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ORIGINAL ARTICLE

Insights from Managing Clinical Issues in Distal Pancreatectomy with En Bloc Celiac Axis Resection: Experiences from 626 Patients

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Running Head

DP-CAR multicenter cohort

Keywords

DP-CAR, pancreatic cancer, celiac axis resection, preoperative arterial embolization

Abstract

Background: Distal pancreatectomy with *en bloc* celiac axis resection (DP-CAR) for pancreatic body cancer has been increasingly reported. However, its large-scale outcomes remain undocumented. This study aimed to evaluate the DP-CAR volume and mortality, preoperative arterial embolization for ischemic gastropathy (IG), oncological benefit for resectable tumors close to the bifurcation of splenic artery (SPA) and celiac artery using propensity score matching (PSM), and prognostic factors in DP-CAR.

Methods: In a multi-institutional analysis, 626 DP-CAR were analyzed retrospectively and compared with 1 325 DP in the same period.

Results: The 90-day mortality was observed in 7 out of 21 high-volume (≥ 1 DP-CAR/year) centers and 1 out of 41 low-volume centers (odds ratio (OR), 20.0; 95% confidence interval (c.i.) 2.26 to 177.26). The incidence of IG was 19.2% in the embolization group and 7.9% in the no embolization group (OR, 2.77; 95% c.i., 1.48–5.19). The PSM analysis showed that the median overall survival was 33.5 months (95% c.i., 27.4–42.0) in the DP-CAR and 37.9 months (95% c.i., 32.8–53.3) in the DP. Multivariable analysis identified age (≥ 67 ; hazard ratio (HR), 1.40; 95 % c.i., 1.12–1.75), preoperative tumor size (≥ 30 mm; HR, 1.42; 95% c.i., 1.12–1.80), and preoperative CA19-9 (>37 U/mL; HR, 1.43; 95% c.i., 1.11–1.83) as adverse prognostic factors.

Conclusion: DP-CAR was safely performed in centers for general pancreatic surgery regardless of DP-CAR volume, and may not be required in preoperative embolization, no oncologic effect for resectable tumor closed to the bifurcation of SPA, and should be performed after appropriate patient selection.

Introduction

Distal pancreatectomy with *en bloc* celiac axis resection (DP-CAR) was developed to accomplish R0 resections for locally advanced pancreatic body cancer invading the celiac artery (CA), providing the prospect of survival to patients with unresectable (UR) lesions¹⁻¹⁷. Owing to recent advances in chemotherapy, DP-CAR is performed more often following preoperative therapy¹⁸; however, mortality rate remained high at the low-volume centers¹², and such a high-risk operation is indicated after proper patient selection only. Preoperative common hepatic arterial embolization and/or additional left gastric arterial embolization techniques have reportedly been used for the development of pancreatic head arterial arcade to prevent ischemic complications such as ischemic gastropathy (IG) and liver ischemia^{19,20}. However, the effect of preoperative embolization remains controversial^{21,22}, and arterial reconstruction is reported as an alternative^{23,24}. The patient selection of potentially resectable pancreatic body cancer, DP-CAR may be performed for tumors close to the bifurcation of the splenic artery (SPA) and CA without CA or common hepatic artery (CHA) invasion, and avoid a risk of microscopic positive cancer cells or dissemination cancer cells during surgery.

This study aimed to evaluate the following: 1) DP-CAR volume and mortality; 2) effectiveness of preoperative arterial embolization for ischemic complications; 3) survival effect of DP-CAR in patients with tumors close to the bifurcation of the SPA and CA without cancer invasion compared with that of DP using propensity score matching (PSM); and 4) preoperative prognostic factors to select patients for whom DP-CAR would have oncological value. The study hypotheses were as follows: the high-volume center would have low mortality in DP-CAR, preoperative arterial embolization would contribute to a low incidence of ischemic complications, and DP-CAR would have an oncological advantage for tumors close to the bifurcation of the SPA. Additionally, the study aimed to identify several prognostic factors.

1 Patients and methods

2 Study design

3 This study was a retrospective cohort analysis of the multicenter, 71 member institutions of the Japanese
4 Society of Pancreatic Surgery that specialized in pancreatic surgery. All patients treated for pancreatic
5 body cancer at these participating institutions were registered in a database. The study protocol was
6 approved by the Institutional Review Board of Hokkaido University (no. 017-0402).

8 Patient population

9 Between September 1987 and December 2017, 1 951 patients with pancreatic invasive ductal
10 adenocarcinomas of the body of the pancreas were enrolled. Patients were divided into two categories:
11 1) tumors involved with or abutting the CHA and/or the CA (T4 tumor) and 2) tumors with an edge near
12 the bifurcation of CHA and SPA without CHA nor CA involvement. Of these patients, 626 received DP-
13 CAR in 63 institutions, and 1 325 received DP in 71 institutions. DP-CAR was mainly performed for
14 category 1 patients; DPs were mainly performed for category 2. Indications for employing the method
15 were decided by each institution. The centers with an annual patient volume of one or more were
16 considered high-volume DP-CAR centers, and others were considered low-volume DP-CAR centers¹².
17 The annual DP-CAR volume per center was based on the mean number of reported procedures between
18 2015 and 2017.

