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RESEARCH

Feasibility of laparoscopic radical antegrade modular pancreatosplenectomy (RAMPS) as a standard treatment for distal resectable pancreatic cancer

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Abstract

Introduction Laparoscopic (Lap-) radical antegrade modular pancreatosplenectomy (RAMPS) is an attractive radical procedure that aims to achieve negative posterior retroperitoneal margin in pancreatic ductal adenocarcinoma (PDAC) resections. However, only few institutions are adapting Lap-RAMPS due to the technical difficulties and the lack of supporting evidence for the clinical applications.

Methods A retrospective cohort study was performed on consecutive patients who underwent RAMPS for distal resectable PDACs. We analyzed the short- and long-term outcomes including local control and the induction of adjuvant chemotherapy compared between Lap- and Open-RAMPS.

Results Of the 118 RAMPS patients, 43 patients underwent Lap-RAMPS and 75 patients underwent Open-RAMPS. The blood loss was lower (125 vs. 390 mL, $p < 0.001$), and postoperative hospital stay was shorter (17 vs. 21 days, $p = 0.018$) in the Lap-RAMPS group. There was no difference in the postoperative complications and no mortality in both groups. R0 resection rate was 100.0% in the Lap-RAMPS and 90.7% in the Open-RAMPS ($p = 0.039$). Among the patients eligible for adjuvant chemotherapy, the Lap-RAMPS group showed a favorable induction rate (100.0 vs. 89.6%, $p = 0.037$). Both groups showed a favorable 3-year local recurrence rate (8.7 vs. 10.0%, $p = 0.976$) and 3-year overall survival (69.8 vs. 71.1%, $p = 0.996$).

Conclusions The safety and efficacy of Lap-RAMPS were comparable to those of Open-RAMPS in terms of achieving local control and adjuvant chemotherapy induction. A higher early induction of adjuvant chemotherapy is an advantage of minimally invasive surgery.

Keywords Pancreatic ductal adenocarcinoma · Radical antegrade modular pancreatosplenectomy · Laparoscopic surgery · Adjuvant chemotherapy

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most fatal malignancies [1, 2]. The number of PDAC patients is expected to increase to 88,000 in 2030 from 43,000 in 2010, with 63,000 deaths in 2030 compared to 36,888 in 2010 in the USA [1]. The distal PDAC usually only presents symptoms during terminal stages [3]. The current only chance of cure for a localized distal PDAC is a surgical resection with negative surgical site margins [4]. Radical antegrade modular pancreatosplenectomy (RAMPS), first reported by Strasberg et al. in 2003 [5], has been an attractive radical procedure for distal PDAC. The concept of this procedure is designed to increase the rate of negative posterior retroperitoneal margin, characterized by en bloc retroperitoneal fat resection (including the left adrenal gland, if necessary) compared with conventional distal pancreatectomy (DP) [6, 7]. With the development of the minimally invasive surgery, laparoscopic RAMPS (Lap-RAMPS) has been performed in

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high-volume centers recently, and several technical reports on Lap-RAMPS that ensure safety and curability have been published [8–10]. While the usefulness of Lap-RAMPS compared to open RAMPS (Open-RAMPS) has been advocated by several retrospective studies, the clinical applicability of the procedure still needs to be further discussed [11–13], particularly by evaluating the clinical outcomes of Lap-RAMPS compared to the current gold standard treatment for resectable PDAC. Knowing the evidence of adjuvant chemotherapy in improving recurrence-free survival (RFS) and overall survival (OS) after resection [14–16], the current best treatment is local control with surgery followed by systemic treatment with adjuvant chemotherapy. Therefore, the benefit of aggressive RAMPS can be proven by high R0 resection rate, a low local recurrence rate, and a high induction rate of adjuvant chemotherapy [17].

The aim of this study is to evaluate the efficacy of Lap-RAMPS compared to Open-RAMPS, while comparing the results to the modern gold standards in treating resectable PDAC.

Methods

Patients

This is a retrospective cohort study performed on consecutive patients who underwent RAMPS with curative intent for the distal anatomically resectable PDAC at Cancer Institutional Hospital of the Japanese Foundation for Cancer Research between January 2016 and March 2021. The indication for Lap-RAMPS was resectable distal PDAC. The exclusion criteria were as follows: (1) patients with distant metastasis, (2) concomitant resection of other organ(s) including celiac axis, portal vein, and colon (except for the left adrenal gland), and (3) initial resectability with borderline resectable or locally advanced PDAC [18], which were basically indication of Open-RAMPS or DP with celiac axis resection. The choice of Lap- or Open-RAMPS was based on the surgeon's skill and preference, but in recent years, Lap-RAMPS has been increasingly selected for the eligible cases. Tumors were evaluated by multidetector computed tomography (CT), contrast-enhanced magnetic resonance imaging (MRI), endoscopic ultrasonography, and/or positron emission tomography CT. The study was approved by the Ethics Committee of Cancer Institute Hospital, Japanese Foundation for Cancer Research, prior to collecting identifiable patient information and analysis (2021-GB 013).

Operation technique

The technical details of Lap-RAMPS and Open-RAMPS have been described previously [7, 10]. In brief, in both Lap- and Open-RAMPS, the root of the splenic artery is dissected and ligated under the anterocranial view (we named "anterocranial splenic artery-first approach") early in the operation to prevent venous congestion in the distal pancreas and spleen [7, 10]. Lap-RAMPS was done by several surgeons who have experienced Open-RAMPS and laparoscopic surgery including conventional distal pancreatectomy, cholecystectomy, hepatectomy, and gastrectomy. According to the temporal distribution between Lap- and Open-RAMPS, there was no clear learning curve formed in the current series (Supplement figure 1). Either anterior or posterior RAMPS was planned at the multidisciplinary conference based on the location of the tumor, so the left adrenal gland is resected en bloc (which case is defined as posterior RAMPS), if necessary, in order to achieve posterior retroperitoneal tumor-free margins (Fig. 1). After resection, drain placement and conservative drain management were done as previously described [10].

