67% b) |
| RS (n = 1,204) | 13 | 1,191 | 1.08% c) |
| No (n = 7,206) | | | |
| SS without SMS (n = 7,206) | 86 | 7,120 | 1.19% d) |
| | a) vs. d) | | ***P* = 0.002** |
| | b) vs. d) | | ***P* = 0.003** |
| | b) vs. c) | | *P* = 0.282 |
| | c) vs. d) | | *P* = 0.885 |

*DSL* duodenal stump leakage; *SS* standard stapler; *SMS* seromuscular suture; *RS* reinforced stapler

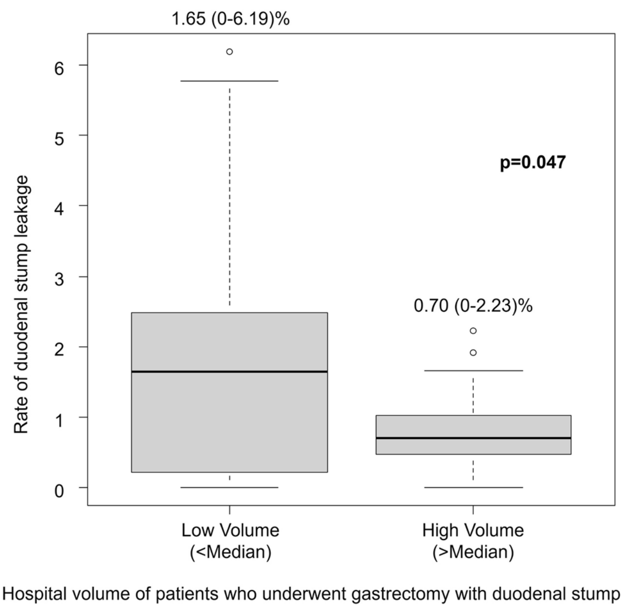


**Fig. 2** Rate of duodenal stump leakage according to the hospital volume of patients who underwent radical gastrectomy with duodenal stump

### Clinicopathological characteristics of patients with DSL according to the presence or absence of duodenal stump reinforcement by seromuscular sutures or reinforced staplers

The clinicopathological characteristics of patients with DSL according to the presence or absence of duodenal stump reinforcement are summarized in Online Resource 1. No significant differences were observed between the clinical features and reinforcement of the duodenal stump.

### Details of duodenal stump reinforcement methods and perioperative data in patients with DSLs

The associations between perioperative data and duodenal stump reinforcement in patients with DSLs are shown in Online Resource 2. Among the 153 patients who developed DSLs, the mortality rate was 7.8% (12 patients). Significantly fewer patients underwent reinforcement of the duodenal stump in MIS than in open surgery ($P < 0.001$). Although there was no significant difference in the operation time, the amount of blood loss was significantly higher in the reinforcement group (373 vs. 230 ml, $P = 0.046$), which was believed to be due to the higher rate of open surgery. The day of DSL onset was significantly shorter in the non-reinforcement group (P = 0.038) than in the reinforcement group. There were no significant between-group differences in the proportion of patients requiring surgical intervention or DSL-related mortality.

### Relationship between the severity of DSL and duodenal stump reinforcement

In total, 131 patients (85.6%) had postoperative complications other than DSLs (all grades), and 103 patients (67.3%) had complications classified as C–D Grade III or higher (Online Resource 3). These serious complications included intra-abdominal abscess, tracheal intubation, sepsis, intra-abdominal hemorrhage, and other organ failures. Notably, reinforcing the duodenal stump did not reduce the severity of DSL.

### Details of surgical intervention for patients with DSLs

Details of the surgical procedures performed after DSL onset (n = 68) are shown in Online Resource 4. Regarding the number of surgeries, 64 (94.1%) patients underwent a single surgery, three (4.4%) underwent two surgeries, and one (1.5%) underwent three surgeries. Intraperitoneal lavage and drainage were performed during all reoperations. Duodenal stump re-closure and duodenostomy were performed in 31 (45.6%) and 28 (41.2%) patients, respectively. None of the reoperation methods showed significant correlations with the reinforcement of the duodenal stump in the initial surgery.