20 Data Collection

21 The following factors were collected and examined: preoperative factors (sex, age, tumor size, serum
22 albumin); C-reactive protein (CRP); carbohydrate Antigen 19-9 (CA19-9); modified Glasgow
23 prognostic score (mGPS); prognostic nutritional index (PNI); neutrophil lymphocyte ratio (NLR);
24 platelet-lymphocyte ratio (PLR); performance status; and preoperative therapy, operative factors
25 (operative time, blood loss, blood transfusion, additional organs resected, and vascular reconstruction),
26 mortality measures (30-day, 90-day), ischemic complications in the stomach, liver, or kidney,
27 gastrointestinal perforation, abdominal abscess, reoperation, and hospital stay. Surgical morbidity was

evaluated based on the Clavien–Dindo classification²⁵. Pancreatic fistula and delayed gastric emptying were evaluated according to the International Study Group of Pancreatic Surgery classification^{26,27}. IG was defined as gastric dysfunction with endoscopic evidence of irregular, shallow, and wide ulcerations, including gastric partial or transmural necrosis, gastric fistula, or perforation due to ischemic changes as evidenced by clinical findings^{28,29}. Hepatic ischemia was defined as radiographic ischemic findings concomitant with abnormal liver function tests^{10,24,29}. Patients with ischemic cholecystitis and kidney disease showed radiographic ischemic findings or symptoms that required intervention. Pathological findings were assessed by pathologists at each hospital, using Union for International Cancer Control - TNM version 7 for principal and initial recurrence patterns. Resectability was assessed based on the guidelines of the National Comprehensive Cancer Network (NCCN 2016 version)³⁰. Overall survival (OS) time was calculated from the time of the first treatment, including preoperative treatment and surgery, to the last follow-up visit or death. Treatment detail and pathological summary were shown in Tables S1 and S2.

Statistical Analysis

Survival results between DP-CAR and DP were compared using PSM analysis, to reduce bias from factors influencing prognostic outcomes. Factors used for matching were preoperative available factors, including age, sex, tumor diameter (imaging diagnosis right before surgery), CA19-9 value (measured right before surgery), and preoperative treatment status. Propensity scores were calculated using a logistic regression model, and one-to-one-matched groups were created with a caliper of 0.2. Data for continuous variables are expressed as median (interquartile rang; i.q.r). Categorical data were expressed in the form of numbers and proportions and were analyzed using Fisher's exact test or χ^2 test. Kaplan–Meier curves were generated to estimate OS, and comparisons between groups were performed using log-rank tests. A P value <0.05 was considered statistically significant. All statistical analyses were performed using JMP® Pro (Version 16.1.0, SAS Institute Inc., Cary, NC, 1989–2023).

Results

DP-CAR volume and mortality

During the study period, DP-CAR was performed in 626 patients; the 30- and 90-day mortality were 1.3% and 2.7%, respectively (Table 1). The number of DP-CAR procedures have increased with approximately 60 patients annually in recent years (Fig. S1). In the past decade, 90-day mortality patients were observed in 8 centers and none in the remaining 54 centers. The incidence of one or more 90-day mortality patients was noted in 33.3% (7/21) of high-volume DP-CAR centers (DP-CAR/year)¹² and 2.4% (1/41) of low-volume DP-CAR centers (odds ratio (OR), 20.0; 95% confidence interval (c.i.), 2.26–177.26; $P = 0.0015$). The DP-CAR mortality in each center is summarized in Table S3.

The left gastric artery-preserving procedure and preoperative arterial embolization for postoperative ischemic gastropathy

Of the 626 patients, 26 patients underwent DP-CAR with total gastrectomy and 600 patients underwent stomach-preserving DP-CAR, categorized as follows: 1) standard DP-CAR (n=442); 2) LGA-preserving DP-CAR (n=109); and 3) LGA-reconstructing DP-CAR (n=49) (Fig. 1). The incidence of IG in the standard DP-CAR was 14.7%, whereas that in the LGA-preserving DP-CAR was reduced to 0.9% (OR, 0.054; 95% c.i., 0.0074–0.39; $P < 0.0001$). Conversely, the incidence of IG in the LGA-reconstructing DP-CAR was 10.2% (OR, 0.66; 95% c.i., 0.25–1.72; $P = 0.52$, compared with standard DP-CAR). As an effect of preoperative arterial embolization, the incidence of IG was 19.2% in the embolization group and 7.9% in the no embolization group (OR, 2.77; 95% c.i., 1.48–5.19; $P = 0.001$). The CHA embolization with additional embolization of LGA including other vessels group, the incidence of IG was 19.2 per cent (OR, 0.99; 95% c.i., 0.52–1.90; $P = 0.98$, compared with the only CHA embolization group). The ischemic morbidity in each procedure is summarized in Table S4.

