Retrospective Cohort Study

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Implications of portal vein/superior mesenteric vein involvement in pancreatic cancer: A comprehensive correlation from preoperative radiological assessment to resection, pathology, and long-term outcomes. A retrospective cohort study

Hyeong Seok Kim, MD, MS[a], Hochang Chae, MD, MS[a], Soo Yeun Lim, MD[a,b], HyeJeong Jeong, MD, MS[a,c], So Jeong Yoon, MD, PhD[a], Sang Hyun Shin, MD, PhD[a], In Woong Han, MD, PhD[a], Jin Seok Heo, MD, PhD[a], Hongbeom Kim, MD, PhD[a]

Background: The incidence of portal vein/superior mesenteric vein (PV/SMV) resection during pancreatoduodenectomy is increasing in clinical practice. This study investigated the clinical significance of preoperative PV/SMV assessment and intraoperative resection and their correlation with pathological results and long-term survival outcomes.

Methods: We analyzed 443 patients undergoing pancreatoduodenectomy at a tertiary center from 2012 to 2017 based on PV/SMV resection. Subgroup analyses were performed based on preoperative PV/SMV involvement, resection, and margin status.

Results: Total of 441 patients were analyzed; 175 had PV/SMV involvement on preoperative radiological assessments and 128 underwent PV/SMV resection. True pathological invasion was observed in 78 patients (60.9%), with 34.3% showing no invasion and negative margins. The positive predictive value for preoperative PV/SMV involvement was 61.7%, with a false-negative value of 28.9%. Overall survival of patients who underwent PV/SMV resection was worse than those who did not (2-year survival rate, 38.1% vs 54.9%, $P < 0.001$). Patients without PV/SMV resection with an rR1/R1 margin showed no decrease in survival compared to those with PV/SMV resection and R0 margins (54.9% vs 40.3%, $P = 0.029$). Prognostic factors included hypertension, PV/SMV resection, PV/SMV R2 margin, T stage, N stage, cell differentiation, adjuvant treatment, and recurrence.

Conclusion: PV/SMV resection could ensure R0 resection but may lead to unnecessary resection. Careful consideration is essential in determining the need for PV/SMV resection. Poor survival in such patients highlights the need for tailored treatments, including neoadjuvant therapy, for those who are expected to undergo PV/SMV resections.

Keywords: margin, pancreatic cancer, pancreatoduodenectomy, portal vein/superior mesenteric vein, vein resection

Introduction

Approximately 20% of patients with pancreatic ductal adenocarcinoma (PDAC) are resectable at diagnosis, while most present with advanced or metastatic disease[1]. Due to the anatomical proximity of the venous confluence to the pancreatic head, portal vein (PV) and superior mesenteric vein (SMV) involvement is common in PDAC[2]. Pancreatoduodenectomy

HIGHLIGHTS

- Patients undergoing portal and superior mesenteric vein resection showed poorer survival outcomes compared to those without vessel resections
- No survival benefit was observed in patients with portal and superior mesenteric vein resection and R0 margins compared to those without resection but with rR1/R1 margins.

[a]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [b]Department of Surgery, Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea and [c]Department of Surgery, Daejeon Eulji Medical Center, Eulji University School of Medicine, Daejeon, South Korea

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Corresponding author. Address: Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwonro, Gangnam-gu, Seoul 06351. Tel.: +82 2 3410 0256. E-mail: (surgeonkhb@gmail.com) (H. Kim).

International Journal of Surgery (2025) 111:2962–2972

Received 16 July 2024; Accepted 3 February 2025

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 24 February 2025

http://dx.doi.org/10.1097/JS9.0000000000002307

(PD) is the treatment of choice for PDAC located at the pancreatic head, and the National Comprehensive Cancer Network (NCCN) criteria has clarified PDAC as resectable or borderline resectable based on PV/SMV involvement[3]. In patients with borderline resectable disease, PV/SMV resection and reconstruction may be necessary to achieve R0 resection, which is associated with improved survival[4,5].

