Does the artery-first approach improve the rate of R0 resection in pancreatoduodenectomy?

A multicenter, randomized, controlled trial

Authors

Luis Sabater[1], Esteban Cugat[2], Alejandro Serrablo[3], Gonzalo Suarez-Artacho[4], Luis Diez-Valladares[5], Julio Santoyo-Santoyo[6], Elena Martín-Pérez[7], Fabio Ausania[8], Santiago López-Ben[9], José María Jover-Navalón[10], Marina Garcés-Albir[1], María Isabel García-Domingo[1], Mario Serradilla[3], Elia Pérez-Aguirre[11], Belinda Sánchez-Pérez[6], Marcello Di Martino[12], Paula Senra-del-Río[8], Laia Falgueras-Verdaguer[9], Alberto Carabias[10], Mari Carmen Gómez-Mateo[13], Antonio Ferrández[14], Dimitri Dorcaratto[15], Elena Muñoz-Forner[1], Constantino Fondevila[16], Javier Padillo[4]

Affiliations

[1] Department of Surgery, Hospital Clínico, University of Valencia, INCLIVA Biomedical Research Institute, Valencia, Spain
[2] Department of Surgery, Hospital Universitario Mutua Terrassa; Hospital Germans Trias i Pujol, Barcelona, Spain
[3] Department of Surgery, Hospital Miguel Servet, Zaragoza, Spain
[4] Department of Surgery, Hospital Virgen del Rocío, Sevilla, Spain
[5] Department of Surgery, Hospital Clínico San Carlos, Madrid, Spain
[6] Department of Surgery, Hospital Regional Universitario Carlos Haya, Málaga, Spain
[7] Department of Surgery, Hospital Universitario La Princesa, Madrid, Spain
[8] Department of Surgery, Hospital Universitario Álvaro Cunqueiro, Vigo, Spain
[9] Department of Surgery, Hospital Universitari de Girona Dr. Josep Trueta, Girona, Spain
[10] Department of Surgery, Hospital Universitario de Getafe, Getafe, Spain
[11] Department of Pathology, Hospital Universitario Donostia, San Sebastián, Spain
[12] Department of Surgery, Hospital Universitario Clínic, Barcelona, Spain
[13] Department of Pathology, Hospital Clínico, University of Valencia, INCLIVA Biomedical Research Institute, Valencia, Spain
[14] Department of Surgery, Hospital Universitario Doctor Peset, Valencia, Spain
[15] Department of Surgery, Hospital Universitario Vall d'Hebron, Barcelona, Spain
[16] Department of Surgery, Hospital Clínic, IDIBAPS, University of Barcelona, Barcelona, Spain

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Abstract

Objective:
To compare the rates of R0 resection in pancreatoduodenectomy (PD) for pancreatic and periampullary malignant tumors using the standard approach (ST-PD) versus the artery-first approach (AFA-PD).

Background:
Standardized histological examination of PD specimens has shown that many resections previously considered R0 are in fact R1, particularly at the margin adjacent to the superior mesenteric artery. The artery-first approach has been proposed to improve oncological clearance, but evidence from randomized studies is lacking.

Methods:
A multicenter, randomized, controlled trial was conducted in 10 university hospitals. Patients with resectable pancreatic head adenocarcinoma and periampullary malignant tumors were randomized to ST-PD or AFA-PD. The primary endpoint was R0 resection rate. Secondary endpoints included postoperative morbidity and mortality. Surgical specimens were evaluated using a standardized pathological protocol by pathologists blinded to the surgical approach.

Results:
A total of 176 patients were randomized, and 153 were included in the final analysis (75 ST-PD, 78 AFA-PD). R0 resection rates were 77.3% in the ST-PD group and 67.9% in the AFA-PD group ($p = 0.194$). No significant differences were observed in postoperative complications or mortality between groups.