Patient demographics and operative and postoperative outcomes

We reviewed the electronic medical records. Patient demographics including age, gender, body mass index (BMI),

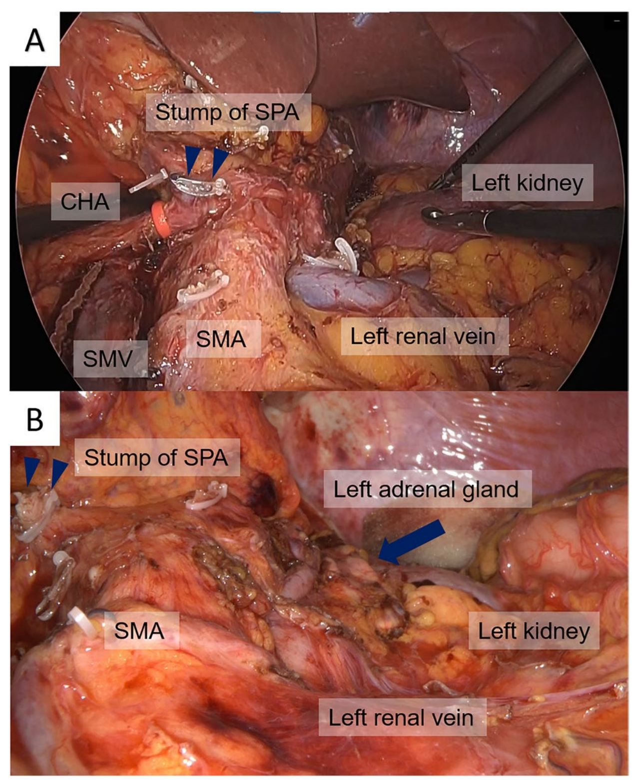

Fig. 1 The view after laparoscopic RAMPS. **A** Posterior RAMPS. **B** Anterior RAMPS. RAMPS: radical antegrade modular pancreatosplenectomy; CHA: common hepatic artery; SPA: splenic artery; SMA: superior mesenteric artery; SMV: superior mesenteric vein

American Society of Anesthesiologists (ASA) score, and presence of diabetes; tumor characteristics including location (body/tail), size (mm), and the serum level of CEA and CA19-9 level at diagnosis and before surgery; and the operative outcomes including the procedure method (Lap- or Open-RAMPS and anterior or posterior RAMPS), operative time, intraoperative blood loss, and hospital stay were recorded. Intraoperative blood loss was calculated in accordance with the conventional method, i.e., as the sum of intraoperative suction fluids (after subtracting the amount of irrigation fluids) and increase in operative gauze weight [19]. Most of the patients remained hospitalized until all drains were removed and were rarely discharged home with drains. The severity of complications was defined according to the Clavien–Dindo classification system [20]. POPF, delayed gastric emptying (DGE), surgical site infection (SSI), and intra-abdominal hemorrhage were defined according to the International Study Group of Pancreatic Surgery [21–23]. Mortality and morbidity were defined as a complication occurring during the hospital stay. The patients were followed up every 3 months after surgery and performed CT and/or MRI every 6 months routinely.

Neoadjuvant and adjuvant chemotherapy

Before December 2018, resectable PDAC was treated by upfront surgery. Thereafter, all patients except for those with clinical stage I received two courses of neoadjuvant gemcitabine (GEM) and tegafur/gimeracil/oteracil (S-1) chemotherapy. After resection, S-1 was administrated as the first choice of adjuvant chemotherapy based on the criteria of the randomized controlled trial (adequate oral intake, Eastern Cooperative Oncology Group performance status of 0 or 1, adequate bone marrow/liver/kidney function) [15, 24]. Four cycles of S-1 were administered, with each cycle having a daily dose of 80 mg/m^2 orally for 28 days, followed by 14 days of rest. GEM was used for patients who could not tolerate S-1 (for example, allergy and nausea). The administration of GEM was repeated every 4 weeks for up to six cycles [15].

Pathologic evaluation

The surgical specimens were assessed according to the Union for International Cancer Control (UICC) 8th edition TNM system [25]. It has been our standard to slice the specimen transversely and evaluate/report microscopic superior, inferior, and posterior margin addition to the pancreas stump margin status. We inked the posterior retroperitoneal margin to ensure accurate histologic evaluation. The posterior retroperitoneal margin was inked before fixation, the fixed specimen was sliced transversely with a 5 mm thickness, and its tangential margin was evaluated. R0 resection was defined by the absence of microscopic cancer cells in all margins, regardless of the distance between the tumor and the closest margin, and also intraoperative abdominal cytopathology negative.

Statistical analysis

Continuous data are presented as a median (range), and categorical data are expressed as a number (percentage). All analyses were performed using StatFlex 6.0 software (Artech Co., Osaka, Japan). The Mann-Whitney U test and the chi-square test were used for comparisons, as appropriate. RFS and OS rates were determined from the time of resection to the time of detection of first recurrence and death or last follow-up, respectively. Survival curves were constructed using the Kaplan–Meier method and compared with the log-rank test. A Cox proportional hazards model was used to assess the prognostic significance of Lap-RAMPS. For Cox model, significant covariates included induction of neoadjuvant chemotherapy, the level of CA19-9, pathological lymph node positive, and induction of adjuvant chemotherapy. Results were considered significant when $p < 0.05$.