The use of PV/SMV resection has increased with advancements in surgical techniques and neoadjuvant therapy. It is common to resect the PV/SMV along with the specimen if the vessel invasion is definite or dissection is considered impossible, as reported in our previous study[6]. However, even when the tumor is dissected from the vessel, the decision to resect the PV/SMV intraoperatively remains complex and must consider both oncological and vascular integrity. Additionally, preoperative imaging often overestimates tumor invasion, leading to potentially unnecessary resections, especially after neoadjuvant therapy[7,8].

Previous studies have attempted to predict PV/SMV involvement preoperatively[9,10], but discrepancies between radiological findings and pathological results remain a challenge. In many cases, radiological signs suggestive of invasion were later identified as inflammation or fibrosis rather than true cancer invasion[11]. This discrepancy raises critical questions about the reliability of imaging as a predictor for vascular resection and demanding surgeons' decision-making processes that lead from radiological suspicion to surgical resection.

The benefit of PV/SMV resection itself is still under debate. While some studies have reported improved outcomes with aggressive resections[12,13], others indicated increased morbidity without clear survival benefits[14]. This ongoing debate highlights the necessity for a more discerning approach to PV/SMV resection and a clearer understanding of its true impact on patient outcomes[15], particularly in cases where the tumor is dissected from the vessel and the specimen has been removed.

Therefore, our study aimed to evaluate the role of preoperative PV/SMV assessment in relation to intraoperative decision-making, postoperative pathological findings, and long-term survival, thereby contributing to the body of evidence for future surgical consensus.

Patients and methods

Patients

This study is in line with the STROCSS criteria[16]. This study included 443 consecutive patients who underwent PD and were pathologically confirmed to have PDAC at a tertiary center in the Republic of Korea between January 2012 and December 2017. Patients who underwent a prior pancreatectomy and the patient diagnosed with distant metastasis during surgery were excluded. All the data were maintained in a prospectively collected database and retrospectively reviewed. This study was approved by the Institutional Review Board, and the requirement for written informed consent for this retrospective study was waived.

Preoperative radiological evaluation

Preoperative radiologic imaging, including computed tomography (CT) and magnetic resonance, was reviewed, and patients were categorized into three groups based on the degree of tumor-vein interface (TVI) of the PV/SMV: no involvement, abutment, and encasement/invasion, as reported in a previous study from our institution[9]. Abutment was defined as tumor contact with vessel within 180° without any deformity of the vessel wall, which corresponded to the NCCN criteria for resectable pancreatic cancer (Fig. 1A). Encasement, characterized by tumor contact with the vessel >180°, and invasion, defined as any deformity, both met the criteria for borderline resectable pancreatic cancer (Fig. 1B). Each category was classified according to the NCCN criteria as either resectable or borderline resectable pancreatic cancer. Following subcategorization, the groups were analyzed.

Operative procedures and postoperative pathologic assessment

Pylorus-preserving pancreatoduodenectomy was defined as the standard procedure, although Whipple operation or pylorus-resecting pancreatoduodenectomy were allowed, depending on the clinical situation. Standard lymphadenectomy, which typically encompasses lymph nodes around the pancreas, the hepatoduodenal ligament, and common hepatic artery, was performed in patients without risk factors such as preoperatively suspected lymph node metastasis or vascular invasion. In patients with such risk factors, extended lymphadenectomy, including vascular skeletonization, was performed. This involved the dissection of lymph nodes deemed necessary based on the individual patient, including areas around the celiac axis, the superior mesenteric artery and vein, and the para-aortic area. Furthermore, in selected cases, the nerve plexus or ganglion on the right side of the celiac axis and superior mesenteric artery was dissected semicircumferentially.