Outcomes of DP-CAR versus DP for pancreatic body cancer in which the tumor edge was close to the SPA bifurcation: propensity score-matched analysis

Of 1951 pancreatic body cancer patients, 551 patients had tumors within 10 mm to the bifurcation of the SPA and the CA without cancer invasion to CA or CHA (Fig. 2a). Of the 551 patients, 414 patients were performed DP, and 137 patients were performed DP-CAR (extended resection). After matching for age, sex, clinical tumor diameter (measured right before surgery), CA19-9 value (measured right before surgery), and preoperative treatment status, 135 patients were matched and included in each group (Fig. 2b). Before and after PSM are shown in Tables S5 and S6. The R0 resection rate (83.0% versus 80.7%; $P = 0.64$), adjuvant therapy (86.7% versus 85.9%; $P = 0.96$), and positive lymph nodes (57.0% versus 56.3%; $P = 0.84$) were similar between the two groups. The median duration of overall survival (OS) was 33.5 months (95% c.i., 27.4–42.0) in the DP-CAR group and 37.9 months (95% c.i., 32.8–53.3) in the DP group ($p = 0.26$; Fig. 2c). Subgroup analysis of both upfront surgery and preoperative therapy showed similar tendency as full set analysis. In the upfront surgery subgroup, the median duration of OS was 31.1 months (95% c.i., 20.3–49.1) in the DP-CAR group and 37.6 months (95% c.i., 24.1–50.4) in the DP group ($p = 0.95$; Fig. S2a). In the preoperative therapy subgroup, the median duration of OS was 27.2 months (95% c.i., 21.3–36.4) in the DP-CAR group and 42.8 months (95% c.i., 26.6–not reached) in the DP group ($p = 0.11$; Fig. S2b).

Preoperative provable prognostic factors for DP-CAR

To identify preoperative prognostic factors for postoperative OS in DP-CAR, clinical factors such as age, sex, tumor size, CA19-9, NLR, mGPS, PLR, and PNI were evaluated by univariable and multivariable analyses using data right before surgery in borderline resectable (BR)/UR patients (Table 2). In the multivariable analysis, age ≥ 67 years (hazard ratio (HR), 1.40; 95% c.i., 1.12–1.75; $P = 0.0036$), clinical tumor size (cTS) ≥ 30 mm (HR, 1.42; 95% c.i., 1.12–1.80; $P = 0.0041$), and CA19-9 > 37 U/ml (HR, 1.43; 95% c.i., 1.11–1.83; $P = 0.0052$) were poor prognostic factors for OS. The median duration of OS was 21.0 months (95% c.i., 17.8–24.2) in the age ≥ 67 group and 29.2 months (95% c.i., 24.9 to 34.0) in the age < 67 group, 22.1 months (95% c.i., 20.4 to 24.5) in the cTS ≥ 30 mm group and 30.9 months (95% c.i., 24.9 to 41.0) in the cTS < 30 mm group, 22.1 months (95% c.i., 18.9 to 24.9) in

the CA19-9 >37 U/ml group and 40.1 months (95% c.i., 25.3 to 46.0) in the CA19-9 ≤37 U/ml group. Survival curves using the Kaplan–Meier and log-rank tests are shown in Fig. S3.

Discussion

Contrary to expectations, in this study, the mortality of DP-CAR in high-volume centers was higher than that in low-volume centers. A previous international multicenter study showed that DP-CAR was associated with a 90-day mortality rate of 5.5% in 5 high-volume centers, and 18% in 18 low-volume centers¹². In our study, 87% of the centers had 0.0% 90-day mortality; therefore, this disparity in results may have been caused by the extremely low mortality rates in each center. One of the reasons for the lower mortality rates for DP-CAR in low-volume centers could have been that the facilities that participated were all high-volume centers for pancreatic surgery, even if they were low-volume for DP-CAR. These institutions held the institutional certification of the Japanese Society of Hepato-Biliary-Pancreatic Surgery, and surgeons held the licensing credentials of board-certified expert surgeons in the hepatobiliary-pancreatic field. Therefore, even if there were <1 DP-CAR/year, we believe that the quality of pancreatic surgery was equal to that of high-volume centers for DP-CAR. Another possibility is that high-risk patients were refused resection at low-volume centers, whereas high-volume centers may accept patients seeking a second or third opinion. Alternatively, a university hospital or cancer center could have taken on more challenging operations. In contrast, low-volume centers may have selected patients with low surgical risk. Working on aggressive surgical procedures such as DP-CAR may present a bias, in which the facility bears the increased risk of mortality. DP-CAR mortality risk score system including factors for low- versus high-volume center was provided by a previous study¹²; however, it was difficult to confirm the risk using our study patients (data not shown).

In our study, preoperative hepatic artery embolization had a higher incidence of postoperative IG than without embolization. Similarly, several studies have recently reported that preoperative hepatic and/or left gastric arterial embolization have no effect^{21,22}. Additionally, a Spanish multicenter study showed that preoperative hepatic artery embolization did not improve morbidity, mortality, or survival probability³³. It is presumed that if the CA is ligated during the operation, the

pancreatic head arcade will develop immediately. Contrast-enhanced findings during embolization supported the assumption that the pancreatic head arcade develops immediately after embolization¹⁹. There are several biases in the current study, such as blood flow from the right gastric artery or communication from the left hepatic artery will affect the gastric arterial supply. Speculating on the cause of the worsened effects of embolization, the embolization of the CHA and LGA develops a pancreatic head arcade, but may also develop the SPA, posterior gastric arteries (PGA), and short gastric arteries (SGA), resulting in enhanced blood flow to the stomach's fundus that is more dependent on the PGA and SGA supply. In this situation, when DP-CAR is performed and the PGA and SGA are both dissected, it is speculated that the blood flow of the stomach fundus will almost instantaneously decrease. Thus, patients who are more dependent on PGA and SGA after embolization may suffer more severe ischemia following DP-CAR. This speculation must be confirmed by future research.

