Surgical Outcomes Following Early Drain Removal After Distal Pancreatectomy in Elderly Patients

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Abstract. Background/Aim: The efficacy and safety of early drain removal following distal pancreatectomy in elderly patients are unclear. We aimed to investigate the short-term surgical outcomes following early drain removal after distal pancreatectomy in elderly patients. Patients and Methods: Fifty-seven patients aged ≥70 years who underwent distal pancreatectomy at our Hospital were enrolled in the study. Data were retrospectively analyzed to evaluate the short-term surgical outcomes following early drain removal after distal pancreatectomy in elderly patients. Results: The incidence of pancreatic fistula following distal pancreatectomy in the early-removal group was significantly lower vs. the conventional group (p=0.022). Multivariate analysis revealed that early drain removal was an independent factor for reducing the risk of pancreatic fistula after distal pancreatectomy in elderly patients (p=0.042). Conclusion: Early drain removal following distal pancreatectomy is an effective and safe surgical perioperative management procedure to prevent pancreatic fistula in elderly patients.

General surgery for elderly patients has been increasing with aging populations, worldwide (1). Additionally, pancreatic resection for elderly patients has been gradually accepted because the surgical outcomes after pancreatectomy were not inferior compared to younger patients (2-5).

Distal pancreatectomy (DP) for benign or malignant disease located in the left pancreas is considered a safe surgical procedure, with low mortality of 0-0.3% with recent advances in surgical techniques and management; however, morbidity associated with DP remains high (6). Pancreatic fistula is one of the main complications after DP, occurring in 18-39% of patients undergoing DP, and can lead to intra-abdominal abscess or postoperative hemorrhage, which prolong the length of postoperative hospital stay and increase medical costs (6-9). Regarding elderly patients with organ functional impairment or frailty, even if not fatal, pancreatic fistula is a more serious complication compared to younger patients because of the possibility of postoperative loss of independence caused by pancreatic fistula. Therefore, safer surgical procedures or perioperative management are needed to minimize the incidence of pancreatic fistula after DP in elderly patients.

Although several randomized control trials closed the stump of remnant pancreas to attempt to decrease pancreatic fistula after DP, no definitive methods exist to prevent or decrease postoperative pancreatic fistula after DP (10-13). Recently, early drain removal has been reported to effectively reduce the incidence of postoperative pancreatic fistula after DP (14, 15). However, the surgical outcomes of early drain removal after DP in elderly patients are uncertain.

Considering population aging (16), studies involving only elderly patients are needed. Therefore, we aimed to assess the short-term surgical outcomes following early drain removal after DP compared with conventional drain removal in a cohort of only elderly patients.

Patients and Methods

Patients. Between August 2010 and August 2019, 95 patients underwent DP at the Tottori University Hospital. We considered patients aged ≥70 years as elderly patients (17), and we reviewed data for 58 patients (61.1%) aged ≥70 years of the 95 patients undergoing DP. Of the 58 patients, we enrolled 57 patients who underwent DP using a stapler to transect the pancreatic parenchyma. We excluded one patient because the parenchyma was transected using an ultrasonically-activated device at the right side of the portal vein.
The Institutional Review Board of approved this retrospective study (No. 17A135) and waived the requirement for informed consent in this retrospective study.

**Determining the pancreatic transection line and measuring pancreatic thickness.** We determined the pancreatic transection line by assessing the tumor location using preoperative multidetector-row computed tomography in the portal phase. Generally, we divided the pancreatic parenchyma above the portal vein. However, in patients with low-grade malignant tumors or metastatic tumors or benign disease located in the pancreatic tail, we shifted the transection line toward the pancreatic tail vs. the left edge of the portal vein. The final decision regarding the transection line was made intraoperatively by the surgeon according to the intraoperative ultrasonographic findings, to obtain safe surgical margins. The thickness of the expected pancreatic transection line was measured preoperatively using the axial view in the preoperative multidetector-row computed tomographic images.