### Results of univariate and multivariate analysis of risk factors for DSL-related mortality

Univariate analysis using a logistic regression model revealed the following clinicopathological characteristics as potentially associated with DSL-related mortality: preoperative cardiovascular disease, renal dysfunction, asthma, duodenal invasion of the tumor, postoperative tracheal intubation, sepsis, intra-abdominal hemorrhage, wound infection, tracheostomy, renal failure, and pneumonia. In the multivariate analysis, preoperative asthma (OR = 11.20; 95% CI 1.770–70.30, $P = 0.010$) and duodenal invasion (OR = 6.720; 95% CI 1.440–31.30, $P = 0.015$) were confirmed as independent preoperative risk factors for DSL-related mortality (Table 4). To identify independent preoperative risk factors for DSL-related mortality, surgical and postoperative factors were excluded from the multivariate analysis.

## Discussion

To the best of our knowledge, this is the largest multicenter retrospective study worldwide investigating DSLs after radical gastrectomies, and the study strongly shows the current real-world data in Japan, where MIS for resectable gastric cancer is increasing. Among our study cohort, the incidences of DSL and DSL-related mortality were 0.93% and 7.8%,

**Table 3** Clinicopathologic characteristics of patients by hospital volume for gastrectomy with the duodenal stump

| Variables | All patients (n = 16,475) | Hospital volume | | *P*-value |
|---|---|---|---|---|
| | | > Median (n = 12,706) | < Median (n = 3,769) | |
| Sex | | | | |
| Male | 11,729 (71.2%) | 8,960 (70.5%) | 2,769 (73.5%) | **< 0.001** |
| Female | 4,746 (28.8%) | 3,746 (29.5%) | 1,000 (26.5%) | |
| Age (years) | | | | |
| < 75 | 10,727 (65.1%) | 8,502 (66.9%) | 2,225 (59.0%) | **< 0.001** |
| ≥ 75 | 5,748 (34.9%) | 4,204 (33.1%) | 1,544 (41.0%) | |
| Tumor location | | | | |
| Lower | 4,488 (27.2%) | 3,462 (27.2%) | 1,026 (27.2%) | 0.983 |
| Middle | 6,905 (41.9%) | 5,413 (42.6%) | 1,492 (39.6%) | |
| Upper | 5,082 (30.9%) | 3,831 (30.2%) | 1,251 (33.2%) | |
| Neoadjuvant chemotherapy | | | | |
| Yes | 1,538 (9.3%) | 1,215 (9.6%) | 323 (8.6%) | 0.069 |
| No | 14,937 (90.7%) | 1,1491 (90.4%) | 3,446 (91.4%) | |
| Approach | | | | |
| Open | 9,046 (54.9%) | 6,657 (52.4%) | 2,389 (63.4%) | **< 0.001** |
| Laparoscopic | 6,556 (39.8%) | 5,210 (41.0%) | 1,346 (35.7%) | |
| Robot assisted | 873 (5.3%) | 839 (6.6%) | 34 (0.9%) | |
| Type of gastrectomy | | | | |
| DG/R-Y | 6,525 (39.6%) | 5,143 (40.5%) | 1,382 (36.7%) | **< 0.001** |
| DG/B-II | 1,359 (8.3%) | 1,176 (9.2%) | 183 (4.8%) | |
| TG/R-Y | 8,591 (52.1%) | 6,387 (50.3%) | 2,204 (58.5%) | |
| Lymph node dissection | | | | |
| < D2 | 7,518 (45.6%) | 5,787 (45.5%) | 1,731 (45.9%) | 0.682 |
| ≥ D2 | 8,957 (54.4%) | 6,919 (54.5%) | 2,038 (54.1%) | |
| pT | | | | |
| ≤ pT1 | 6,247 (37.9%) | 5,081 (40.0%) | 1,166 (30.9%) | 0.682 |
| pT2 | 1,759 (10.7%) | 1,289 (10.2%) | 470 (12.5%) | |
| pT3 | 4,213 (25.6%) | 3,156 (24.8%) | 1,057 (28.0%) | |
| pT4 | 4,256 (25.8%) | 3,180 (25.0%) | 1,076 (28.6%) | |
| pN | | | | |
| pN0 | 8,362 (50.8%) | 6,629 (52.2%) | 1,733 (46.0%) | **< 0.001** |
| ≥ pN1 | 8,113 (49.2%) | 6,077 (47.8%) | 2,036 (54.0%) | |
| Method of duodenal stump closure | | | | |
| SS without SMS | 7,206 (43.7%) | 5,161 (40.6%) | 2,045 (54.2%) | **< 0.001** |
| SS with SMS | 8,065 (49.0%) | 6,374 (50.2%) | 1,691 (44.9%) | |
| RS | 1,204 (7.3%) | 1,171 (9.2%) | 33 (0.9%) | |
| Duodenal stump leakage | | | | |
| Yes | 153 (0.9%) | 92 (0.7%) | 61 (1.6%) | **< 0.001** |
| No | 16,322 (99.1%) | 12,614 (99.3%) | 3,708 (98.4%) | |