Alternative to the embolization method, a blood flow-preserving technique is recommended for patients with IG, which preserves the LGA and/or left inferior phrenic arteries³². However, the LGA-preserving DP-CAR had limited indications for patients without LGA-tumor involvement. In contrast, arterial reconstruction methods such as LGA reconstruction should be more widely acceptable^{23,24}. Our results showed that the arterial reconstruction DP-CAR had 10.2% of IG. There may be technical problems with arterial patency after reconstruction or insufficient blood flow from the selected supply artery. Oba et al. have evaluated reconstruction quality using intraoperative angiography with indocyanine green-fluorescence (ICG) imaging for LGA, showing that 39% (7/18) of patients had poor flow following initial reconstruction, and five required LGA re-anastomosis³⁴. Further, comparisons of clinical and vascular geometry data by Egorov et al. have revealed fast adaptation of collateral circulation, insignificant changes in the proper hepatic artery diameter, and a high risk of IG if the preoperative diameter of the pancreaticoduodenal artery was <2 mm³⁵. Hence, preoperative embolization remains controversial; however, arterial reconstruction is for selected patients at risk of IG before surgery or have poor stomach blood flow as seen on ICG angiography during surgery. Thus, the arterial reconstruction team should be available in patients with a high risk of IG for DP-CAR.

In this study, DP-CAR (extended resection) and DP (standard resection) were compared by PSM for pancreatic body cancer close to the bifurcation of SPA and CHA within 10 mm; however, no

1 difference was noted in R0 resection rates and survival. One of the possibilities for the lack of effect
2 of oncological outcomes was that the DP R0 resection rate was unexpectedly high (80.7%), even if
3 the tumor was located close to the bifurcation of the artery. The other possibility was that adjuvant
4 therapy performed similar rate between DP patients (85.9%) and DP-CAR patients (86.7%).
5 According to our results, it may be crucial to perform standard DP so that adjuvant chemotherapy
6 could be immediately administered following surgery rather than providing extended resection.
7 Conversely, as a strategy to improve the prognosis of locally advanced pancreatic body cancer, it is
8 recommended that patient selection is conducted during preoperative treatment, safe surgery should
9 be performed, and postoperative therapy must be administered to all patients. We posit that the
10 preoperative prognostic factors such as age ≥ 67 years, clinical tumor size ≥ 30 mm, and CA19-9 > 37
11 U/ml may be helpful in selecting the patients for DP-CAR.

12 This study had some limitations. First, it was a retrospective analysis of long-term data;
13 therefore, biases were included, such as differences in collection periods between institutions and the
14 numbers of DP-CAR procedures (even among high-volume centers), and varying provisions for DP-
15 CAR procedures in high-volume centers for pancreatic surgeries. Second, patients who initially required
16 DP-CAR, but achieved tumor shrinkage after preoperative therapy and underwent standard DP, were
17 included in the DP group. In conclusion, DP-CAR was safely performed in centers for general
18 pancreatic surgery regardless of DP-CAR volume, and may not be required in preoperative arterial
19 embolization, no oncologic effect for resectable tumor closed to the bifurcation of SPA and CA, and
20 should be performed after appropriate patient selection.

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2 **Disclosure**

3 No conflict of interests relevant to the current study are reported by any of the authors.

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5 **Data availability**

6 Data used for the manuscript will be available from the corresponding author upon reasonable request.

References

1. Hishinuma S, Ogata Y, Matsui J, Ozawa I, Inada T, Shimizu H, et al. Two cases of cancer of the pancreatic body undergoing gastric preservation with distal pancreatectomy combined with resection of the celiac axis. *Jpn J Gastroenterol Surg* 1991;24:2782-6 (in Japanese with English abstract)
2. Mayumi T, Nimura Y, Kamiya J, Kondo S, Nagino M, Kanai M, et al. Distal pancreatectomy with en bloc resection of the celiac artery for carcinoma of the body and tail of the pancreas. *Int J Pancreatol* 1997;22:15-21.
3. Kondo S, Katoh H, Shimizu T, Omi M, Hirano S, Ambo Y, et al. Preoperative embolization of the common hepatic artery in preparation for radical pancreatectomy for pancreas body cancer. *Hepato-Gastroenterology* 2000;47:1447-9.
4. Hishinuma S, Ogata Y, Tomikawa M, Ozawa I. Stomach-preserving distal pancreatectomy with combined resection of the celiac artery: radical procedure for locally advanced cancer of the pancreatic body. *J Gastrointest Surg* 2007;11:743-9.
5. Hirano S, Kondo S, Hara T, Ambo Y, Tanaka E, Shichinohe T, et al. Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer: Long-term results. *Ann Surg* 2007;246:46-51.
6. Okada K, Kawai M, Tani M, Hirono S, Miyazawa M, Shimizu A, et al. Surgical strategy for patients with pancreatic body/tail carcinoma: who should undergo distal pancreatectomy with en-bloc celiac axis resection? *Surgery* 2013;153:365-72.
7. Nakamura T, Hirano S, Noji T, Asano T, Okamura K, Tsuchikawa T, et al. Distal pancreatectomy with en bloc celiac axis resection (modified appleby procedure) for locally advanced pancreatic body cancer: A Single-center review of 80 consecutive patients. *Ann Surg Oncol* 2016;23:969-75.
8. Yoshitomi H, Sakai N, Kagawa S, Takano S, Ueda A, Kato A, et al. Feasibility and safety of distal pancreatectomy with en bloc celiac axis resection (DP-CAR) combined with neoadjuvant therapy for