During surgery, operators decided whether to resect the PV/SMV after dissection around the PV/SMV, as reported in a previous study[6]. En-bloc resection with the vessel was typically performed when vessel invasion was definite or dissection is considered impossible. However, if upon separation of the tumor from the vessel, the vessel wall appeared discolored, showing a darkened or irregular color differing from the normal appearance of other parts of the PV/SMV, showed signs of dissection, or if the tumor was very close to the PV/SMV margin with suspected preoperative vessel involvement, additional resection of the vessel was performed post-specimen extraction. Vessel resection was performed by either segmental or wedge resection, based on the vascular surgeon's preference or degree

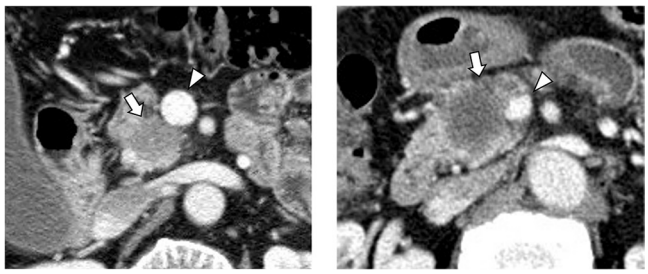

Figure 1. Contrast-enhanced computed tomography image showing portal vein/superior mesenteric vein (arrowhead) involvement by the tumor (arrow); abutment (A) and encasement/invasion (B).

of tumor contact. Reconstruction was either primarily repaired or performed using a graft (autologous vein, allograft, or synthetic graft, based on the consulted vascular surgeon's preference and the circumstances).

Pathological examination of the margin status was reviewed by a pancreas-biliary system-specialized pathologist with more than 10 years of experience. As reported in a previous study, resection margin status was divided into 3 groups: (1) R0 (grossly and microscopically negative resection margin, microscopic safety margin ≥1 mm); (2) rR1 (revised grossly negative but microscopically positive resection margin, 0 mm < safety margin < 1 mm); (3) R1 (classic microscopic positive resection margin, safety margin = 0 mm)[17–19].

Postoperative complication and surveillance strategy following surgical resection

All patients underwent CT 5 or 7 days postoperatively for evaluation of complications, and complications were graded based on the Clavien–Dindo classification[20]. Postoperative surgical complications categorized as ≥ Clavien–Dindo grade 3 that occurred within 30 days were analyzed. A postoperative pancreatic fistula (POPF) was defined according to the International Study Group for Pancreatic Fistula[21]. Postpancreatectomy hemorrhage (PPH) was also defined according to the International Study Group of Pancreatic Surgery[22].

At our institute, comprehensive postoperative surveillance, including CA19-9 levels and contrast-enhanced abdominopelvic CT, was implemented after treatment. Recurrence was primarily diagnosed using radiologic modalities or an increase in CA19-9 levels. As previously reported, local recurrence was defined as follows: if a local ill-defined mass or soft tissue or increase in the size of lymph nodes along visceral vessels around the pancreatic bed was found[19]. When combined with distant recurrence, such as liver, lung, or peritoneal seeding, we did not regard it as local recurrence.

The follow-up period for our patients extended from the time of surgery until either the patient's death or last recorded follow-up appointment. We calculated the overall survival (OS) as the duration from surgery to the occurrence of death by any cause.

Statistical analysis

Statistical analyses were conducted using IBM SPSS version 28.0 and R software version 4.3.2. We employed the χ^2 test or Fisher's exact test for nominal variables, and the Student's *t*-test or analysis of variance for continuous variables. A *P*-value of <0.05 was considered at significant, and $P < 0.1$ marginally significant. Survival data were analyzed using the Kaplan–Meier method and compared using the log-rank test. Significant variables from univariate analysis were further examined by multivariate analysis using a Cox proportional hazards regression model.