*DG* distal gastrectomy; *TG* total gastrectomy; *R-Y* Roux-en-Y reconstruction; *B-II* Billroth-II reconstruction; *SS* standard stapler; *SMS* seromuscular suture; *RS* reinforced stapler; *pT* pathological T factor; *pN* pathological N factor

respectively. The most effective method to prevent DSL is to transect the duodenum using a SS and then reinforce the staple line with SMS. However, the safety of using a stapler with a reinforcing material was not found to be statistically significant compared with reinforcement with SMS. We found no significant correlation between reinforcement and severe complications (C–D grade ≥ III) or DSL-related mortality after the onset of DSL; thus, reinforcement of the duodenal stump may not influence DSL severity.

Among various risk factors for DSL, an unreinforced duodenal stump has been identified as an independent risk factor for DSL [2, 7, 16]. Reinforcement of the duodenal stump

**Table 4** Results of univariate and multivariate analyses of risk factors for DSL-related mortality

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95% CI | *P*-value | Odds ratio | 95% CI | *P*-value |
| Preoperative factors | | | | | | |
| Sex, female | 2.860 | 0.789–10.3 | 0.110 | NA | | |
| Age, ≥ 75 years | 1.200 | 0.370–3.910 | 0.759 | NA | | |
| BMI, > median | 0.986 | 0.303–3.200 | 0.981 | NA | | |
| Tumor location, lower | 2.990 | 0.899–9.930 | 0.074 | NA | | |
| ASA-PS, ≥ III | 3.160 | 0.929–10.70 | 0.066 | NA | | |
| Lauren classification, diffuse | 2.260 | 0.682–7.460 | 0.183 | NA | | |
| Preoperative comorbidities | | | | | | |
| Hypertension | 0.905 | 0.279–2.940 | 0.869 | NA | | |
| Cardiovascular disease | 3.700 | 1.110–12.30 | **0.033** | 2.840 | 0.762–10.60 | 0.120 |
| Diabetes mellitus | 1.180 | 0.302–4.640 | 0.810 | NA | | |
| Renal dysfunction | 5.540 | 1.250–24.60 | **0.025** | 3.180 | 0.586–17.30 | 0.180 |
| COPD | 1.510 | 0.173–13.20 | 0.709 | NA | | |
| Asthma | 11.400 | 2.210–59.00 | **0.004** | 11.200 | 1.770–70.30 | **0.010** |
| Liver dysfunction | 2.050 | 0.226–18.50 | 0.525 | NA | | |
| Steroid administration | 6.320 | 0.530–75.30 | 0.145 | NA | | |
| Pyloric stenosis | 2.150 | 0.422–11.00 | 0.357 | NA | | |
| Duodenal invasion | 8.310 | 2.060–33.60 | **0.003** | 6.720 | 1.440–31.30 | **0.015** |
| pT, pT4 | 1.800 | 0.541–6.020 | 0.337 | NA | | |
| pN, ≥ pN1 | 0.978 | 0.296–3.230 | 0.971 | NA | | |
| Surgical/postoperative factors | | | | | | |
| Operation time, > median | 1.010 | 0.312–3.300 | 0.981 | NA | | |
| Estimated blood loss, > median | 0.479 | 0.138–1.660 | 0.247 | NA | | |
| Approach, MIS | 1.610 | 0.494–5.250 | 0.429 | NA | | |
| Type of gastrectomy, TG | 0.789 | 0.239–2.600 | 0.697 | NA | | |
| Lymph node dissection, ≥ D2 | 0.339 | 0.098–1.180 | 0.089 | NA | | |
| Methods of duodenal stump closure | | | | | | |
| SS with SMS | 2.800 | 0.843–9.290 | 0.093 | NA | | |
| Complications (≥ Grade 3a) | | | | | | |
| Intra-abdominal abscess | 1.460 | 0.443–4.820 | 0.534 | NA | | |
| Tracheal intubation | 29.500 | 7.100–123.0 | **< 0.001** | NA | | |
| Sepsis | 35.500 | 8.360–150.0 | **< 0.001** | NA | | |
| Intra-abdominal hemorrhage | 33.200 | 8.230–134.0 | **< 0.001** | NA | | |
| Wound infection | 5.370 | 1.410–20.50 | **0.014** | NA | | |