Conclusions:
Despite theoretical oncological advantages associated with the artery-first approach, this multicenter randomized trial found no differences in R0 resection rates or postoperative outcomes compared with the standard approach.

Keywords

Artery-first approach; Pancreatic cancer; Pancreatoduodenectomy; Periampullary tumors; R0 resection

Introduction

Surgical resection in combination with adjuvant chemotherapy currently represents the only potentially curative treatment for patients with pancreatic and periampullary malignant tumors. Despite advances in surgical technique and perioperative management, long-term outcomes remain poor, and a large proportion of patients experience disease recurrence and cancer-related death within a few years after surgery.

Historically, reported rates of R0 resection after pancreatoduodenectomy (PD) were consistently higher than 70%. However, this perception changed after studies by Verbeke et al. and Esposito et al. demonstrated that when PD specimens are evaluated using standardized

pathological protocols, many resections previously considered R0 are in fact R1. In particular, the circumferential resection margin adjacent to the superior mesenteric artery (SMA) has been identified as the most frequent site of microscopic margin involvement and is now recognized as a key prognostic factor influencing survival.

These findings have led to increasing interest in surgical strategies aimed at improving clearance of the retropancreatic tissue and the medial margin adjacent to the SMA. One such strategy is the so-called “artery-first approach” to pancreatoduodenectomy (AFA-PD). This approach is characterized by early dissection and assessment of the main arterial structures, particularly the SMA, before irreversible surgical steps are undertaken. It also involves meticulous clearance of the retropancreatic tissue along the arterial plane, with the theoretical aim of increasing the likelihood of achieving a true R0 resection.

Two main factors have contributed to the widespread adoption of artery-first techniques over the past decade. First, criteria for local resectability have progressively shifted from venous involvement toward arterial involvement, emphasizing the importance of assessing arterial encasement early during surgery. Second, there is growing recognition of the oncological relevance of the resection margin along the right lateral border of the SMA, which is now considered the most critical margin in pancreatic head cancer surgery.

Several potential advantages have been attributed to the artery-first approach, including early determination of unresectability, avoidance of futile surgery, improved oncological clearance, reduced intraoperative blood loss due to early ligation of the inferior pancreatoduodenal artery, and improved lymph node retrieval. However, despite these theoretical benefits, evidence supporting the superiority of AFA-PD over standard pancreatoduodenectomy (ST-PD) remains limited.

To date, studies comparing artery-first and standard approaches have largely consisted of retrospective cohort studies or case-control series, often with heterogeneous definitions of the artery-first technique and without standardized pathological assessment of resection margins. Consequently, the true impact of the artery-first approach on R0 resection rates and postoperative outcomes remains unclear.

Therefore, the aim of this multicenter, randomized, controlled trial was to compare the rate of tumor-free resection margins (R0) in patients undergoing pancreatoduodenectomy for pancreatic head adenocarcinoma and other periampullary malignant tumors using either the standard surgical approach or the artery-first approach. Secondary objectives included the evaluation of postoperative morbidity and mortality associated with each technique.

Patients and Methods

Study design and setting

This study was designed as a multicenter, randomized, controlled trial comparing the rate of tumor-free resection margins in patients undergoing pancreatoduodenectomy (PD) using either the standard approach (ST-PD) or the artery-first approach (AFA-PD). The trial was conducted in 10 university hospitals with specialized hepatopancreatobiliary surgery units. The study was registered at ClinicalTrials.gov (NCT02803814), and the protocol was approved by the ethics committee of each participating center. All patients provided specific written informed consent prior to inclusion.

The primary endpoint of the study was the rate of R0 resection. Secondary endpoints included postoperative complications, intraoperative and postoperative transfusions, operative time, lymph node retrieval, reoperation, hospital stay, readmissions, and postoperative mortality.