Results

Patients' characteristics

178 patients underwent RAMPS for PDAC during this period (January 2016 to March 2021). 60 patients were excluded in the analysis: 44 underwent RAMPS with another organ(s) resection and 13 and 3 with initially borderline resectable/unresectable PDAC. Finally, 118 patients were included in the analysis. 43 patients underwent Lap-RAMPS and 75 patients underwent Open-RAMPS for the localized distal PDAC. The patients' characteristics are shown in Table 1. The Lap-RAMPS group received neoadjuvant chemotherapy more frequently (Lap-RAMPS vs. Open-RAMPS, 53.5% vs. 17.3%, $p < 0.001$).

Operative and postoperative outcomes

The details of operative and postoperative outcomes are shown in Table 2. The median operative time was longer (364 min [250–547] vs. 303 min [182–579] $p < 0.001$), and the median blood loss was lower (125 mL [5–500] vs. 390 mL [40–1340], $p < 0.001$) in the Lap-RAMPS group. The anterior RAMPS procedure was performed more frequent in the Lap-RAMPS (anterior/posterior 26/17 vs. 24/51, $p = 0.003$). The postoperative stay was shorter (17 days vs. 21 days, $p = 0.018$) in the Lap-RAMPS group. The details of postoperative complications are shown in Table 2. The incidence of POPF, DGE, SSI, and hemorrhage was not different

Table 1 Patients' characteristics data

Characteristics	Lap-RAMPS (*n*=43)	Open-RAMPS (*n*=75)	*p* value
Age	69 (35–84)	70 (37–89)	0.327
Gender (male/female)	18/25	49/26	0.013
BMI	21.1 (14.6–29.6)	21.8 (15.6–30.1)	0.114
Diabetes mellitus	11 (25.6%)	24 (32.0%)	0.463
ASA class 1/2/3	6/36/1	20/39/6	0.254
Tumor site (body/tail)	20/23	46/29	0.119
Neoadjuvant chemotherapy	23 (53.5%)	13 (17.3%)	<0.001
Tumor size (mm)			
At diagnosis	22 (6–59)	22 (8–55)	0.284
Before surgery	17 (3–59)	22 (8–60)	0.004
CEA (ng/mL)			
At diagnosis	2.8 (0.7–31.6)	2.6 (0.7–16.6)	0.836
Before surgery	2.8 (0.7–31.6)	2.8 (0.7–15.7)	0.644
CA19-9 (U/mL)			
At diagnosis	29.7 (2.0–6743.7)	114.6 (2.0–27719.6)	0.046
Before surgery	27.7 (2.0–6743.7)	52.3 (2.0–27719.6)	0.030
		Median (range)	

BMI body mass index, *ASA* American Society of Anesthesiologists class

Table 2 Operative and postoperative outcome

Variables	Lap-RAMPS (*n*=43)	Open-RAMPS (*n*=75)	*p* value
Operative time (min)	364 (250–547)	303 (182–579)	0.0002
Blood loss (g)	125 (5–500)	390 (40–1340)	<0.0001
Blood transfusion (%)	0 (0%)	1 (1.3%)	0.447
Anterior/posterior RAMPS	26/17	24/51	0.0026
Postoperative stay (day)	17 (8–47)	21 (10–80)	0.018
POPF ISGPF grade BL/B/C	3/16/0	9/20/0	0.612
DGE (%)	3 (7.0%)	5 (6.7%)	0.949
SSI (%)	2 (4.7%)	10 (13.3%)	0.133
Hemorrhage (%)	0 (0%)	1 (1.3%)	0.447
CD grade 3a or higher (%)	8 (18.6%)	13 (17.8%)	0.862
Mortality (%)	0 (0%)	0 (0%)	1.00
		Median (range)	

POPF postoperative pancreatic fistula, *ISGPF* International Study Group on Pancreatic Fistula Definition, *DGE* delayed gastric emptying, *SSI* surgical site infection, *CD* Clavien–Dindo

between the two groups. There was no significant difference in complication of Clavien–Dindo grade 3a or higher (p = 0.862). There was no postoperative mortality in both groups, and there was no open conversion in the Lap-RAMPS group.

Histopathological outcomes

Histopathological outcomes are shown in Table 3. Pathological tumor size in the Lap-RAMPS group was smaller than that in the Open-RAMPS group (24 mm [4–78] vs. 30mm [2–70], p = 0.013). Lymph node metastases were observed in 18 patients (41.9%) of the Lap-RAMPS group and 40 patients (53.3%) of the Open-RAMPS group (p = 0.230). There was no significant difference in UICC stage between two groups. The achievement rate of R0 resection was 100.0% in the Lap-RAMPS and 90.7% in the Open-RAMPS (p = 0.039). In the Open-RAMPS group, R1 resection was observed in seven patients: positive posterior retroperitoneal margin in three patients, positive proximal pancreatic stump in two patients, positive nerve plexus stump in one patient, and intraoperative abdominal cytopathology positive in one patient.