| Anastomotic leakage | 3.940 | 0.929–16.70 | 0.063 | NA | | |
| Tracheostomy | 22.500 | 5.570–90.90 | **< 0.001** | NA | | |
| Renal failure | 27.200 | 6.440–115.0 | **< 0.001** | NA | | |
| Pneumonia | 19.400 | 4.540–83.10 | **< 0.001** | NA | | |
| Acute pancreatitis | 4.500 | 0.802–25.20 | 0.087 | NA | | |
| Arrhythmia | 12.700 | 0.744–218.0 | 0.079 | NA | | |
| Day of DSL onset, > median | 1.550 | 0.468–5.100 | 0.474 | NA | | |
| Surgical intervention | 1.840 | 0.556–6.070 | 0.319 | NA | | |
| Main nutritional methods, TPN | 0.629 | 0.190–2.080 | 0.446 | NA | | |
| Octreotide administration | 2.200 | 0.673–7.220 | 0.192 | NA | | |

*DSL* duodenal stump leakage; *BMI* body mass index; *ASA-PS* American Society of Anesthesiologists-Physical Status; *COPD* chronic obstructive pulmonary disease; *MIS* minimally invasive surgery; *TG* total gastrectomy; *SS* standard stapler; *SMS* seromuscular suture; *TPN* total parenteral nutrition; *CI* confidence interval with SMS is often omitted during laparoscopic gastrectomy because of its technical difficulty [5, 10]. Our study similarly showed that among patients with DSL, significantly fewer patients treated with MIS than those treated with open surgery underwent duodenal stump reinforcement using SMS or RS. The incidence of DSL has previously been suggested to be higher after laparoscopic gastrectomies than open gastrectomies [16–18], and it is assumed that the main reason for this is that duodenal stump reinforcement by SMS is omitted. Although Ri et al. [6] reported that the operative duration is extended by 33 min for laparoscopic distal gastrectomy and 40 min for laparoscopic total gastrectomy in the reinforcement group using buried sutures compared with that in the non-reinforcement group, a significant reduction in the incidence of DSL would be of greater benefit to patients undergoing gastrectomies, even if the operative time is extended. Our study showed that the incidence of DSL was significantly lower in high-volume institutions, where many gastrectomies with duodenal stumps are performed. A detailed comparison of high- and low-volume institutions showed that although there were various clinicopathological differences, high-volume institutions had a significantly higher rate of duodenal stump reinforcement. This also suggests the importance of reinforcing the duodenal stump with SMS to prevent DSL. Suturing methods for reinforcing the staple line at the duodenal stump include Lembert's sutures [19], the barbed suture method [20], the single-purse string suture method [21], and the handover method [22]. Each surgeon can use the most suitable method to reinforce the duodenal stump even during laparoscopic surgery because data on direct comparison among these reinforcement methods are not available [23]. Irrespective of the method used, it is important to bury the staple line and surrounding duodenal wall sufficiently so that the duodenal stump can withstand peristaltic pressure. Recently, robot-assisted gastrectomy has become increasingly popular in gastric cancer surgery. Technical difficulties associated with duodenal stump reinforcement with SMS may be overcome in robot-assisted surgery.