Surgical specimens were evaluated according to a standardized histopathological protocol, with pathologists blinded to the surgical approach. Independent data monitors from the Spanish Clinical Research Network reviewed all procedures and data included in the trial. Data were recorded in electronic case report forms and sent directly to the statistics core facility for analysis. Participating centers were required to perform a minimum of 20 pancreatic resections per year, and all surgeons involved had extensive experience in both surgical techniques. To avoid imbalanced recruitment, no center was allowed to include more than 25 patients. Before patient recruitment, a consensus meeting was held to standardize the technical aspects of both operative procedures.

Patients

Between January 2016 and December 2017, all patients aged 18 years or older with resectable pancreatic and periampullary malignant tumors were evaluated for inclusion. Eligible diagnoses included pancreatic head adenocarcinoma, ampullary adenocarcinoma, distal cholangiocarcinoma, and duodenal adenocarcinoma.

Exclusion criteria were the presence of liver metastases or peritoneal carcinomatosis, high surgical risk defined as American Society of Anesthesiologists (ASA) physical status IV, prior neoadjuvant treatment, history of other malignant tumors, residual macroscopic disease (R2 resection), and definitive histopathological diagnosis other than the eligible tumor types.

Randomization

Patients were randomly assigned to either ST-PD or AFA-PD using block randomization stratified by participating center in order to ensure balanced group allocation. Randomization codes consisted of a three-letter center identifier followed by the patient number and were accessible only to the research team of each center. Treatment allocations were sealed in numbered envelopes and opened in the operating room after intraoperative confirmation that the tumor was resectable.

Sample size calculation

Sample size was calculated using the GRANMO program. Based on previous studies, the R1 resection rate with standardized pathological assessment was estimated to be approximately 50% for pancreatic and periampullary malignant tumors. In published series evaluating the artery-first approach, reported R1 rates ranged from 18% to 27%. Assuming a clinically significant reduction in R1 rate from 50% with ST-PD to 25% with AFA-PD, a total of 144 patients (72 per group) were required to achieve a statistical power of 80% with a two-sided significance level of 5%, accounting for an anticipated dropout rate of 20%. The arcsine method was used for this calculation.

Surgical technique

Standard pancreatoduodenectomy

Following abdominal exploration, a wide Kocher maneuver and mobilization of the right colon were performed. The greater omentum was separated from the mesocolon and removed. The superior mesenteric vein and pancreatic neck were exposed after dissection of the colonic

mesentery from the anterior surface of the duodenum. The gastrocolic trunk was dissected and divided, allowing exposure of the anterior surface of the superior mesenteric vein below the pancreas.

Cholecystectomy was performed, the lesser sac was opened, and the hepatoduodenal ligament was completely dissected with division of the gastroduodenal artery. The bile duct was divided and the portal vein circumferentially dissected, removing all surrounding lymphatic tissue. Gastric or duodenal transection was carried out using a linear stapler. The jejunum was divided at the angle of Treitz and passed to the right side behind the mesenteric vessels. The pancreatic neck was divided, and small vessels from the portomesenteric axis to the pancreatic head were ligated and divided. Finally, the retroperitoneal border of the pancreas was sectioned and the specimen removed.

Artery-first approach pancreatoduodenectomy

A wide Kocher maneuver was performed to expose the anterior surface of the inferior vena cava and the left renal vein. The assistant retracted the mesentery toward the left shoulder, facilitating exposure of the superior mesenteric artery (SMA) above the left renal vein. The SMA was encircled with a vessel loop, and attachments between the SMA, the uncinate process, and the portal vein were divided. The inferior and posterior pancreatoduodenal arteries were identified and divided.

Dissection of the hepatic pedicle and hepatoduodenal ligament was then carried out. Transection of the stomach or duodenum, jejunum, and pancreatic neck was performed in the same manner as in the standard approach. The posterolateral aspect of the portal vein was dissected, dividing its tributary branches to allow clearance of the retroperitoneal tissue along the right lateral edge of the SMA, after which the specimen was removed.