Table 3 Histopathological outcome and adjuvant chemotherapy data

Variables	Lap-RAMPS (*n*=43)	Open-RAMPS (*n*=75)	*p* value
Pathological tumor size (mm)	24 (4–78)	30 (2–70)	0.013
Lymph node metastasis (%)	18 (41.9%)	40 (53.3%)	0.230
UICC (8th) stage			
0/IA/IB/IIA/IIB/III	3/10/8/4/15/3	2/10/18/5/32/8	0.520
Resected lymph node numbers	24 (8–49)	32 (3–83)	0.005
R0/R1	43/0	68/7	0.039
Introduction of AC (%)	39 (90.7%)	60 (80.0%)	0.128
Use of AC			0.326
S-1 (%)	37 (94.9%)	59 (98.3%)	
GEM (%)	2 (5.1%)	1 (1.7%)	
Time until starting AC (day)	54 (26–115)	59.5 (33–125)	0.026
Follow-up month	23.1 (8.6–42.2)	31.5 (7.1–71.6)	0.0002
		Median (range)	

UICC Union for International Cancer Control, *AC* adjuvant chemotherapy, *S-1* tegafur/gimeracil/oteracil, *GEM* gemcitabine

Adjuvant chemotherapy

Patients not eligible for adjuvant chemotherapy were as follows: 4 elderly patients (Lap: 2, Open: 2), 3 pathological stage 0 (Lap: 1, Open: 2), 4 patients with early recurrence (Lap: 1, Open: 3), and 1 patient treated for another malignancy (Lap: 0, Open: 1). Of the candidates for adjuvant chemotherapy excluding those, 39 patients (100.0%) received adjuvant chemotherapy in the Lap-RAMPS group and 60 out of 67 patients (89.6%) received adjuvant chemotherapy in the Open-RAMPS group (p = 0.037) (Fig. 2). The reasons for not receiving adjuvant chemotherapy in the Open-RAMPS group were as follows. In the Open-RAMPS group: an impaired performance status after surgery in 5 patients and refusal of adjuvant chemotherapy in 2 patients. The intervals between initiation of adjuvant chemotherapy and resection were shorter in the Lap-RAMPS group compared to the Open-RAMPS group (54.0 days vs. 59.5 days, p = 0.026).

Overall survival outcome

The median follow-up month of all patients was 23.1 months (8.6–42.2) in the LAP-RAMPS group and 31.5 months (7.1–71.6) in the Open-RAMPS group (p = 0.0002). Figure 3 shows Kaplan–Meier curves for OS, RFS, local recurrence, and distant metastasis among all patients. Three-year OS, RFS, local recurrence rates, and distant metastasis rate after resection in the Lap-RAMPS group were 69.8%, 58.1%, 8.7%, and 33.6%, respectively, compared to 71.1%, 58.3%, 10.0%, and 35.8% in the Open-RAMPS group, respectively (RFS: p = 0.433, OS: p = 0.996, local recurrence rates: p = 0.976, and distant metastasis rates: p = 0.391). Among the patients with distant

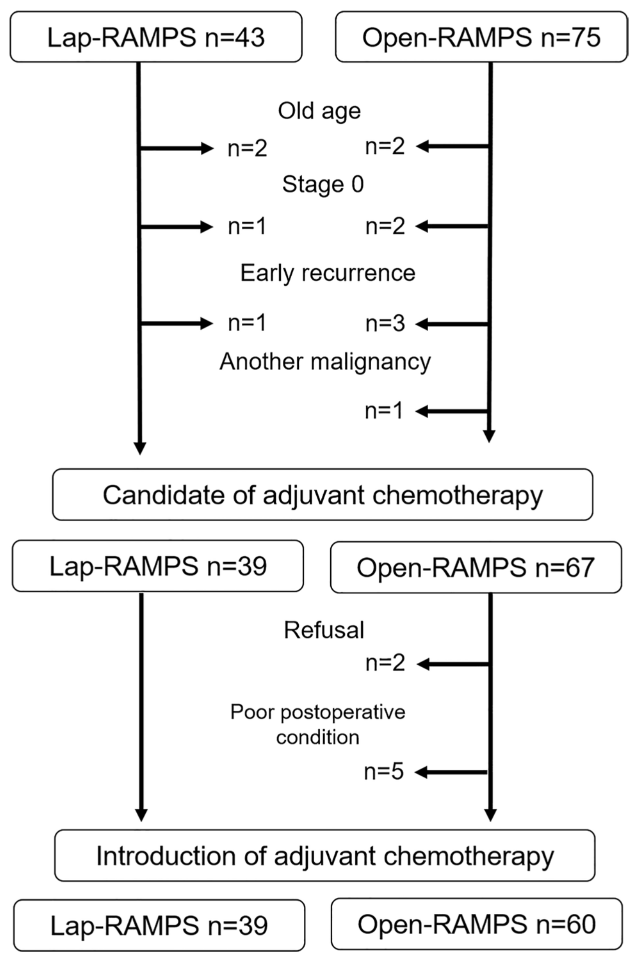

Fig. 2 The induction rate of postoperative adjuvant chemotherapy between the Lap-RAMPS and the Open-RAMPS group