As an alternative to sutures, the use of a reinforced linear stapler with PGA sheets [11] has the advantages of shortening the reinforcement time and good generalizability for these applications regardless of technical difficulties. Bleeding from the staple line and minor postoperative anastomotic leakage can be reduced using linear staplers with PGA sheets during gastroduodenal anastomosis [24]. However, the incidence of DSL using this RS is 2% [11], which is by no means low. In our present study, resection with the use of RS is statistically equivalent to resection using a SS with SMS and may be acceptable as a method of duodenal stump reinforcement. However, it also shows a statistically similar DSL rate to resection using a SS without SMS reinforcement. If the tumor extends beyond the pylorus into the duodenum, suture reinforcement may not be performed as there is an insufficient vertical margin after resection, making it difficult to perform seromuscular suturing of the staple line of the duodenal stump. In such patients, duodenal resection using a linear stapler with PGA sheets may be effective. Further studies focusing on the usefulness of a linear stapler with PGA sheets for such patients are needed.

After DSL onset, nonsurgical treatments are typically the preferred choice in patients with a stable general condition, localized intra-abdominal abscess, and adequate drainage. Surgical treatment should be reserved for cases in which nonoperative management does not allow adequate leakage drainage, leading to secondary complications such as intra-abdominal bleeding, sepsis, other leakage, and intestinal obstruction [4, 7, 25, 26]. When duodenal fluid leakage is combined with infection, the ability of the duodenal fluid to digest proteins becomes high, causing surrounding blood vessels and anastomoses to rupture, which can lead to death. Abdominal abscess drainage, transhepatic biliary drainage [27, 28], duodenostomy [29], fistula obliteration by glue injection [30], and endoscopic procedures such as DSL closure by over-the-scope clip [31] are nonsurgical treatments for DSL. Patients with sepsis and/or hemodynamic instability often require surgical intervention. In our study, 44.4% of patients underwent surgical treatment, mainly peritoneal drainage, for infection control. Other procedures include abdominal drainage-to-tube duodenostomy [32], fistula repair with a rectus abdominis flap [33], fistula closure by Roux-en-Y duodenojejunostomy [34], biliogastric diversion [35], and pancreatoduodenectomy [36]. Patients with DSL who require surgical intervention usually have sepsis, intra-abdominal hemorrhage, respiratory failure, and renal failure, resulting in poor prognosis. Our study showed that the presence or absence of surgical intervention was not significantly correlated with DSL-related mortality, which may be a result of appropriate surgery being performed in patients who required it.

Among the risk factors for DSL-related mortality, the identification of preoperative factors is important in clinical practice. Asthma, which was identified as an independent risk factor for mortality in this study, is a significant risk factor for postoperative complications in major surgery [37, 38]. Lin et al. [39] further reported that asthma increased the incidence of postoperative pneumonia (OR = 1.48; 95% CI 1.34–1.64), septicemia (OR = 1.11; 95% CI 1.02–1.21), and urinary tract infection (OR = 1.17; 95% CI 1.09–1.26) when compared with patients without asthma. Furthermore, preoperative emergency care for asthma was significantly associated with postoperative 30 day in-hospital mortality (OR = 1.84; 95% CI 1.11–3.04). Careful preoperative control of active asthma is important when planning gastrectomy with a duodenal stump for patients with gastric cancer. Although only preoperative asthma was identified as an independent risk factor for mortality, other preoperative underlying diseases such as cardiovascular disease and renal dysfunction were also risk factors in the univariate analyses. We believe that it is important to pay closer attention to the early detection of DSL onset and careful management for such patients. Placing an additional drainage tube near the duodenal stump may prevent subsequent serious illness, even if DSL does occur.