Results

Demographics and clinicopathological characteristics between patients with PV/SMV resection and without PV/SMV Resection

A total of 441 patients were included in the analysis. The male-to-female ratio was 1.67:1, with a mean patient age of 63.5 years. Preoperative radiological assessment showed that 175 patients were suspected to have PV/SMV involvement of the tumor, consisting of abutments from 85 and 90 patients with encasement or invasion. PV/SMV resection was performed in 128 patients (29.0%), and the results were compared with those without PV/SMV resection (Table 1).

Patients who underwent PV/SMV resection had a higher proportion of neoadjuvant treatment (14.1% vs 2.9%, $P < 0.001$) and preoperative radiological PV/SMV involvement (80.5% vs 23.0%, $P < 0.001$). The operation time was longer in patients who underwent PV/SMV resection (391.7 vs 332.0 min, $P < 0.001$), and estimated blood loss was also greater compared to those without PV/SMV resection (670.2 vs 413.0 mL, $P < 0.001$). In patients undergoing PV/SMV resection, 113 patients (88.3%) had segmental resections, while the remaining 15 patients (11.7%) underwent wedge resections. Of these, 120 patients (93.8%) underwent en-bloc resections, while 8 patients (6.3%) had sequential resections. Of these patients, 20 (15.6%) required a graft for vascular reconstruction. Pathologic tumor size was larger (3.1 vs 2.8 cm, $P < 0.001$) with advanced T stages ($P = 0.022$) in patients with PV/SMV resection, despite similar total number of retrieved lymph node (21.6 vs 21.4, $P = 0.884$). Postoperative outcomes, including complications of Clavien–Dindo grade ≥3 (25.8% vs 23.6%, $P = 0.724$), clinically relevant POPF (6.2% vs 8.3%, $P = 0.590$), and PPH grade ≥B (6.2% vs 5.4%, $P = 0.912$) were equivalent between the two groups.

Preoperative radiologic involvement of PV/SMV and subsequent surgical resection with following pathological margin status

Fig. 2 shows the pathological margin status of the PV/SMV according to preoperative radiologic involvement of the PV/SMV and intraoperative resection. Preoperative radiological assessment showed that 175 patients were suspected of having PV/SMV involvement. Among them, 100 patients underwent PV/SMV resection, whereas 25 patients without preoperative involvement underwent resection.

In patients with PV/SMV resection, true pathologic invasion was in 78 patients (60.9%), and when the PV/SMV groove margin was evaluated, 44 patients had R0 and six rR1 cases in 50 patients without PV/SMV invasion despite resection. Among the 25 patients with PV/SMV resection who were not suspicious of preoperative involvement, 12 patients had true pathologic invasion, and 10 patients had R0, with three rR1 for the PV/SMV groove margin. When the PV/SMV was not resected in patients with preoperative PV/SMV involvement (n = 72), R0 resection was achieved in 34 patients with 32 rR1, four R1, and two R2 margin statuses (Fig. 2).

When we evaluated the accuracy of preoperative PV/SMV involvement, the positive predictive value was 61.1% (107/175) and the negative predictive value was 28.6% (76/266). These parameters were evaluated after excluding patients who received neoadjuvant treatment; the positive and negative predictive values were 60.5% and 29.0%, respectively.

Survival analysis according to preoperative PV/SMV involvement, PV/SMV resection, margin status, and neoadjuvant/adjuvant therapy

After a median follow-up of 22.0 months (interquartile rage, 11.0–42.0 months), the median survival time for all patients in

Table 1

Demographic and clinicopathologic characteristics of patients with and without PV/SMV resection.