**Closing the pancreatic stump and inserting the drain.** After January 2017, in all but one patient, we transected the pancreatic parenchyma using the Endo GIA tri-staple (Covidien, Tokyo, Japan), which is a triple-row stapler reinforced with a polyglycolic acid sheet (Neoveil®; GUNZE, Kyoto, Japan). One patient underwent pancreatic transection using the Endo GIA tri-staple without a polyglycolic acid sheet. From August 2010 to December 2016, we used an Endo GIA tri-staple with reinforcement for 4 patients and without reinforcement for 26 patients. We used the Endo GIA with double-row staples (Covidien) with reinforcement in seven patients; We used the Echelon 60 (Ethicon Endo-Surgery, Cincinnati, OH, USA), which is a triple-row stapler, with a green cartridge and 4.3-mm staple height, to divide the pancreatic parenchyma in one patient. Regarding the Endo GIA stapler, one of three cartridge types was selected depending on the thickness of the expected pancreatic transection line. We used the black cartridge with a 4.0-5.0-mm staple height for pancreatic parenchyma ≥10 mm thick and a purple cartridge with a 3.0-4.0-mm staple height for pancreatic parenchyma <10 mm. From August 2010 to July 2011, we used a green cartridge with a 4.3-mm staple height to divide the pancreatic parenchyma, regardless of the pancreatic thickness. The pancreas was compressed slowly for more than 10 minutes and transected carefully over 5 min. We then examined the stump of the remnant pancreas, namely, the staple line at the stump or the pancreatic parenchyma near the stump. Pancreatic parenchymal injury to the remnant pancreas and hemorrhage along the staple line were repaired immediately, if present. After peritoneal lavage, we placed a closed drain near the stump of the remnant pancreas. If necessary, another drain was placed in the left subphrenic space.

**Postoperative management.** Prophylactic antibiotics were administered until postoperative day (POD) 2 or earlier in all patients. Oral intake was started on POD 3 or 4 if no severe postoperative surgical complications occurred, such as severe pneumonia or paralytic ileus. Routinely, we measured the drain amylase level on POD 1 and 3. We also performed bacterial culture and a bacterial smear test of the drainage fluid to detect infection on POD 1 and 3. Regarding the criteria for removing the drain in our institution, from August 2010 to December 2016, we removed the drain on POD 3 or 4 if the amylase level in the drainage fluid on POD 3 was less than three times the serum value or less than <800 IU/l as an absolute value, and the drainage fluid was clear. After POD 5, the drain was maintained until the postoperative pancreatic fistula resolved, according to the judgment of the chief hepatobiliary–pancreatic surgeon in our institution. We considered the patients receiving drain removal according to this old criteria to constitute the conventional group. In contrast, after January 2017, we removed the drain on POD 3 or 4, regardless of the amylase level and drainage fluid volume, if infection was confirmed to be absent according to the bacterial smear test performed on POD 3. We considered the patients receiving drain removal based on the new criteria to constitute the early removal group.

**Definition of pancreatic fistula after DP.** Pancreatic fistula was defined according to the definition of the International Study Group on Pancreatic Surgery (18). Namely, in this study, we defined pancreatic fistula as follows: persistent drainage of >3 weeks, reinsertion of an intra-abdominal drain, and angiographic procedures for hemorrhage, which were classified as grade B, and reoperation classified as grade C.

**Clinicopathological variables.** We collected data for the following clinicopathological variables from the patients’ medical records: age, body mass index, and pancreatic ductal adenocarcinoma. Table I. Overall patient clinicopathological variables.

| Variable                         | Value          |
|----------------------------------|----------------|
| Age, median (range), (year)      | 77 (70-87)     |
| Gender (n, %)                    |                |
| Male                             | 38 (66.7%)     |
| Female                           | 19 (33.3%)     |
| Body mass index, median (range), (kg/m²) | 21.3 (14.0-28.8) |
| Histological diagnosis (n, %)    |                |
| Pancreatic ductal adenocarcinoma | 31 (54.4%)     |
| Acinar cell cancer               | 1 (1.8%)       |
| IPMN                             | 11 (19.3%)     |
| ITPN                             | 1 (1.8%)       |
| PNEN                             | 5 (8.8%)       |
| MCN                              | 2 (3.5%)       |
| SPN                              | 1 (1.8%)       |
| Metastatic pancreatic tumor      | 2 (3.5%)       |
| Other disease                    | 3 (5.3%)       |
| Surgical approach (n, %)         |                |
| Laparoscopy                      | 12 (21.1%)     |
| Spleen preservation (n, %)       |                |
| Present                          | 2 (3.5%)       |
| Absent                           | 55 (96.5%)     |
| Thickness of the pancreatic transection, median (range), (mm) | 11.1 (4.0-20.4) |
| Type of stapler (n, %)            |                |
| Triple-row stapler               | 50 (87.7%)     |
| Double-row stapler               | 7 (12.3%)      |
| Reinforcement (n, %)             |                |
| Present                          | 29 (50.9%)     |
| Absent                           | 28 (49.1%)     |
| Pancreatic fistula, (n, %)       | 17 (29.8%)     |

IPMN, Intraductal papillary mucinous neoplasm; ITPN, intraductal tubulopapillary neoplasm; PNEN, pancreatic neuroendocrine neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm.