This study had some limitations. First, this was a retrospective observational study in which surgeons from multiple institutions participated, and the answers to the enrollment questionnaire were retrospectively derived on the basis of medical records. Second, because the aggregated data for each facility were collected via an all-case survey, although it was possible to compare the presence or absence of DSL onset and various clinicopathological factors among all patients with duodenal stumps, it was not possible to perform a multivariate analysis to investigate the correlation between each clinicopathological factor and the risk factors for developing DSL. Third, the RS group may have included patients in whom it was not practical to bury the stump owing to duodenal invasion, which may have resulted in a selection bias. Although there are some limitations, this study is, to the best of our knowledge, the largest survey to date to investigate the number of gastric cancer surgeries using real-world data. This is especially important as MIS is becoming increasingly widespread. Mortality due to postoperative complications of radical gastrectomy for gastric cancer should be prevented in all patients. Therefore, we anticipate that our findings will contribute to providing novel and valuable information about this rare but severe complication. However, the usefulness of a RS for patients with duodenal invasion requires further large-scale investigation.

## Conclusions

The present study revealed that the incidence of DSLs after gastrectomies with duodenal stumps was 0.93%, which was lower than that found in previous estimations. However, the mortality rate was 7.8% (12/153) when DSL developed. Duodenal stump reinforcement should be performed to prevent DSL, a complication associated with a high mortality rate if its development is not prevented. While SMS stands as the preferable method of reinforcement, the use of a RS may also be acceptable. For patients who are at a high risk of mortality after the onset of DSLs (i.e., those with poor general conditions or duodenal invasions), it is important to be more careful to prevent subsequent serious events.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s10120-024-01538-x.

**Acknowledgements** We would like to thank the individuals from each participating institution (Online Resource 5) who responded to our questionnaire survey. We would also like to thank Ms. Sanae Sakamoto and the staff at KSCC for their excellent data collection and management, secretarial assistance, and support. The authors thank Editage (www.editage.com) for English language editing.

**Author contributions** Drs. Sano and Saeki had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Sano, Hiki, Oki, Baba, Shirabe, and Saeki. Acquisition, analysis, or interpretation of data: Sano, Imai, Yamaguchi, Bamba, Shinno, Kawashima, Tokunaga, Enokida, Tsukada, Hatakeyama, Koga, Kuwabara, Urakawa, Arai, Yamamoto, Yasufuku, Iwasaki, Sakon, Honboh, Kawaguchi, Kusumoto, and Shibao. Drafting of the manuscript: Sano, Hiki, Nakazawa, Sakai, Sohda, Oki, Baba, and Saeki. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Sano, Hiki, Sohda, and Saeki. Administrative, technical, or material support: Nakazawa, Sakai, and Sohda. Supervision: Hiki, Oki, Baba, and Shirabe.

**Funding** The authors declare no sources of funding.

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

## Declarations

**Conflicts of interest** The authors declare that they have no conflicts of interest.

**Ethical approval** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent to be included in the study, or the equivalent, was obtained from all patients.

## References

1. Kajiwara Y, Takahashi A, Ueno H, Kakeji Y, Hasegawa H, Eguchi S, et al. Annual report on National clinical database 2020 for gastroenterological surgery in Japan. Ann Gastroenterol Surg. 2023;7:367–406.
2. Paik HJ, Lee SH, Choi CI, Kim DH, Jeon TY, Kim DH, et al. Duodenal stump fistula after gastrectomy for gastric cancer: risk factors, prevention, and management. Ann Surg Treat Res. 2016;90:157–63.
3. Patricia YP, Ka Fai Kevin W, Fong Yee L, Kiu Jing F, Kylie S, Siu KL. Duodenal stump leakage. Lessons to learn from a large-scale 15-year cohort study. Am J Surg. 2020;220(4):976–81.
4. Cozzaglio L, Coladonato M, Biffi R, Coniglio A, Corso V, Dionigi P, et al. Duodenal fistula after elective gastrectomy for malignant disease: an Italian retrospective multicenter study. J Gastrointest Surg. 2010;14:805–11.
5. Cozzaglio L, Giovenzana M, Biffi R, Cobianchi L, Coniglio A, Framarini M, et al. Surgical management of duodenal stump fistula after elective gastrectomy for malignancy: an Italian retrospective multicenter study. Gastric Cancer. 2016;19:273–9.
6. Ri M, Hiki N, Ishizuka N, Ida S, Kumagai K, Nunobe S, et al. Duodenal stump reinforcement might reduce both incidence and severity of duodenal stump leakage after laparoscopic gastrectomy with Roux-en-Y reconstruction for gastric cancer. Gastric Cancer. 2019;22:1053–9.