- borderline resectable and unresectable pancreatic body/tail cancer. *Langenbecks Arch Surg* 2019;404:451-8.
9. Murakami Y, Nakagawa N, Kondo N, Hashimoto Y, Okada K, Seo S, et al. Survival impact of distal pancreatectomy with en bloc celiac axis resection combined with neoadjuvant chemotherapy for borderline resectable or locally advanced pancreatic body carcinoma. *Pancreatology* 2021;21:564-72.
 10. Truty MJ, Colglazier JJ, Mendes BC, Nagorney DM, Bower TC, Smoot RL, et al. En Bloc Celiac Axis Resection for Pancreatic Cancer: Classification of Anatomical Variants Based on Tumor Extent. *J Am Coll Surg* 2020;231:8-29.
 11. Yamamoto T, Satoi S, Kawai M, Motoi F, Sho M, Uemura KI, et al. Is distal pancreatectomy with en-bloc celiac axis resection effective for patients with locally advanced pancreatic ductal adenocarcinoma? -Multicenter surgical group study. *Pancreatology* 2018;18:106-13.
 12. Klompmaker S, Peters NA, van Hilst J, Bassi C, Boggi U, Busch OR, et al. Outcomes and risk Score for distal pancreatectomy with celiac axis resection (DP-CAR): An International Multicenter Analysis. *Ann Surg Oncol* 2019;26:772-81.
 13. Klompmaker S, De Rooij T, Korteweg JJ, van Dieren S, van Lienden KP, van Gulik TM, et al. Systematic review of outcomes after distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer. *Br J Surg* 2016;103:941-9.
 14. Gong H, Ma R, Gong J, Cai C, Song Z, Xu B. Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic cancer: A systematic review and meta-analysis. *Med (Baltim)* 2016;95:e3061. doi: [10.1097/MD.0000000000003061](https://doi.org/10.1097/MD.0000000000003061), PMID: [26962836](https://pubmed.ncbi.nlm.nih.gov/26962836/).
 15. Feng Q, Xin Z, Du Y, Mao F, Li L, Zhai H, et al. Distal pancreatectomy with en bloc celiac axis resection does not improve the R0 rate or median survival time of patients with locally advanced pancreatic cancer: A systematic review and meta-analysis. *Transl Cancer Res* 2020;9:7205-13.
 16. Nigri G, Petrucciani N, Belloni E, Lucarini A, Aurello P, D'Angelo F, et al. Distal pancreatectomy with celiac axis resection: Systematic review and meta-analysis. *Cancers (Basel)* 2021;13:1967. doi: [10.3390/cancers13081967](https://doi.org/10.3390/cancers13081967), PMID: [33921838](https://pubmed.ncbi.nlm.nih.gov/33921838/).

17. Liu L, Liu TX, Huang WX, Yang Z, Wang S, Da MX, et al. Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body/tail cancer: A systematic review and meta-analysis. *Asian J Surg* 2022;45:51-61.
18. Schmocker RK, Wright MJ, Ding D, Beckman MJ, Javed AA, Cameron JL, et al. An aggressive approach to locally confined pancreatic cancer: defining surgical and oncologic outcomes unique to pancreatectomy with celiac axis resection (DP-CAR). *Ann Surg Oncol* 2021;28:3125-34.
19. Abo D, Hasegawa Y, Sakuhara Y, Terae S, Shimizu T, Tha KK, et al. Feasibility of a dual microcatheter-dual interlockingdetachable coil technique in preoperative embolization in preparation for distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer. *J Hepato-Bil Pancreat Sci* 2012;19:431-7.
20. Fuji T, Yamagami T, Fukumoto W, Baba Y, Chosa K, Ishikawa M, et al. Usefulness of Amplatzer vascular plug for preoperative embolization before distal pancreatectomy with en bloc celiac axis resection. *Cardiovasc Interv Radiol* 2019;42:1352-7.
21. Ueda A, Sakai N, Yoshitomi H, Furukawa K, Takayashiki T, Kuboki S, et al. Is hepatic artery coil embolization useful in distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic cancer? *World J Surg Oncol* 2019;17:124. doi: [10.1186/s12957-019-1667-8](https://doi.org/10.1186/s12957-019-1667-8).
22. Storkholm JH, Burgdorf SK, Hansen CP. Distal pancreas-coeliac axis resection with preoperative selective embolization of the coeliac axis: A single high-volume centre experience. *Langenbecks Arch Surg* 2020;405:635-45.
23. Sato T, Inoue Y, Takahashi Y, Mise Y, Ishizawa T, Tanakura K, et al. Distal pancreatectomy with celiac axis resection combined with reconstruction of the left gastric artery. *J Gastrointest Surg* 2017;21:910-7.
24. Inoue Y, Saiura A, Sato T, Oba A, Ono Y, Mise Y, et al. Details and outcomes of distal pancreatectomy with celiac axis resection preserving the left gastric arterial flow. *Ann Surg Oncol* 2021;28:8283-94.
25. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: Five-year experience. *Ann Surg* 2009;250:187-96.