Continuous variables are expressed as median with range.
using SPSS software (Version 24; IBM Corp., Armonk, NY, USA). statistically significant, and all statistical analyses were performed
receiver operating characteristic curve analysis to determine the cutoff
and multivariate logistic regression analyses were performed to clarify
clinicopathological variables between the two groups. We used

| Variable                                                                 | Early removal group (n=19) | Conventional group (n=38) | p-Value |
|-------------------------------------------------------------------------|-----------------------------|---------------------------|---------|
| Age, median (range), (year)                                             | 78.0 (70-87)                | 77.0 (70-87)              | 0.541   |
| Gender, male (n, %)                                                     | 11 (57.9%)                  | 27 (71.1%)                | 0.321   |
| Body mass index, median (range), (kg/m²)                                | 21.4 (18.0-27.8)            | 21.2 (14.0-28.8)          | 0.553   |
| Histological diagnosis (n, %)                                           |                             |                           | 0.132   |
| Pancreatic ductal adenocarcinoma                                        | 13 (68.4%)                  | 18 (47.4%)                |         |
| Other disease                                                           | 6 (31.6%)                   | 20 (52.6%)                |         |
| Preoperative prognostic nutritional index, median (range)               | 48.2 (40.7-69.1)            | 49.0 (19.8-59.2)          | 0.919   |
| Operative time, median (range), (min)                                   | 345 (272-537)               | 345.5 (175-779)           | 0.226   |
| Intraoperative blood loss volume, median (range), (ml)                  | 240 (15-1,285)              | 405 (10-1,565)            | 0.119   |
| Surgical approach (n, %)                                                |                             |                           |         |
| Laparoscopy                                                             | 7 (36.8%)                   | 5 (13.2%)                 | 0.045   |
| Spleen preservation (n, %)                                              |                             |                           | 0.440   |
| Present                                                                 | 0 (0%)                      | 2 (5.3%)                  |         |
| Absent                                                                  | 19 (100.0%)                 | 36 (94.7%)                |         |
| Thickness of the pancreatic transection line, median (range) (mm)       | 11.7 (8.8-17.1)             | 11.1 (4.0-20.4)           | 0.525   |
| Type of stapler (n, %)                                                  |                             |                           | 0.048   |
| Triple-row stapler                                                      | 19 (100.0%)                 | 31 (81.6%)                |         |
| Double-row stapler                                                      | 0 (0%)                      | 7 (18.4%)                 |         |
| Reinforcement (n, %)                                                    |                             |                           | <0.001  |
| Present                                                                 | 18 (94.7%)                  | 11 (28.9%)                |         |
| Absent                                                                  | 1 (5.3 %)                   | 27 (71.7%)                |         |
| Combined with gastrectomy, colectomy, enterectomy (n, %)                | 0 (0%)                      | 6 (15.8%)                 | 0.076   |

Continuous variables are expressed as median with range.

sex, body mass index (BMI), histological diagnosis, preoperative prognostic nutritional index, operation time, intraoperative blood loss volume, surgical approach, spleen preservation, thickness of the pancreatic transection line, type of staple, use of reinforcement, combined with gastrectomy or colectomy or enterectomy, drain amylase levels and serum C-reactive protein levels on POD 1 and 3, bacterial culture and bacterial smear tests of the drainage fluid on POD 1 and 3, duration of drain insertion, length of postoperative hospital stay, postoperative fluid collection at the stump of the remnant pancreas ≥3 months postoperatively, readmission and mortality within 90 days after surgery, and pancreatic fistula.

Statistical analysis. The continuous variables were expressed as median with range, and categorical variables were expressed as number (proportions, %). The Chi-square test, Fisher’s exact test, and the Mann–Whitney U-test were used to evaluate differences in the clinicopathological variables between the two groups. We used receiver operating characteristic curve analysis to determine the cutoff value for the thickness of the pancreatic transection line. Univariate and multivariate logistic regression analyses were performed to clarify the risk factors for pancreatic fistula after DP. p<0.05 was considered statistically significant, and all statistical analyses were performed using SPSS software (Version 24; IBM Corp., Armonk, NY, USA).