	PV/SMV resection (+)(n = 128)	PV/SMV resection (–)(n = 313)	*P*-value
Age	62.9 ± 10.7	63.7 ± 10.0	0.474
Sex (M/F)	84/44	192/121	0.462
Body mass index	22.7 ± 3.1	22.9 ± 3.1	0.541
Preoperative hypertension	56 (43.8%)	127 (40.6%)	0.612
Preoperative diabetes	50 (39.1%)	127 (40.6%)	0.852
ASA class (1/2/3)	15/97/16	49/238/26	0.266
CA19-9 (median, IQR)	69.5 (21.5–375.9)	122.6 (30.8–406.9)	0.130
Neoadjuvant therapy	18 (14.1%)	9 (2.9%)	<0.001
FFX + GnP/5-FU/Gem	6/3/9	4/2/3	0.714
Radiologic PV/SMV involvement	103 (80.5%)	72 (23.0%)	<0.001
Abutment	36 (28.1%)	49 (15.7%)	
Encasement/invasion	67 (52.3%)	23 (7.3%)	
NCCN criteria (R/BR)	61/67	290/23	<0.001
Operation (PPPD/Whipple/PrPD)	54/20/54	168/31/114	0.057
Operation time (minute)	391.7 ± 68.1	332.0 ± 64.2	<0.001
Estimated blood loss (mL)	670.2 ± 496.7	413.0 ± 339.9	<0.001
PV/SMV resection			NA
Resection type (segmental/wedge)	113/15	NA	
Resection timing (en-bloc/sequential)	120/8	NA	
Reconstruction (primary/graft)	108/20	NA	
Pathologic tumor size (cm)	3.1 ± 0.9	2.8 ± 1.0	<0.001
Total retrieved lymph node	21.5 ± 9.8	21.5 ± 10.4	0.997
Positive lymph node	2.3 ± 3.6	1.6 ± 2.0	0.051
T stage (1/2/3/4)	17/91/19/1	67/219/27/0	0.022
N stage (0/1/2)	31/66/31	102/134/77	0.161
Cell differentiation (well/mod/poor/un)	4/86/37/1	20/209/76/8	0.268
R status (R0/rR1/R1/R2)	66/47/14/1	183/110/14/6	0.065
PV/SMV margin (R0/rR1/R1/R2)	89/32/6/1	214/90/6/3	0.354
Lymphovascular invasion	91 (72.8%)	204 (66.7%)	0.259
Perineural invasion	124 (97.6%)	297 (94.9%)	0.304
Postoperative hospital stay (days)	12.6 ± 5.7	14.2 ± 10.3	0.043
Complication Clavien–Dindo grade ≥3	33 (25.8%)	74 (23.6%)	0.724
Clinically relevant POPF	8 (6.2%)	26 (8.3%)	0.590
Postpancreatectomy hemorrhage grade ≥B	8 (6.2%)	17 (5.4%)	0.912
Adjuvant treatment	77 (60.6%)	200 (66.4%)	0.299
FFX + GnP/5-FU/Gem/outside	4/38/26/9	5/123/49/23	0.220
Recurrence	92 (71.9%)	203 (65.7%)	0.253
Recurrence pattern (local/systemic/both)	20/48/24	62/110/31	0.055

ASA, American Society of Anesthesiologists; BR, borderline resectable; CA19-9, carbohydrate antigen 19-9; FFX, FOLFIRINOX; GnP, Gemcitabine + nab-Paclitaxel; IQR, interquartile range; NA, not available; POPF, postoperative pancreatic fistula; PPPD, pylorus-preserving pancreatoduodenectomy; PrPD, pylorus-resecting pancreatoduodenectomy; PV, portal vein; R, resectable; SMV, superior mesenteric vein.

the study was 25.0 months (95% CI: 22.0–28.0 months), with 2-year and 5-year survival rates (YSR) of 50.0% and 22.0%, respectively (Supplementary Figure 1, http://links.lww.com/JS9/D960). Patients who underwent PV/SMV resection had significantly poorer survival rates than those who did not (2YSR, 38.1% vs 54.9%, $P < 0.001$) (Fig. 3A), and a similar pattern was observed when the patients were limited to those with preoperative PV/SMV involvement (37.8% vs 59.5%, $P = 0.015$) (Supplementary Figure 2, http://links.lww.com/JS9/D960). When comparing disease-free survival (2-year disease-free survival rate: 15.2% vs 29.2%, $P < 0.001$) and cumulative recurrence rate (2-year recurrence rate: 80.0% vs 64.8%, $P = 0.002$) based on PV/SMV resection, patients with resection showed poorer prognosis (Fig. 3B and C).