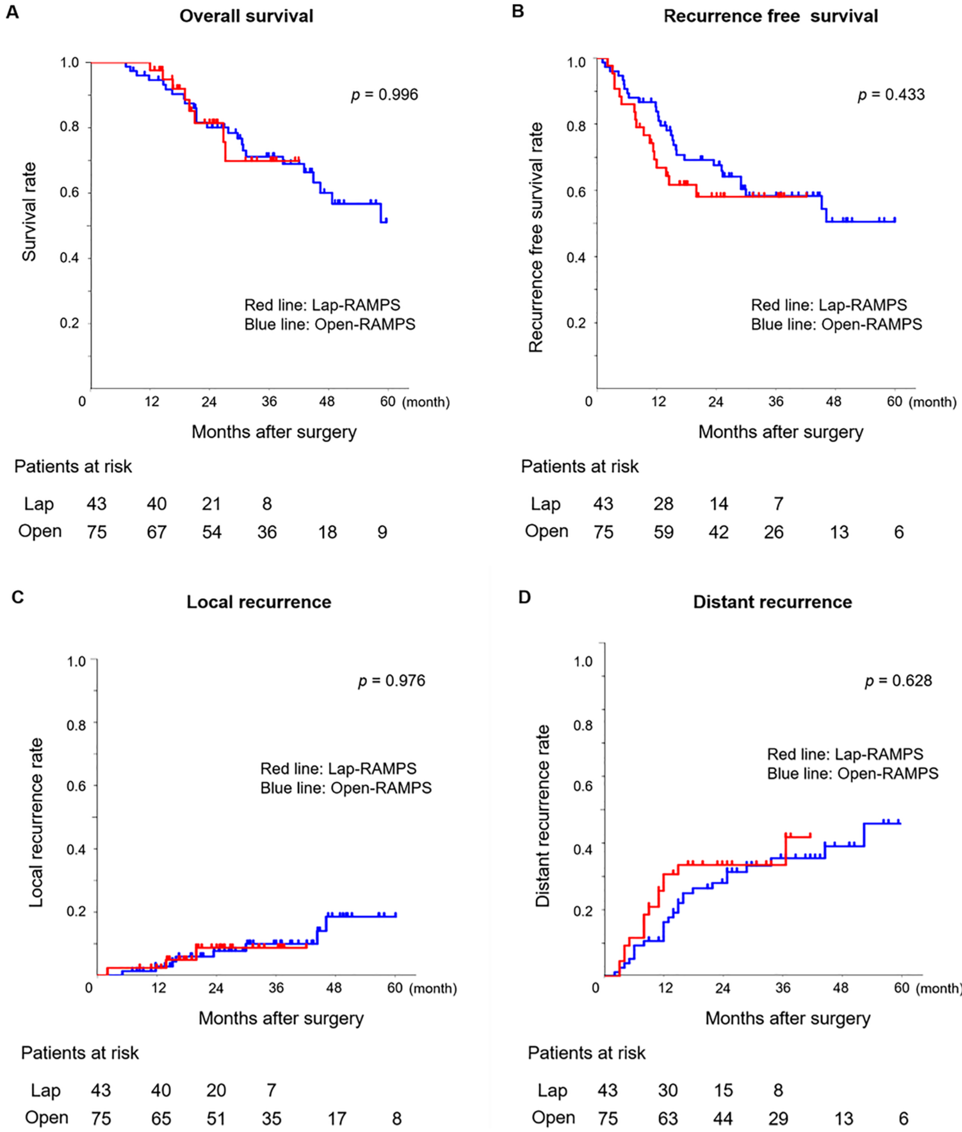

Fig. 3 Kaplan–Meier analysis of overall survival (**A**), recurrence-free survival (**B**), local recurrence (**C**), and distant metastasis (**D**) between the Lap-RAMPS group and the Open-RAMPS group

metastases, 8 patients (18.6%) had liver metastases, 1 patient (2.3%) had peritoneal metastases, and 3 patients (7.0%) had para-aortic lymph node metastases in the Lap-RAMPS group; and 7 patients (9.3%) had liver metastases, 7 patients (9.3%) had peritoneal metastases, and 5 patients (6.7%) had para-aortic lymph node metastases in the Open-RAMPS group. Lap-RAMPS was not associated with poor prognosis compared to Open-RAMPS even after adjusting for induction of neoadjuvant chemotherapy, the level of CA19-9, pathological lymph node positive, and induction of adjuvant chemotherapy (the hazard ratio 1.185, 95% CI = 0.480–2.927; $p = 0.713$) (Table 4).

Table 4 Results of Cox multivariate analyses of open/laparoscopic and other prognostic factors after surgical treatment

Multivariate analysis			
Variables	*p* value	Hazard ratio	95% CI
Induction of neoadjuvant chemotherapy	0.317	1.636	0.623–4.299
CA19-9 level > 500	0.005	3.045	1.400–6.622
Induction of adjuvant chemotherapy	0.859	1.097	0.397–3.031
Pathological lymph node positive	0.955	0.978	0.460–2.081
Lap-RAMPS	0.713	1.185	0.480–2.927

Lap-RAMPS laparoscopic radical antegrade modular pancreatosplenectomy

Discussion

Although the RAMPS continues to be the attractive and reasonable procedure for adequate local control of resectable distal PDAC with sufficient posterior retroperitoneal margin, its usefulness needs to be reevaluated since it is more technically demanding than the conventional DP and its short- or long-term outcomes have not been discussed extensively in literature [5, 6, 26, 27]. PDAC is a systemic disease with a recurrence rate after curative resection of 70% to 80%, with 70% to 80% of which being distant metastases. Since adjuvant chemotherapy plays an important role in controlling recurrence [28, 29], the rate of induction of adjuvant chemotherapy is an important factor in evaluating the outcome of radical PDAC resection, which should be accompanied by pathologic evaluation of the resected specimen and the local recurrence rate after resection. We have previously reported on the technical aspects of Open-RAMPS [7] and later on Lap-RAMPS ("anterocranial splenic artery-first approach") as the minimally invasive surgery progressed [10]. The present study demonstrated that these efforts have resulted in a high induction rate of adjuvant chemotherapy (Lap-RAMPS: 100.0%, Open-RAMPS: 89.6%), a high R0 rate (Lap-RAMPS: 100.0%, Open-RAMPS: 90.7%), and a low 3-year local recurrence rate (Lap-RAMPS: 8.7%, Open-RAMPS: 10.0%) and shows the certain usefulness of RAMPS in short- and long-term outcomes. Lap-RAMPS was not associated with poor prognosis compared to Open-RAMPS even after adjusting for other prognostic factors (hazard ratio 1.185; $p = 0.713$). On the other hand, Lap-RAMPS was able to introduce adjuvant chemotherapy earlier postoperatively at a higher induction rate than Open-RAMPS (100.0% vs. 89.6%, $p = 0.037$), suggesting that Lap-RAMPS may be a useful procedure that combines the benefits of minimally invasive surgery with the radicality of RAMPS. It is practically difficult to plan a randomized control trial comparing conventional DP and RAMPS since the decision to perform conventional DP or RAMPS is dependent on location and institution, just as the reason why conventional DP for PDAC is rarely performed in our institution [7]. The results of the LEOPARD-2 study, which compared the time to functional recovery between laparoscopic and open pancreatoduodenectomy and failed to demonstrate the safety of laparoscopic pancreatoduodenectomy, suggest that the quality control of RCTs of minimally invasive surgery can be challenging [30]. Considering this fact, the result of this study should be thoroughly taken into account when implementing evidence-based practice for resectable PDAC.