Results

Overall, patient characteristics are summarized in Table 1. The median patient age was 77 years (range=70-87 years) and the male:female ratio was 2.1. The median BMI was 21.3 (range=14.0-28.8) kg/m². This study included 31 patients (54.4%) diagnosed as having pancreatic ductal adenocarcinoma histologically. Laparoscopic surgery was performed in 12/57 (12.1%) patients, and two patients (3.5%) underwent DP with spleen preservation. The median thickness of the pancreatic transection line was 11.0 mm (range=4.0-20.4 mm). A triple-row stapler was used to divide the pancreas in 50 patients (87.7%), and reinforcement was used in 29 patients (50.9%). Pancreatic fistula occurred in 17/57 (29.8%) of patients.

Table II shows a comparison of the pre- and intraoperative clinicopathological variables in the patients who underwent DP between the early-removal group (n=19) and the conventional group (n=38). Laparoscopic surgery, the rate of using a triple-row stapler, and the use of reinforcement were significantly higher in the early-removal group vs. the conventional group. There were no significant correlations between the two groups regarding age, sex, BMI, histological diagnosis, preoperative prognostic nutritional index, operative time, intraoperative blood loss volume, spleen preservation, thickness of the pancreatic transection line, and whether DP was combined with gastrectomy, colectomy, or enterectomy.

Regarding the postoperative surgical outcomes (Table III) between the early-removal group and the conventional group, the incidence of pancreatic fistula in the early-removal group was significantly lower than that in the
conventional group \((p=0.022)\). Additionally, the duration of drain insertion \((p<0.001)\) and postoperative hospital stay \((p=0.036)\) were significantly shorter in the early-removal group vs. the conventional group. There were no significant differences in the drain amylase levels and serum C-reactive protein levels on POD 1 and 3 between the two groups. There were also no significant differences regarding the bacterial smear test results on POD 3, postoperative fluid collection at the stump of the remnant pancreas, and readmission within 90 days after surgery. There was no mortality within 90 days after surgery in either group.

Multivariate analysis revealed that early drain removal was an independent factor regarding reducing the risk of pancreatic fistula after DP in elderly patients \((p=0.042, \text{Table IV})\).

**Discussion**

Increasing life expectancy is associated with a higher incidence of cancer (19). As a result, the rate of surgical resection in elderly patients has increased (1). However, elderly patients often have multiple comorbidities with functional impairment, tissue vulnerability, and are generally considered to have a high risk of postoperative complications after highly invasive surgery, such as pancreatectomy, which might cause protracted decline in their activities of daily living (20-23). Therefore, for elderly patients, safer surgical techniques or management to minimize complications following pancreatic resection, namely, pancreatic fistula, are required so that patients suffer no loss of independence or productivity. Studies limited to cohorts of only elderly patients are needed to evaluate elderly patients correctly because of large differences between elderly and younger patients regarding physiological function, such as organ dysfunction, or physical characteristics, such as frailty; thus, we designed this study to involve only elderly patients.

Early drain removal after pancreatectoduodenectomy effectively reduced the incidence of postoperative pancreatic fistula in one study (24). The study focused on postoperative surgical management and was based on the concept that long-term drain insertion may induce retrograde intraperitoneal infections that lead to postoperative pancreatic fistula. Additionally, in our previous report, a positive bacterial smear test early postoperatively was significantly associated with pancreatic fistula after pancreatectoduodenectomy (25). Regarding DP, a small number of reports have evaluated early vs. late drain removal. Adachi et al. discussed the possibility of a close relationship between intraperitoneal infection via the drain and subsequent pancreatic fistula, and concluded that early drain removal after DP provided favorable postoperative outcomes (26). Another study reported that late drain removal was significantly associated with complications after DP (15). Furthermore, Yang et al. reported a close relationship between pancreatic fistula following DP and positive bacterial culture in the drainage fluid, and demonstrated that Staphylococcus spp. were isolated more frequently from the culture in the drainage fluid, and demonstrated that

### Table III. Comparison of postoperative surgical outcomes in elderly patients undergoing distal pancreatectomy between the early drain removal group and the conventional drain removal group.