In both techniques, standard lymphadenectomy was performed, including lymph node stations 5, 6, 8a, 12, 13, 14a and 14b, and 17. Intraoperative frozen-section analysis of the pancreatic transection margin was routinely performed. If the margin was positive, additional pancreatic tissue was resected. Completion pancreatectomy was indicated in cases of a second positive transection margin or when the remaining pancreatic remnant was too small to allow safe reconstruction.

End-point definitions

R0 resection was defined as noninvolvement of circumferential resection margins, with a minimum distance of more than 1 mm between tumor cells and the resection margin. The histopathological protocol included identification and inking of the pancreatic transection margin and the circumferential resection margin, which comprised both the medial (vascular) and posterior (retroperitoneal) margins.

Postoperative morbidity was defined according to international consensus criteria. Pancreatic fistula, delayed gastric emptying, and postoperative hemorrhage were classified according to the International Study Group of Pancreatic Surgery definitions. Biliary leak was defined according to the International Study Group of Liver Surgery. Chylous fistula was defined as the presence of milky, amylase-poor, triglyceride-rich drainage. Diarrhea was defined as an increase in bowel movements to more than three per day. Complications were graded using the Clavien–Dindo classification and summarized using the Comprehensive Complication Index.

Intraoperative transfusion was defined as administration of blood or blood products during surgery or immediately afterward. Reoperation was defined as any surgical procedure requiring general anesthesia. Readmission was defined as rehospitalization within 30 days after discharge. Mortality was defined as death during the same hospital admission or within 90 days following surgery.

Statistical analysis

All analyses were performed on an intention-to-treat basis. Categorical variables were expressed as counts and percentages, and continuous variables as mean ± standard deviation or median with interquartile range, as appropriate. A log-binomial regression model including the surgical approach as a covariate was used to compare R0 resection rates between groups.

Continuous secondary outcomes were analyzed using the Student t test, categorical variables using Fisher's exact test, and ordinal variables using the Mann–Whitney U test. Statistical significance was set at a two-sided p value of < 0.05. The primary endpoint was also analyzed in the subgroup of patients with pancreatic ductal adenocarcinoma.

All statistical analyses were conducted by an independent medical statistics core facility using SAS version 9.4.

Results

Patient flow and study population

Between January 2016 and December 2017, a total of 179 patients were assessed for eligibility. Of these, 176 patients met the inclusion criteria and were randomized to undergo either standard pancreatoduodenectomy (ST-PD) or artery-first approach pancreatoduodenectomy (AFA-PD). After randomization, 23 patients were excluded from the final analysis due to intraoperative findings or definitive histopathological diagnoses not meeting inclusion criteria. The final study population consisted of 153 patients: 75 patients in the ST-PD group and 78 patients in the AFA-PD group. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram is shown in Figure 2.

Patient and surgical characteristics

Baseline patient characteristics and details of the surgical procedures are summarized in Table 1. Mean patient age was similar between groups (67.7 ± 10.2 years in the ST-PD group and 67.9 ± 9.7 years in the AFA-PD group). Sex distribution, prevalence of diabetes mellitus, American Society of Anesthesiologists (ASA) physical status, and rates of preoperative biliary drainage did not differ significantly between groups.

The most frequent pathological diagnosis was pancreatic ductal adenocarcinoma, accounting for 58% of cases overall, followed by ampullary adenocarcinoma (31.4%), distal cholangiocarcinoma (9.2%), and duodenal adenocarcinoma (1.3%). The proportion of pancreatic ductal adenocarcinoma was higher in the AFA-PD group, although this difference did not reach statistical significance.

Surgical variables, including the proportion of pylorus-preserving pancreatoduodenectomy, type of pancreatic anastomosis, need for vascular resection, and rate of completion pancreatectomy, were comparable between the two groups. Venous resection was performed in 19.6% of patients overall. Completion pancreatectomy was required in 10.5% of cases, with no significant difference between groups.