The current results showed that the rate of R0 in the Lap-RAMPS group was higher than that of the Open-RAMPS group (Lap vs. Open: 100% vs. 90.9%, $p = 0.039$). A major reason could be that the patients having tumor near the splenic artery or the superior mesenteric vein are often considered ineligible for Lap-RAMPS. Neoadjuvant chemo(radio)therapy has been shown to reduce preoperative tumor size and the level of CA19-9 and to increase the rate of R0 achievement in postoperative outcomes [31, 32] and to improve OS compared with upfront surgery in the patients with borderline resectable pancreatic cancer [33]. The difference in the rate of neoadjuvant chemotherapy could also play in the difference in R0 rate due to the overlapping period during which Lap-RAMPS and neoadjuvant treatment were introduced. The preoperative tumor size was smaller in the Lap-RAMPS group, and as a result, the anterior RAMPS was selected more often (Lap vs. Open: 60.4% vs. 32.0%, $p < 0.001$).

Caudal approach during Lap-RAMPS that includes opening of the mesotransverse colon to secure a surgical margin in advanced cases with transverse mesocolon invasion or tumor adjacency to the superior mesenteric artery has been advocated as well. However, there are few literatures that show short- and long-term outcomes of this approach [34–36]. We have recently reported the anterocranial splenic artery-first approach contributed to reduction of blood loss during dissection following our open-RAMPS concept. The current results demonstrated that the anterocranial splenic artery-first approach can achieve high rates of negative posterior retroperitoneal margin, low rate of local recurrence, and low volume of intraoperative blood loss [10]. It can be explained that these good results were achieved by initially ligating the splenic artery blood inflow to prevent congestion, thereby ensuring a dry field of vision, and by unifying the left-sided dissection of the superior mesenteric artery and en bloc dissection of the retroperitoneum procedures.

Induction of postoperative adjuvant chemotherapy is indispensable in maximizing OS in the treatment of PDAC. Currently, S-1 and FOLFIRINOX are the best adjuvant chemotherapy with comparable efficacy in terms of hazard ratio for OS compared to GEM, and oral S-1 continues to be the first choice in clinical practice in Japan due to its convenient mode of administration along with minimal side effects [14, 15, 37]. Regardless of which drug is used, the currently available evidence suggests that adjuvant chemotherapy following radical surgery is the best treatment for OS extension. In this study, 39 patients (100.0%) in the Lap-RAMPS group and 60 patients (89.6%) in the Open-RAMPS group were induced adjuvant chemotherapy. Five patients in the Open-RAMPS group could not initiate adjuvant chemotherapy due to their impaired performance status after surgery, whereas all patients in the Lap-RAMPS underwent adjuvant treatment. Although the present results showed somehow short-term advantage of minimally invasive Lap-RAMPS with less body wall destruction and intestinal dryness, the positive impact on long-term outcomes (RFS, OS) could not be demonstrated.

There are some limitations in this study. First, patient selection bias could not be excluded due to the retrospective nature of the study. Second, the patient backgrounds between two groups are different since the induction of neoadjuvant chemotherapy and Lap-RAMPS at our hospital started later in the study period. However, the current results also showed that Lap-RAMPS can be safely performed after neoadjuvant treatment, and moreover, Lap-RAMPS was not associated with poor prognosis compared to Open-RAMPS even after adjusting for significant covariates including neoadjuvant chemotherapy (the hazard ratio 1.185; $p = 0.713$). These are considered important results that could justify the continued adoption of this relatively new technique. Further prospective multicenter trials are essential to demonstrate the true efficacy and non-inferiority of Lap-RAMPS to Open-RAMPS. Third, our discharge criteria were not strictly defined. This might affect the results of postoperative hospital stay.

In conclusion, the safety and efficacy of Lap-RAMPS were comparable to those of Open-RAMPS in terms of achieving local control and adjuvant chemotherapy induction, which are deemed as the current treatment gold standards for resectable distal PDAC. Higher induction rate of adjuvant chemotherapy in Lap-RAMPS might suggest that minimally invasive approach for a radical resection may be promising in improving the care and outcomes of patients.

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Authors' contributions Study conception and design: Shoki Sato and Atsushi Oba. Acquisition of data: Shoki Sato and Atsushi Oba. Analysis and interpretation of data: Shoki Sato. Drafting of manuscript: Shoki Sato, Atsushi Oba, and Y.H. Andrew Wu. Critical revision of manuscript: Atsushi Oba, Tomotaka Kato, Kosuke Kobayashi, Y.H. Andrew Wu, Yoshihiro Ono, Takafumi Sato, Hiromichi Ito, Yosuke Inoue, and Yu Takahashi.

Declarations

Ethical approval All authors comply with the journal's ethical policies.

Consent to participate Informed consent was obtained from all individual participants included in the study.