| Variables                                                                 | Early removal group \((n=19)\) | Conventional group \((n=38)\) | \(p\)-Value |
|--------------------------------------------------------------------------|-------------------------------|-------------------------------|-------------|
| Pancreatic fistula, \((n, \%)\)                                           | 2 \((10.5\%)\)                | 15 \((39.5\%)\)               | 0.022       |
| Drain amylase level on POD 1, median \((\text{range})\), (IU/l)          | 4,120 \((756-13,035)\)        | 3,613 \((45-19,178)\)         | 0.421       |
| Drain amylase level on POD 3, median \((\text{range})\), (IU/l)          | 416 \((68-6,997)\)           | 242 \((17-7,490)\)           | 0.544       |
| Serum C-reactive protein level on POD 1, median \((\text{range})\), (mg/dl) | 5.01 \((1.74-12.06)\)        | 5.86 \((1.46-18.44)\)        | 0.660       |
| Serum C-reactive protein level on POD 3, median \((\text{range})\), (mg/dl) | 19.21 \((5.03-32.21)\)       | 13.86 \((5.76-29.46)\)       | 0.101       |
| Positive bacterial smear test result on POD 3, \((n, \%)\)              | 0 \((\%)\)                   | 1 \((2.9\%)\)                | 0.642       |
| Duration of drain insertion, median \((\text{range})\), \((\text{days})\) | 4 \((3-4)\)                  | 6 \((3-148)\)                | <0.001      |
| Postoperative hospital stay, median \((\text{range})\), \((\text{days})\) | 18 \((10-52)\)               | 22 \((11-151)\)              | 0.036       |
| Postoperative fluid collection at the stump of the remnant pancreas \((\text{days})\)  | 2 \((10.5\%)\)               | 3 \((8.3\%)\)                | 0.570       |
| Readmission within 90 days after surgery, \((n, \%)\)                  | 1 \((5.3\%)\)                | 0 \((0\%)\)                  | 0.333       |
| Mortality within 90 days after surgery, \((n, \%)\)                     | 0 \((0\%)\)                  | 0 \((0\%)\)                  | N/A         |

POD, Postoperative day. \(^4\)Data for one patient not available; \(^5\)data for three patients not available; \(^6\)data for four patients not available; \(^7\)data for two patients not available. N/A: Not available. Continuous variables are expressed as median with range.
with mortality. In addition, no patients in the early-removal group had a positive bacterial smear test results in the drainage fluid. Consistent with previous reports in younger patients, our results support a relationship between retrograde drain infection and subsequent pancreatic fistula following DP in elderly patients.

As for reinforcement near the pancreatic stump, the reinforced stapler was reportedly reduced the incidence of pancreatic fistula after DP (28, 29). However, the usefulness of reinforced staple to decrease pancreatic fistula could not be drawn in our study.

Regarding not placing a drainage tube after DP, a recent randomized multicenter controlled trial showed that clinical outcomes were comparable following DP with or without intraperitoneal drainage; however, the study also reported that the DP group without routine intraperitoneal drainage had a higher incidence of intra-abdominal fluid collection near the pancreatic stump (30). Another study reported that fluid collection volume was significantly associated with postoperative pancreatic fistula after DP (31). Moreover, no drain placement after DP was significantly associated with an increased risk of death or serious morbidity compared with early drain removal after DP (14). Therefore, the efficacy of omitting routine drainage in DP is controversial, especially for elderly patients.

In this study, early drain removal after DP was indicated to decrease postoperative pancreatic fistula safety and shorten hospital stay in elderly patients, so that the surgical procedure might contribute to maintain independence or productivity after DP for elderly patients. However, there were 2 patients that needed the reinsertion of an intra-abdominal drain near the pancreatic stump for postoperative pancreatic fistula. The risk factor for reinsertion of a drain to abdominal cavity could not be identified in this study.

Our study has several limitations. First, this was a retrospective analysis involving a small cohort, which can generate bias, although the cohort was composed of only elderly patients. Therefore, a prospective randomized multicenter trial is desirable to validate the efficacy of early drain removal after DP in elderly patients. Second, we defined early drain removal as removing the drain on POD 3 or 4, while the optimal time for early removal after DP is unclear.

**Conclusion**

Early drain removal is useful and safer surgical perioperative management to decrease the risk of pancreatic fistula and to shorten the postoperative hospital stay in elderly patients undergoing DP.

**Conflicts of Interest**

The Authors declare that they have no conflicts of interest.

**Author’s Contributions**

Study concept: Teruhisa Sakamoto. Study design: Teruhisa Sakamoto. Acquisition of data: Takuki Yagyu, Ei Uchinaka and Takehiko Hanaki. Analysis and interpretation of data: Kozo Miyatani and Kyoichi Kihara. Statistical analysis: Manabu Yamamoto, Tomoyuki Matsunaga and Naruo Tokuyasu. Drafting of manuscript: Teruhisa Sakamoto. Critical revision of manuscript: Soichiro Honjo and Yoshiyuki Fujiwara. Final approval of the article: all Authors.

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