Primary endpoint: R0 resection rate

R0 resection rates for pancreatic and periampullary malignant tumors were 77.3% (95% CI: 68.4–87.4) in the ST-PD group and 67.9% (95% CI: 58.3–79.1) in the AFA-PD group. This difference was not statistically significant (p = 0.194).

In the subgroup of patients with pancreatic ductal adenocarcinoma (n = 87), R0 resection rates were 57.9% in the ST-PD group and 58.8% in the AFA-PD group (p = 0.930), indicating no difference between surgical approaches in this subgroup.

Resection margin involvement

Overall, 42 patients (27.4%) had at least one involved resection margin. Margin involvement occurred in 22.7% of patients in the ST-PD group and 32.1% in the AFA-PD group. The most frequently affected margin was the posterior circumferential (retroperitoneal) margin, involved in 88% of cases with margin positivity in the ST-PD group and 56% in the AFA-PD group. Although there was a trend toward fewer posterior margin involvements in the AFA-PD group, this difference did not reach statistical significance (p = 0.069).

Involvement of the transection margin and medial (vascular) margin was infrequent and did not differ significantly between groups.

Operative and perioperative outcomes

Operative outcomes are detailed in Table 2. Median operative time was 330 minutes (interquartile range [IQR] 285–390) in the ST-PD group and 360 minutes (IQR 300–420) in the AFA-PD group (p = 0.430). Mean intraoperative blood loss was similar between groups (303 ± 408 mL in ST-PD versus 344 ± 304 mL in AFA-PD; p = 0.525). Rates of intraoperative blood transfusion did not differ significantly.

Overall postoperative morbidity occurred in 73.3% of patients undergoing ST-PD and 67.9% of those undergoing AFA-PD (p = 0.484). There were no statistically significant differences between groups in the incidence of postoperative pancreatic fistula, delayed gastric emptying, postoperative hemorrhage, biliary fistula, gastrointestinal fistula, abdominal abscess, chylous fistula, or diarrhea.

The severity of postoperative complications, assessed using the Clavien–Dindo classification and the Comprehensive Complication Index, was comparable between groups. Rates of reoperation and hospital readmission within 30 days were also similar.

Median postoperative hospital stay was 15 days (range 11–22) in the ST-PD group and 17 days (range 13–25) in the AFA-PD group (p = 0.182).

Mortality

Thirty-day mortality was 4.0% in the ST-PD group and 6.4% in the AFA-PD group. Ninety-day mortality rates were 4.0% and 7.7%, respectively. These differences were not statistically significant.

Discussion

This study represents the first multicenter, randomized, controlled trial comparing R0 resection rates between two different surgical approaches to pancreatoduodenectomy for pancreatic head and periampullary malignant tumors. The most complex anatomical area of the

pancreatoduodenectomy procedure was approached either from the portal vein–superior mesenteric vein axis (standard approach) or from the superior mesenteric artery (artery-first approach). According to the results of this trial, the choice of surgical approach had no impact on the rate of tumor-free resection margins.

Despite the increasing popularity of the artery-first approach, the concept is not new. It was first described in the 1990s by Nakao and Takagi and by Leach and colleagues, and subsequently refined by several groups who emphasized early evaluation of arterial involvement and systematic clearance of retropancreatic tissue. Over time, the term “artery-first approach” has been used to describe a variety of techniques sharing the common principle of early dissection of the superior mesenteric artery. However, the heterogeneity of these approaches and the lack of standardized pathological assessment have limited the interpretability of previously published studies.

Several theoretical advantages have been attributed to the artery-first approach, including early determination of unresectability, avoidance of futile surgery, increased lymph node retrieval, shorter operative time, reduced intraoperative blood loss, and lower transfusion requirements due to early ligation of the inferior pancreatoduodenal artery. Nevertheless, none of these advantages were confirmed in the present randomized trial. In our series, artery-first pancreatoduodenectomy tended to be associated with a longer operative time, while blood loss, transfusion rates, and postoperative morbidity were comparable between the two groups.