References

1. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM (2014) Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res 74:2913–2921. https://doi.org/10.1158/0008-5472.can-14-0155
2. Siegel RL, Miller KD, Jemal A (2017) Cancer statistics, 2017. CA Cancer J Clin 1:7–30. https://doi.org/10.3322/caac.21590
3. van Erning FN, Mackay TM, van der Geest LGM, Groot Koerkamp B, van Laarhoven HWM, Bonsing BA, Wilmink JW, van Santvoort HC, de Vos-Geelen J, van Eijck CHJ, Busch OR, Lemmens VE, Besselink MG (2018) Association of the location of pancreatic ductal adenocarcinoma (head, body, tail) with tumor stage, treatment, and survival: a population-based analysis. Acta Oncol 57:1655–1662. https://doi.org/10.1080/0284186X.2018.1518593
4. Strasberg SM, Fields R (2012) Left-sided pancreatic cancer: distal pancreatectomy and its variants: radical antegrade modular pancreatosplenectomy and distal pancreatectomy with celiac axis resection. Cancer J 18:562–570. https://doi.org/10.1097/PPO.0b013e31827596c5
5. Strasberg SM, Drebin JA, Linehan D (2003) Radical antegrade modular pancreatosplenectomy. Surgery. 133:521–527. https://doi.org/10.1067/msy.2003.146
6. Strasberg SM, Linehan DC, Hawkins WG (2007) Radical antegrade modular pancreatosplenectomy procedure for adenocarcinoma of the body and tail of the pancreas: ability to obtain negative tangential margins. J Am Coll Surg 204:244–249. https://doi.org/10.1016/j.jamcollsurg.2006.11.002
7. Watanabe G, Ito H, Sato T, Ono Y, Mise Y, Inoue Y, Takahashi Y, Saiura A (2019) Left kidney mobilization technique during radical antegrade modular pancreatosplenectomy (RAMPS). Langenbecks Arch Surg 404:247–252. https://doi.org/10.1007/s00423-019-01767-0
8. Kim EY, Hong TH (2017) Initial experience with laparoscopic radical antegrade modular pancreatosplenectomy for left-sided pancreatic cancer in a single institution: technical aspects and oncological outcomes. BMC Surg 17:2. https://doi.org/10.1186/s12893-016-0200-z
9. Rosso E, Manzoni A, Zimmitti G (2020) Laparoscopic radical antegrade modular pancreatosplenectomy with venous tangential resection: focus on periadventitial dissection of the superior mesenteric artery for obtaining negative margin and a safe vascular resection. Ann Surg Oncol 27:2902–2903. https://doi.org/10.1245/s10434-020-08271-6
10. Kato T, Inoue Y, Oba A, Ono Y, Sato T, Ito H, Takahashi Y (2022) Laparoscopic radical antegrade modular pancreatosplenectomy with anterocranial splenic artery-first approach for left-sided resectable pancreatic cancer (with videos). Ann Surg Oncol 29:3505–3514. https://doi.org/10.1245/s10434-022-11382-x
11. Kawabata Y, Hayashi H, Kaji S, Fujii Y, Nishi T, Tajima Y (2020) Laparoscopic versus open radical antegrade modular pancreatosplenectomy with artery–first approach in pancreatic cancer. Langenbecks Arch Surg 405:647–656. https://doi.org/10.1007/s00423-020-01887-y
12. Zhang H, Li Y, Liao Q, Xing C, Ding C, Zhang T, Guo J, Han X, Xu Q, Wu W, Zhao Y, Dai M (2021) Comparison of minimal invasive versus open radical antegrade modular pancreatosplenectomy (RAMPS) for pancreatic ductal adenocarcinoma: a single center retrospective study. Surg Endosc 35:3763–3773. https://doi.org/10.1007/s00464-020-07938-1
13. Hirashita T, Iwashita Y, Fujinaga A, Nakanuma H, Tada K, Masuda T, Endo Y, Ohta M, Inomata M (2022) Surgical and oncological outcomes of laparoscopic versus open radical antegrade modular pancreatosplenectomy for pancreatic ductal adenocarcinoma. Surg Today 52:224–230. https://doi.org/10.1007/s00595-021-02326-1
14. Oettle H, Neuhaus P, Hochhaus A, Hartmann JT, Gellert K, Ridwelski K, Niedergethmann M, Zülke C, Fahlke J, Arning MB, Sinn M, Hinke A, Riess H (2013) Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. Jama. 310:1473–1481. https://doi.org/10.1001/jama.2013.279201
15. Uesaka K, Boku N, Fukutomi A, Okamura Y, Konishi M, Matsumoto I, Kaneoka Y, Shimizu Y, Nakamori S, Sakamoto H, Morinaga S, Kainuma O, Imai K et al (2016) Adjuvant chemotherapy of S-1 versus gemcitabine for resected pancreatic cancer: a phase 3,