26. Bassi C, Marchegiani G, Dervenis C, Sarr M, Hilal MA, Adham M, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years After. *Surgery* 2017;161:584-91.
27. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: A suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2007;142:761-8.
28. Kondo S, Katoh H, Hirano S, Ambo Y, Tanaka E, Maeyama Y, et al. Ischemic gastropathy after distal pancreatectomy with celiac axis resection. *Surg Today* 2004;34:337-40.
29. Okada KI, Kawai M, Hirono S, Miyazawa M, Kitahata Y, Ueno M, et al. Ischemic gastropathy after distal pancreatectomy with en bloc celiac axis resection for pancreatic body cancer. *Langenbecks Arch Surg* 2018;403:561-71
- 30.. Tempero MA, Malafa MP, Behrman SW, Benson 3rd AB, Casper ES, Chiorean EG, et al. Pancreatic Adenocarcinoma, Version 2.2014. *J Natl Compr Canc Netw*, version 2.2014: featured updates to the NCCN guidelines 2014;12:1083-93.
31. Nishino H, Takano S, Yoshitomi H, Furukawa K, Takayashiki T, Kuboni S, et al. Ischemic gastropathy after distal pancreatectomy with en bloc celiac axis resection versus distal pancreatectomy for pancreatic body/tail cancer. *Surg Open Sci* 2019;1:14-9.
32. Okada K, Kawai M, Tani M, Hirono S, Miyazawa M, Shimizu A, et al. Preservation of the left gastric artery on the basis of anatomical features in patients undergoing distal pancreatectomy with celiac axis en-bloc resection (DP-CAR). *World J Surg* 2014;38:2980-5.
33. Ramia JM, de Vicente E, Pardo F, Sabater L, Lopez-Ben S, Quijano Y, et al. Preoperative hepatic artery embolization before distal pancreatectomy plus celiac axis resection does not improve surgical results: A Spanish multicentre study. *Surgeon* 2021;19:e117-24. doi: [10.1016/j.surge.2020.08.012](https://doi.org/10.1016/j.surge.2020.08.012). Epub 2020 October 3. PMID: [33023848](https://pubmed.ncbi.nlm.nih.gov/33023848/).

34. Oba A, Inoue Y, Sato T, Ono Y, Mise Y, Ito H, et al. Impact of indocyanine green-fluorescence imaging on distal pancreatectomy with celiac axis resection combined with reconstruction of the left gastric artery. *HPB (Oxford)* 2019;21:619-25.
35. Egorov V, Kim P, Kharazov A, Dzigasov S, Popov P, Rykova S, et al. Hemodynamic, surgical and oncological outcomes of 40 distal pancreatectomies with celiac and left gastric arteries resection (DP CAR) without arterial reconstructions and preoperative embolization. *Cancers (Basel)* 2022;14:1254. doi: [10.3390/cancers14051254](https://doi.org/10.3390/cancers14051254), PMID: [35267562](https://pubmed.ncbi.nlm.nih.gov/35267562/).

Figure Legends

Fig.1 Preoperative embolization and ischemic gastropathy

The frequency of IG is shown for 600 stomach-preserving, DP-CAR procedures according to the status of preoperative embolization. The LGA-preserving DP-CAR group had excellent results (0.9%); however, standard groups and LGA reconstruction groups had worse results, with >10% of IG. Moreover, preoperative embolization of the CHA did not improve IG, even with additional arterial embolization of the LGA or other additional arterial embolization. The no embolization group demonstrated reduced IG compared with the preoperative embolization group (7.9% vs 19.2%, $P=0.001$).

* Includes additional other arterial embolization procedures. IG, ischemic gastropathy. DP-CAR, distal pancreatectomy with *en bloc* celiac axis resection. LGA, left gastric artery. CHA, common hepatic artery.

Fig. 2 Propensity score matching analysis to compare DP-CAR and DP for pancreatic body cancer in which the tumor edge was close to the SPA bifurcation

- a. Pancreatic body cancer situated close to the root of the SPA carries a risk of tumor exposure during DP, especially those near the SPA stump (yellow line). DP-CAR should be effective in reducing the risk of tumor exposure (blue line).

- b. Among patients with a tumor edge close to the splenic artery bifurcation within 10 mm (<0 mm– ≤ 10 mm), 414 patients received DP, whereas 137 patients received DP-CAR. We performed propensity score matching on these groups using five factors: age, sex, tumor diameter (imaging diagnosis done right before surgery), CA19-9 value (measured right before surgery), and preoperative treatment status. We matched 414 DP and 137 DP-CAR patients, and finally, 135 DP and 135 DP-CAR were analyzed (1:1 matching, Caliper 0.2).
- c. After propensity score matching, using the Kaplan–Meier and log-rank tests was shown. The median duration of overall survival was 33.5 months (95% c.i., 27.4–42.0) in the DP-CAR group and 37.9 months (95% c.i., 32.8–53.3) in the DP group ($p = 0.26$).

DP, Distal pancreatectomy. DP-CAR, Distal pancreatectomy with *en bloc* celiac axis resection. SPA, splenic artery. CHA, common hepatic artery. GDA, gastroduodenal artery. CA, celiac artery. PSM, propensity score matching.