Two meta-analyses comparing artery-first and standard pancreatoduodenectomy have been published. In the first, Negoi et al. reported reduced blood loss, fewer transfusions, lower rates of pancreatic fistula and delayed gastric emptying, shorter hospital stay, and lower local recurrence rates with the artery-first approach, but no differences in R0 resection rates, major postoperative complications, mortality, lymph node retrieval, or long-term survival. A more recent meta-analysis by Ironside et al. suggested advantages of the artery-first approach in terms of R0 resection, perioperative outcomes, and overall survival. However, both meta-analyses included exclusively retrospective studies with heterogeneous surgical techniques and non-standardized margin assessment, limiting the strength of their conclusions.

In our trial, no difference in R0 resection rates was observed when considering all tumor types or when restricting the analysis to patients with pancreatic ductal adenocarcinoma. The similarity of R0 resection rates between groups in the pancreatic adenocarcinoma subgroup suggests that increasing the sample size would be unlikely to reveal a clinically meaningful difference. These findings are particularly relevant in light of ongoing randomized trials, such as the MAPLE-PD study, which focuses on overall survival rather than margin status as the primary endpoint.

The inclusion of periampullary tumors may be considered a limitation, as many studies evaluating margin status have focused exclusively on pancreatic ductal adenocarcinoma. However, this decision was deliberate. Preoperative biopsy is not mandatory in resectable periampullary tumors, and many patients undergo surgery without a definitive histological diagnosis. Moreover, growing evidence suggests that prognostic factors such as lymph node involvement and perineural invasion may be more relevant than tumor location alone. Including all periampullary malignancies allowed assessment of the oncological effectiveness of both techniques across the full spectrum of resectable tumors encountered in clinical practice.

Another potential limitation is the relatively high rate of completion pancreatectomy. In this study, completion pancreatectomy was performed according to predefined intraoperative criteria following frozen-section analysis of the pancreatic transection margin and was not related to borderline resectable disease. The similar rates of completion pancreatectomy in both groups and the intention-to-treat analysis mitigate the potential impact of this factor on the primary outcome.

This trial has several strengths, including its randomized design, multicenter participation, standardized surgical techniques agreed upon before patient recruitment, and blinded pathological assessment using a standardized margin protocol. These methodological features address the main weaknesses of previous studies and provide a high level of evidence regarding the comparative effectiveness of artery-first and standard pancreatoduodenectomy.

In summary, despite theoretical oncological advantages and encouraging results from low-level evidence, this multicenter, randomized, controlled trial demonstrates that the artery-first approach does not improve R0 resection rates or postoperative outcomes compared with the standard approach in patients undergoing pancreatoduodenectomy for pancreatic head adenocarcinoma and other periampullary malignant tumors.

References

1. Hester CA, Dogeas E, Augustine MM, et al. Incidence and comparative outcomes of periampullary cancer: a population-based analysis demonstrating improved outcomes and increased use of adjuvant therapy from 2004 to 2012. *J Surg Oncol*. 2019;119:303–317.
2. Plichta JK, Godambe AS, Fridirici Z, et al. The association between survival and the pathologic features of periampullary tumors varies over time. *HPB Surg*. 2014;2014:890530.
3. Van Roest MH, Gouw AS, Peeters PM, et al. Results of pancreaticoduodenectomy in patients with periampullary adenocarcinoma: perineural growth more important prognostic factor than tumor localization. *Ann Surg*. 2008;248:97–103.
4. Verbeke CS, Leitch D, Menon KV, et al. Redefining the R1 resection in pancreatic cancer. *Br J Surg*. 2006;93:1232–1237.
5. Esposito I, Kleeff J, Bergmann F, et al. Most pancreatic cancer resections are R1 resections. *Ann Surg Oncol*. 2008;15:1651–1660.
6. Gómez-Mateo MC, Sabater-Ortí L, Ruiz-Montesinos I, et al. Pathology reporting of resected pancreatic/periampullary cancer specimen. In: Tewari M, ed. *Surgery for Pancreatic and Periampullary Cancer: Principles and Practice*. Singapore: Springer Nature; 2018:247–280.
7. Campbell F, Cairns A, Duthie F, et al. Dataset for the histopathological reporting of carcinomas of the pancreas, ampulla of Vater and common bile duct. The Royal College of Pathologists; 2017. London.
8. Soer E, Brosens L, van de Vijver M, et al. Dilemmas for the pathologist in the oncologic assessment of pancreatoduodenectomy specimens. *Virchows Arch*. 2018;472:533–543.