open-label, randomised, non-inferiority trial (JASPAC 01). Lancet 388:248–257. https://doi.org/10.1016/s0140-6736(16)30583-9
16. Neoptolemos JP, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, Halloran CM, Faluyi O, O'Reilly DA, Cunningham D, Wadsley J, Darby S, Meyer T, Gillmore R et al (2017) Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet 389:1011–1024. https://doi.org/10.1016/s0140-6736(16)32409-6
17. Altman AM, Wirth K, Marmor S, Lou E, Chang K, Hui JYC, Tuttle TM, Jensen EH, Denbo JW (2019) Completion of adjuvant chemotherapy after upfront surgical resection for pancreatic cancer is uncommon yet associated with improved survival. Ann Surg Oncol 26:4108–4116. https://doi.org/10.1245/s10434-019-07602-6
18. Tempero MA, Malafa MP, Chiorean EG, Czito B, Scaife C, Narang AK, Fountzilas C, Wolpin BM, Al-Hawary M, Asbun H, Behrman SW, Benson AB, Binder E et al (2019) Pancreatic adenocarcinoma, version 1.2019. J Natl Compr Canc Netw 17:202–210. https://doi.org/10.6004/jnccn.2019.0014
19. Oba A, Ishizawa T, Mise Y, Inoue Y, Ito H, Ono Y, Sato T, Takahashi Y, Saiura A (2019) Possible underestimation of blood loss during laparoscopic hepatectomy. BJS Open 3:336–343. https://doi.org/10.1002/bjs5.50145
20. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213. https://doi.org/10.1097/01.sla.0000133083.54934.ae
21. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ, Büchler MW (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 142:761–768. https://doi.org/10.1016/j.surg.2007.05.005
22. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Yeo CJ, Büchler MW (2007) Postpancreatectomy hemorrhage (PPH);an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery. 142:20–25. https://doi.org/10.1016/j.surg.2007.02.001
23. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M et al (2017) The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery. 161:584–591. https://doi.org/10.1016/j.surg.2016.11.014
24. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 5: 649-655
25. Brierley JD, Gospodarowicz MK, Wittekind C (2016) TNM classification of malignant tumours, 8th edn
26. Park HJ, You DD, Choi DW, Heo JS, Choi SH (2014) Role of radical antegrade modular pancreatosplenectomy for adenocarcinoma of the body and tail of the pancreas. World J Surg 38:186–193. https://doi.org/10.1007/s00268-013-2254-8
27. Abe T, Ohuchida K, Miyasaka Y, Ohtsuka T, Oda Y, Nakamura M (2016) Comparison of surgical outcomes between radical antegrade modular pancreatosplenectomy (RAMPS) and standard retrograde pancreatosplenectomy (SPRS) for left-sided pancreatic cancer. World J Surg 40:2267–2275. https://doi.org/10.1007/s00268-016-3526-x
28. Groot VP, Rezaee N, Wu W, Cameron JL, Fishman EK, Hruban RH, Weiss MJ, Zheng L, Wolfgang CL, He J (2018) Patterns, timing, and predictors of recurrence following pancreatectomy for pancreatic ductal adenocarcinoma. Ann Surg 267:936–945. https://doi.org/10.1097/sla.0000000000002234
29. Oba A, Del Chiaro M, Satoi S, Kim S-W, Takahashi H, Yu J, Hioki M, Tanaka M, Kato Y, Ariake K, Wu YHA, Inoue Y, Takahashi Y et al (2022) New criteria of resectability for pancreatic cancer: a position paper by the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS). J Hepatobiliary Pancreat Sci 29:725–731. https://doi.org/10.1002/jhbp.1049
30. van Hilst J, de Rooij T, Bosscha K, Brinkman DJ, van Dieren S, Dijkgraaf MG, Gerhards MF, de Hingh IH, Karsten TM, Lips DJ, Luyer MD, Busch OR, Festen S et al (2019) Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. Lancet Gastroenterol Hepatol 4:199–207. https://doi.org/10.1016/s2468-1253(19)30004-4
31. Sho M, Akahori T, Tanaka T, Kinoshita S, Nagai M, Tamamoto T, Ohbayashi C, Hasegawa M, Kichikawa K, Nakajima Y (2015) Importance of resectability status in neoadjuvant treatment for pancreatic cancer. J Hepatobiliary Pancreat Sci 22:563–570. https://doi.org/10.1002/jhbp.258
32. Fujii T, Satoi S, Yamada S, Murotani K, Yanagimoto H, Takami H, Yamamoto T, Kanda M, Yamaki S, Hirooka S, Kon M, Kodera Y (2017) Clinical benefits of neoadjuvant chemoradiotherapy for adenocarcinoma of the pancreatic head: an observational study using inverse probability of treatment weighting. J Gastroenterol 52:81–93. https://doi.org/10.1007/s00535-016-1217-x
33. van Dam JL, Janssen QP, Besselink MG, Homs MYV, van Santvoort HC, van Tienhoven G, de Wilde RF, Wilmink JW, van Eijck CHJ, Groot KB (2022) Neoadjuvant therapy or upfront surgery for resectable and borderline resectable pancreatic cancer: a meta-analysis of randomised controlled trials. Eur J Cancer 160:140–149. https://doi.org/10.1016/j.ejca.2021.10.023
34. Ban D, Garbarino GM, Ishikawa Y, Honda G, Jang JY, Kang CM, Maekawa A, Murase Y, Nagakawa Y, Nishino H, Ohtsuka T, Yiengpruksawan A, Endo I et al (2022) Surgical approaches for minimally invasive distal pancreatectomy: a systematic review. J Hepatobiliary Pancreat Sci 29:151–160. https://doi.org/10.1002/jhbp.902
35. Ome Y, Hashida K, Yokota M, Nagahisa Y, Michio O, Kawamoto K (2017) Laparoscopic radical antegrade modular pancreatosplenectomy for left-sided pancreatic cancer using the ligament of Treitz approach. Surg Endosc 31:4836–4837. https://doi.org/10.1007/s00464-017-5561-6
36. Nagai K, Kiguchi G, Yogo A, Anazawa T, Yagi S, Taura K, Takaori K, Masui T (2020) Left-posterior approach for artery-first en bloc resection in laparoscopic distal pancreatectomy for left-sided pancreatic cancer. Langenbecks Arch Surg 405:1251–1258. https://doi.org/10.1007/s00423-020-02021-8
37. Conroy T, Castan F, Lopez A, Turpin A, Ben Abdelghani M, Wei AC, Mitry E, Biagi JJ, Evesque L, Artru P, Lecomte T, Assenat E, Bauguion L et al (2022) Five-year outcomes of FOLFIRINOX vs gemcitabine as adjuvant therapy for pancreatic cancer: a randomized clinical trial. JAMA Oncol. https://doi.org/10.1001/jamaoncol.2022.3829