Table 1. Baseline patient characteristics and surgical outcomes

Factor	DP-CAR (n=626)	DP (n=1325)
Age (years), median (i.q.r.)	66 (59-72)	70 (64-76)
Sex ratio (M:F)	362:264	714:611
Upfront surgery	269 (43.0)	991 (74.8)
Preoperative therapy	357 (57.0)	334 (25.2)
Systemic therapy	357 (57.0)	332 (25.1)
Radiation therapy	160 (25.6)	176 (13.3)
Resectability		
Resectable	124 (19.8)	1165 (87.9)
Borderline resectable	327 (52.2)	111 (8.4)
Unresectable	173 (27.6)	47 (3.6)
Unknown	2 (0.3)	2 (0.2)
cTS (mm), median (i.q.r.)	29 (22-40)	21 (16–30)
CA19-9 (U/ml), median (i.q.r.)	58.3 (15.6-261.9)	46.2 (14.0–183.3)
modified GPS		
0	478 (76.4)	1072 (80.9)
1/2	111 (17.7)	177 (13.4)
Unknown	7 (5.9)	76 (5.7)
PNI, median (i.q.r.)	46.5 (42.7-50.1)	47.7 (43.8-51.1)
NLR, median (i.q.r.)	2.5 (1.8-3.7)	2.3 (1.7-3.2)
PLR, median (i.q.r.)	152.2 (111.3-209.2)	141.0 (109.3-196.1)
With total gastrectomy	26 (4.2)	31 (2.3)
Clavien-Dindo grade $\geq$ IIIa	273 (43.6)	294 (22.2)
Ischemic gastropathy	71 (11.3)	2 (0.2)
Liver ischemia	64 (10.2)	0 (0.0)
DGE grade B/C	89 (14.6)	48 (3.6)
Pancreatic fistula grade B/C	226 (36.1)	294 (22.2)
Hospital stay (days), median (i.q.r.)	32 (20-52.5)	21 (14-35)
Adjuvant therapy	486 (77.8)	1057 (79.8)
Reoperation	36 (5.8)	20 (1.5)
30-day mortality	8 (1.3)	3 (0.2)
90-day mortality	18 (2.9)	7 (0.5)

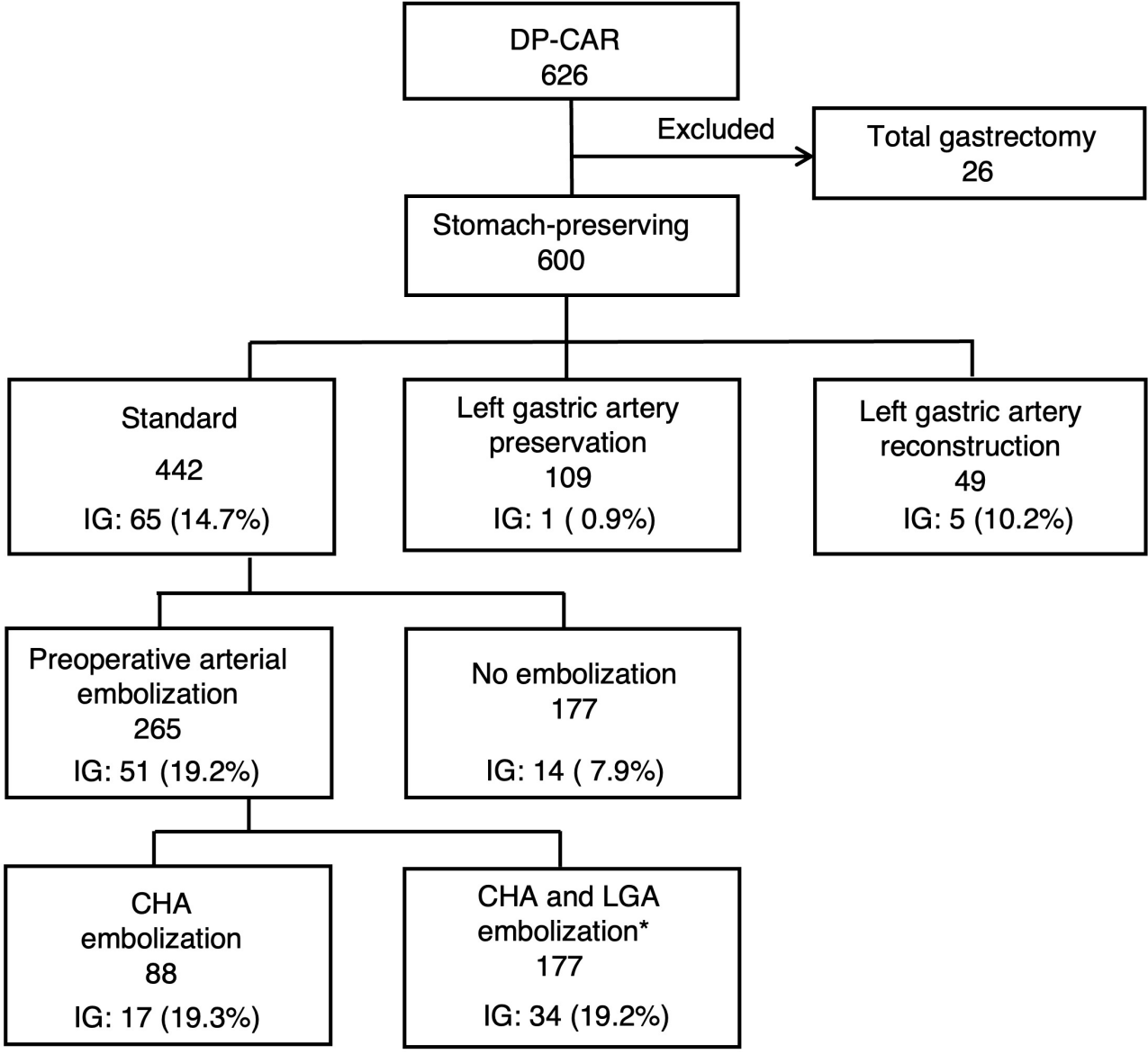
Values are n (%) unless otherwise indicated.

i.q.r., interquartile range; cTS, clinical tumor size of imaging study right before surgery; CA19-9, carbohydrate antigen 19-9; GPS, Glasgow prognostic score; PNI, prognostic nutritional index; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; DGE, delayed gastric emptying.