7. Gu L, Zhang K, Shen Z, Wang X, Zhu H, Pan J, et al. Risk factors for duodenal stump leakage after laparoscopic gastrectomy for gastric cancer. J Gastric Cancer. 2020;20:81–94.
8. Aurello P, Sirimarco D, Magistri P, Petrucciani N, Berardi G, Amato S, et al. Management of duodenal stump fistula after gastrectomy for gastric cancer: systematic review. World J Gastroenterol. 2015;21:7571–6.
9. Pugliese R, Maggioni D, Sansonna F, Scandroglio I, Ferrari GC, Di Lernia S, et al. Total and subtotal laparoscopic gastrectomy for adenocarcinoma. Surg Endosc. 2007;21:21–7.
10. Cai ZH, Zang L, Yang HK, Kitano S, Zheng MH. Survey on laparoscopic total gastrectomy at the 11th China-Korea-Japan laparoscopic gastrectomy joint seminar. Asian J Endosc Surg. 2017;10:259–67.
11. Misawa K, Yoshikawa T, Ito S, Cho H, Ito Y, Ogata T. Safety and feasibility of linear stapling device with bioabsorbable polyglycolic acid sheet for duodenal closure in gastric cancer surgery: a multi-institutional phase II study. World J Surg. 2019;43:192–8.
12. Ali BI, Park CH, Song KY. Outcomes of non-operative treatment for duodenal stump leakage after gastrectomy in patients with gastric cancer. J Gastric Cancer. 2016;16:28–33.
13. Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). Gastric Cancer. 2023;26:1–25.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–13.
15. Kanda Y. Investigation of the freely available easy-to-use software "EZR" for medical statistics. Bone Marrow Transpl. 2013;48:452–8.
16. Orsenigo E, Bissolati M, Socci C, Chiari D, Muffatti F, Nifosi J, et al. Duodenal stump fistula after gastric surgery for malignancies: a retrospective analysis of risk factors in a single centre experience. Gastric Cancer. 2014;17:733–44.
17. Kostakis ID, Alexandrou A, Armeni E, Damaskos C, Kouraklis G, Diamantis T, et al. Comparison between minimally invasive and open gastrectomy for gastric cancer in Europe: a systematic review and meta-analysis. Scand J Surg. 2017;106:3–20.
18. Sarela AI. Entirely laparoscopic radical gastrectomy for adenocarcinoma: lymph node yield and resection margins. Surg Endosc. 2009;23:153–60.
19. Inoue K, Michiura T, Fukui J, Mukaide H, Ozaki T, Miki H, et al. Staple–line reinforcement of the duodenal stump with intracorporeal lembert's sutures in laparoscopic distal gastrectomy with Roux-en-Y reconstruction for gastric cancer. Surg Laparosc Endosc Percutan Tech. 2016;26:338–42.
20. Kim SY, Nam SH, Min JS, Kim MC. Laparoscopic reinforcement suture on staple-line of duodenal stump using barbed suture during laparoscopic gastrectomy for gastric cancer. Ann Surg Treat Res. 2017;93:305–9.
21. He H, Li H, Ye B, Liu F. Single purse-string suture for reinforcement of duodenal stump during laparoscopic radical gastrectomy for gastric cancer. Front Oncol. 2019;9:1020.
22. Du J, Xue H, Zhao L, Zhang Z, Hu J. Handover method: simple, classic and harmonized intracorporeal closure of stapled duodenal stump during laparoscopic gastrectomy. J Surg Oncol. 2021;124:41–8.
23. Liu X, Kong W, Ying R, Shan Y, Yin G. Reinforcement methods of duodenal stump after laparoscopic gastrectomy for gastric cancer: a review. Heliyon. 2023;9: e17272.