When patients with preoperative radiologic PV/SMV involvement were compared to those without involvement, a marginally significant difference in survival was observed (2YSR, 46.8% vs 52.2%, $P = 0.057$) (Fig. 4A). There was no significant difference in survival between patients who received neoadjuvant therapy and those who did not (48.1% vs 50.1%, $P = 0.344$); however, patients who received adjuvant therapy demonstrated significantly better survival compared to those who did not (60.5% vs 31.6%, $P < 0.001$) (Fig. 4B and C).

When patients who underwent PV/SMV resection with an R0 resection were compared to those who did not undergo PV/SMV resection with a margin of rR1 or R1 status, there was no observed survival gain (2YSR, 40.3% vs 54.9%, $P = 0.029$) (Fig. 5A). When these patients were further divided according to pathological PV/SMV involvement, no significant survival difference was observed between patients who achieved R0 margins with PV/SMV resection and pathological PV/SMV involvement, and those without PV/SMV resection whose margins were rR1 or R1 (39.1% vs 54.9%, $P = 0.233$) (Fig. 5B). Patients who underwent PV/SMV resection with an R0 margin and no pathological PV/SMV involvement also did not demonstrate better survival compared to those without PV/SMV

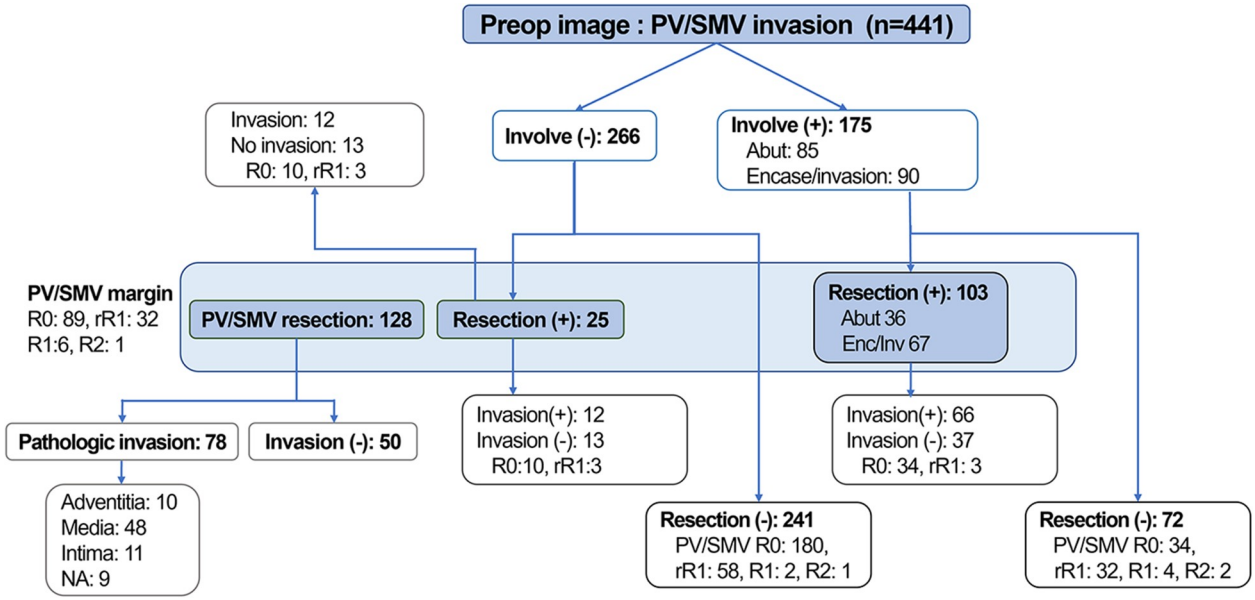

Figure 2. Flowchart of study patients based on preoperative radiological involvement, resection, and its margin status. NA, not available; PV, portal vein; SMV, superior mesenteric vein.