9. Menon KV, Gomez D, Smith AM, et al. Impact of margin status on survival following pancreatoduodenectomy for cancer: the Leeds Pathology Protocol. *HPB (Oxford)*. 2009;11:18–24.

10. Strobel O, Hank T, Hinz U, et al. Pancreatic cancer surgery: the new R-status counts. *Ann Surg*. 2017;265:565–573.

11. Chandrasegaram MD, Goldstein D, Simes J, et al. Meta-analysis of radical resection rates and margin assessment in pancreatic cancer. *Br J Surg*. 2015;102:1459–1472.

12. Ghaneh P, Kleeff J, Halloran CM, et al. The impact of positive resection margins on survival and recurrence following resection and adjuvant chemotherapy for pancreatic ductal adenocarcinoma. *Ann Surg*. 2017;269:520–529.

13. Markov P, Satoi S, Kon M. Redefining the R1 resection in patients with pancreatic ductal adenocarcinoma. *J Hepatobiliary Pancreat Sci*. 2016;23:523–532.

14. Horiguchi A, Ishihara S, Ito M, et al. Pancreatoduodenectomy in which dissection of the efferent arteries of the head of the pancreas is performed first. *J Hepatobiliary Pancreat Surg*. 2007;14:575–578.

15. Figueras J, Codina-Barreras A, López-Ben S, et al. Cephalic duodenopancreatectomy in periampullary tumors. *Cir Esp*. 2008;83:186–193.

16. Kawai M, Tani M, Ina S, et al. CLIP method reduces intraoperative bleeding during pancreaticoduodenectomy. *World J Surg*. 2008;32:82–87.

17. Dumitrascu T, David L, Popescu I. Posterior versus standard approach in pancreatoduodenectomy. *Langenbecks Arch Surg*. 2010;395:677–684.

18. Ishizaki Y, Sugo H, Yoshimoto J, et al. Pancreatoduodenectomy with or without early ligation of the inferior pancreatoduodenal artery. *World J Surg*. 2010;34:2939–2944.

19. Kurosaki I, Minagawa M, Takano K, et al. Left posterior approach to the superior mesenteric vascular pedicle. *JOP*. 2011;12:220–229.

20. Shrikhande SV, Barreto SG, Bodhankar YD, et al. Superior mesenteric artery first approach. *Langenbecks Arch Surg*. 2011;396:1205–1212.

21. Kawabata Y, Tanaka T, Nishi T, et al. Total mesopancreatoduodenum excision. *Eur J Surg Oncol*. 2012;38:574–579.

22. Gundara JS, Wang F, Alvarado-Bachmann R, et al. Early complete pancreatic head devascularisation. *Am J Surg*. 2013;206:518–525.

23. Aimoto T, Mizutani S, Kawano Y, et al. Left posterior approach pancreatoduodenectomy. *J Nippon Med Sch*. 2013;80:438–445.

24. Shah OJ, Gagloo MA, Khan IJ, et al. Pancreaticoduodenectomy: superior approach versus classical Whipple. *Hepatobiliary Pancreat Dis Int*. 2013;12:196–203.