24. Nagahisa Y, Morikawa A, Kato T, Hashida K, Ome Y, Kawamoto K. Feasibility of endo GIA™ reinforced reload with tri-staple™ technology for delta-shaped anastomosis. Asian J Surg. 2018;41:448–53.
25. Babu BI, Finch JG. Current status in the multidisciplinary management of duodenal fistula. Surgeon. 2013;11:158–64.
26. Zizzo M, Ugoletti L, Manzini L, Castro Ruiz C, Nita GE, Zanelli M, et al. Management of duodenal stump fistula after gastrectomy for malignant disease: a systematic review of the literature. BMC Surg. 2019;19:55.
27. Cozzaglio L, Cimino M, Mauri G, Ardito A, Pedicini V, Poretti D, et al. Percutaneous transhepatic biliary drainage and occlusion balloon in the management of duodenal stump fistula. J Gastrointest Surg. 2011;15:1977–81.
28. Villar R, Fernàndez R, Gonzàlez J, Oliver JM, Parga G, Garcìa-Hidalgo E. High-output external duodenal fistula: treatment with percutaneous transhepatic biliary/duodenal drainage. Cardiovasc Intervent Radiol. 1996;19:371–3.
29. Oh JS, Lee HG, Chun HJ, Choi BG, Lee SH, Hahn ST, et al. Percutaneous management of postoperative duodenal stump leakage with foley catheter. Cardiovasc Intervent Radiol. 2013;36:1344–9.
30. Bianchi A, Solduga C, Ubach M. Percutaneous obliteration of a chronic duodenal fistula. Br J Surg. 1988;75:572.
31. Bini R, Coppola F, Recchia S, Fusca M, Gaia S, Leli R. Endoscopic treatment of postgastrectomy duodenal fistula with an over-the-scope clip. Surg Innov. 2011;18:102–4.
32. Levy E, Cugnenc PH, Frileux P, Hannoun L, Parc R, Huguet C, et al. Postoperative peritonitis due to gastric and duodenal fistulas. Operative management by continuous intraluminal infusion and aspiration: report of 23 cases. Br J Surg. 1984;71(7):543–6.
33. Chander J, Lal P, Ramteke VK. Rectus abdominis muscle flap for high-output duodenal fistula: novel technique. World J Surg. 2004;28:179–82.
34. Ujiki GT, Shields TW. Roux-en-Y operation in the management of postoperative fistula. Arch Surg. 1981;116:614–7.
35. Milias K, Deligiannidis N, Papavramidis TS, Ioannidis K, Xiros N, Papavramidis S. Biliogastric diversion for the management of high-output duodenal fistula: report of two cases and literature review. J Gastrointest Surg. 2009;13:299–303.
36. Musicant ME, Thompson JC. The emergency management of lateral duodenal fistula by pancreaticoduodenectomy. Surg Gynecol Obstet. 1969;128:108–14.
37. İlhan S, Özkan S, Baştopçu M, Koçoğullari CU. Investigation of the effect of asthma on mortality and morbidity after coronary artery bypass surgery. Turk Thorac J. 2020;21:163–8.
38. Motono N, Ishikawa M, Iwai S, Yamagata A, Iijima Y, Uramoto H. Analysis of risk factors for postoperative complications in non-small cell lung cancer: comparison with the Japanese National Clinical Database risk calculator. BMC Surg. 2022;22:180.
39. Lin CS, Chang CC, Yeh CC, Chung CL, Chen TL, Liao CC. Postoperative adverse outcomes in patients with asthma: a nationwide population-based cohort study. Medicine (Baltimore). 2016;95: e2548.

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