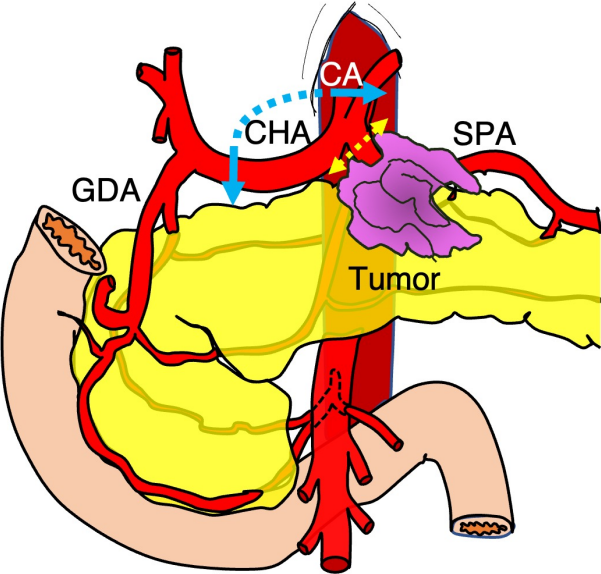
Table 2. Univariable and multivariable analysis of preoperative available prognostic factors for DP-CAR (BR / UR)

		Univariable		Multivariable	
		HR (95% c.i.)	<i>P</i> value	HR (95% c.i.)	<i>P</i> value
Age (years)	≥67	1.42 (1.13-1.78)	0.002	1.40 (1.12-1.75)	0.004
	<67				
Male		1.06 (0.84-1.34)	0.600		
Female					
cTS (mm)	≥30	1.55 (0.75-1.57)	0.0002	1.42 (1.12-1.80)	0.004
	<30				
CA19-9 (U/ml)	>37	1.57 (1.24-2.00)	0.0002	1.43 (1.11-1.83)	0.005
	≤37				
m GPS	2	1.09 (0.60-1.99)	0.783		
	0/1				
NLR	≥5	1.09 (0.77-1.53)	0.622		
	<5				
PLR	<150	1.23 (0.64-1.01)	0.061	1.21 (0.97-1.52)	0.090
	≥150				
PNI	<45	1.08 (0.86-1.36)	0.524		
	≥45				

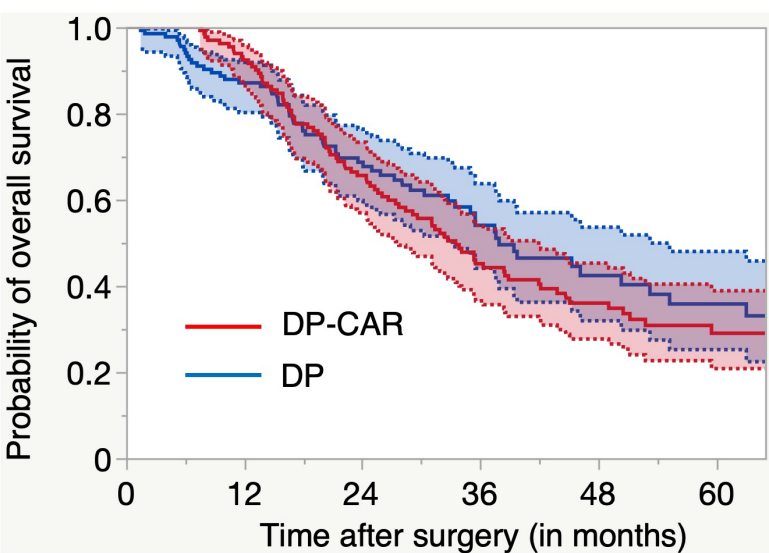
CA19-9, Carbohydrate antigen 19-9; m GPS, modified Glasgow prognostic score; NLR, Neutrophil lymphocyte ratio; PLR, Platelet lymphocyte ratio; PNI, Prognostic nutritional index
Modified Glasgow prognostic score was defined as follows: patients with both an elevated C-reactive protein (>1.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were allocated a score of 2. Patients with only one of these biochemical abnormalities were given a score of 1. Patients with neither of these abnormalities were given a score of 0. PNI was calculated as follows: $10 \times \text{Albumin (g/dl)} + 0.005 \times \text{total lymphocyte count (/}\mu\text{l)}$
BR, borderline resectable; UR, locally advanced unresectable, HR; hazard ratio



a The arterial resection margin in DP and DP-CAR



c Overall survival after PSM



No. at risk

DP-CAR	135	121	82	51	32	17
DP	135	108	70	38	21	15

b Propensity score matching using five factors