25. Nakamura M, Nakashima H, Tsutsumi K, et al. First jejunal vein oriented mesenteric excision. *J Gastroenterol*. 2013;48:989–995.

26. Zhou HY, Wang Y, Zhang J, et al. Retrograde vs conventional dissection technique. *JAMA Surg*. 2014;149:604–607.

27. Inoue Y, Saiura A, Yoshioka R, et al. Systematic mesopancreas dissection. *Ann Surg*. 2015;262:1092–1101.

28. Vallance A, Young A, Pandanaboyana S, et al. Posterior SMA-first dissection. *Pancreas*. 2017;46:276–281.

29. Hirono S, Kawai M, Okada K, et al. Mesenteric approach during pancreatoduodenectomy. *Ann Gastroenterol Surg*. 2017;1:208–218.

30. Sabater L, Gómez-Mateo MC, López-Sebastián J, et al. Prognostic implications of standardized margin study. *Cir Esp*. 2014;92:532–538.

31. Tol JA, Gouma DJ, Bassi C, et al. Definition of standard lymphadenectomy. *Surgery*. 2014;156:591–600.

32. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula definition. *Surgery*. 2005;138:8–13.

33. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying definition. *Surgery*. 2007;142:761–768.

34. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage definition. *Surgery*. 2007;142:20–25.

35. Koch M, Garden OJ, Padbury R, et al. Bile leakage definition. *Surgery*. 2011;149:680–688.

36. Assumpcao L, Cameron JL, Wolfgang CL, et al. Chyle leaks following pancreatic resection. *J Gastrointest Surg*. 2008;12:1915–1923.

37. Dindo D, Demartines N, Clavien PA. Classification of surgical complications. *Ann Surg*. 2004;240:205–213.

38. Slankamenac K, Graf R, Barkun J, et al. Comprehensive Complication Index. *Ann Surg*. 2013;258:1–7.

39. Nakao A, Takagi H. Isolated pancreatectomy for pancreatic head carcinoma. *Hepatogastroenterology*. 1993;40:426–429.

40. Leach SD, Davidson BS, Ames FC, et al. Alternative exposure of retropancreatic vasculature. *J Surg Oncol*. 1996;61:163–165.

41. Machado MC, Penteado S, Cunha JE, et al. Pancreatic head tumors with portal vein involvement. *Hepatogastroenterology*. 2001;48:1486–1487.

42. Pessaux P, Varma D, Arnaud JP. SMA-first pancreatoduodenectomy. *J Gastrointest Surg*. 2006;10:607–611.

43. Varty PP, Yamamoto H, Farges O, et al. Early retropancreatic dissection. *Am J Surg*. 2005;189:488–491.

44. Weitz J, Rahbari N, Koch M, et al. The artery-first approach. *J Am Coll Surg*. 2010;210:e1–e4.

45. Sanjay P, Takaori K, Govil S, et al. Artery-first approaches. *Br J Surg*. 2012;99:1027–1035.

46. Negoi I, Hostiuc S, Runcanu A, et al. SMA-first versus standard PD. *Hepatobiliary Pancreat Dis Int*. 2017;16:127–138.

47. Ironside N, Barreto SG, Loveday B, et al. Meta-analysis of artery-first approach. *Br J Surg*. 2018;105:628–636.

48. Gall TM, Jacob J, Frampton A, et al. No-touch isolation technique. *JAMA Surg*. 2014;149:482–485.

49. Nakao A. The mesenteric approach in pancreatoduodenectomy. *Dig Surg*. 2016;33:308–313.

50. Asbun HJ, Conlon K, Fernandez-Cruz L, et al. When to perform PD without biopsy. *Surgery*. 2014;155:887–892.

51. Hirono S, Kawai M, Okada KI, et al. MAPLE-PD trial protocol. *Trials*. 2018;19:613.