resection whose margins were rR1 or R1 (41.1% vs 54.9%, $P = 0.011$) (Fig. 5C). The 2YSR was equivalent to that of patients who underwent PV/SMV resection with rR1 or R1 margins and no pathological PV/SMV involvement (54.9% vs 66.7%, $P = 0.185$), although this group had a small number of patients (n = 6).

Prognostic factors for OS

Table 2 presents the prognostic factors for OS in patients after surgical resection. Univariate analysis revealed that age, body mass index, preoperative hypertension, initial CA19-9, preoperative radiologic PV/SMV involvement, estimated blood loss, intraoperative PV/SMV resection, pathologic PV/SMV invasion, PV/SMV margin status, pathologic tumor size, T stage, N stage, cell differentiation, lymphovascular invasion, perineural invasion, adjuvant treatment, and recurrence were significantly associated with survival following resection of PDAC.

Multivariate Cox regression model revealed preoperative hypertension (hazard ratio [HR]: 1.552, $P < 0.001$), intraoperative PV/SMV resection (HR: 1.343, $P = 0.018$), PV/SMV R2 margin (HR: 6.024, $P = 0.001$), T stage ($P = 0.025$), N2 stage (HR: 2.217, $P < 0.001$) compared to N0 stage, moderate differentiation (HR: 1.778, $P = 0.035$), poor differentiation (HR: 3.428, $P < 0.001$) and undifferentiation (HR: 4.047, $P = 0.009$) compared to well differentiation, adjuvant treatment (HR: 0.398, $P < 0.001$), and recurrence (HR: 2.310, $P < 0.001$) remained significant.

Discussion

The management of PDAC remains a formidable challenge in surgical oncology due to its aggressive nature and the close anatomical proximity of the major vasculature, including the PV/SMV. Surgical resection offers the only potential cure; however, only a small proportion of patients are eligible for this treatment. Some patients may require more aggressive treatments including combined PV/SMV resection with the tumor. Although advancements in radiological imaging techniques have made preoperative assessments of PV/SMV involvement helpful in deciding whether to resect the PV/SMV intraoperatively, there remains a gap in its pathological correlation. Furthermore, the controversy surrounding the survival benefits of aggressive PV/SMV resection versus more conservative approaches has not been resolved.

In this study, 175 patients (39.7%) who underwent PD for PDAC had preoperative radiological PV/SMV involvement. A total of 128 patients (29.0%) underwent combined PV/SMV resection, and true pathological invasion was confirmed in 78 patients (60.9%). Patients who underwent PV/SMV resection had significantly poorer survival and recurrence outcomes than those who did not undergo resection. Moreover, patients who underwent PV/SMV resection with R0 margins demonstrated no survival benefit compared to those who did not undergo PV/SMV resection with rR1 or R1 margins. Multivariate Cox regression analysis revealed that preoperative hypertension, intraoperative PV/SMV resection, PV/SMV R2 margin, T stage, N2 stage compared to N0 stage, moderate, poor, and undifferentiation compared to well differentiation, adjuvant treatment, and recurrence were significantly associated with OS.

The role of preoperative radiological assessment in determining PV/SMV involvement and guiding resection decisions has been a subject of long-standing debate, with varying degrees of success in predicting actual tumor invasion. In this study, preoperative radiological assessment did not definitely predict the need for PV/SMV resection, yielding a positive predictive value of 61.1% and a false-negative value of 28.6%. A previous study conducted by our institute, which utilized CT to predict vessel invasion based on parameters such as tumor size, length of vessel involvement, and TVI, reported a sensitivity of 87% and

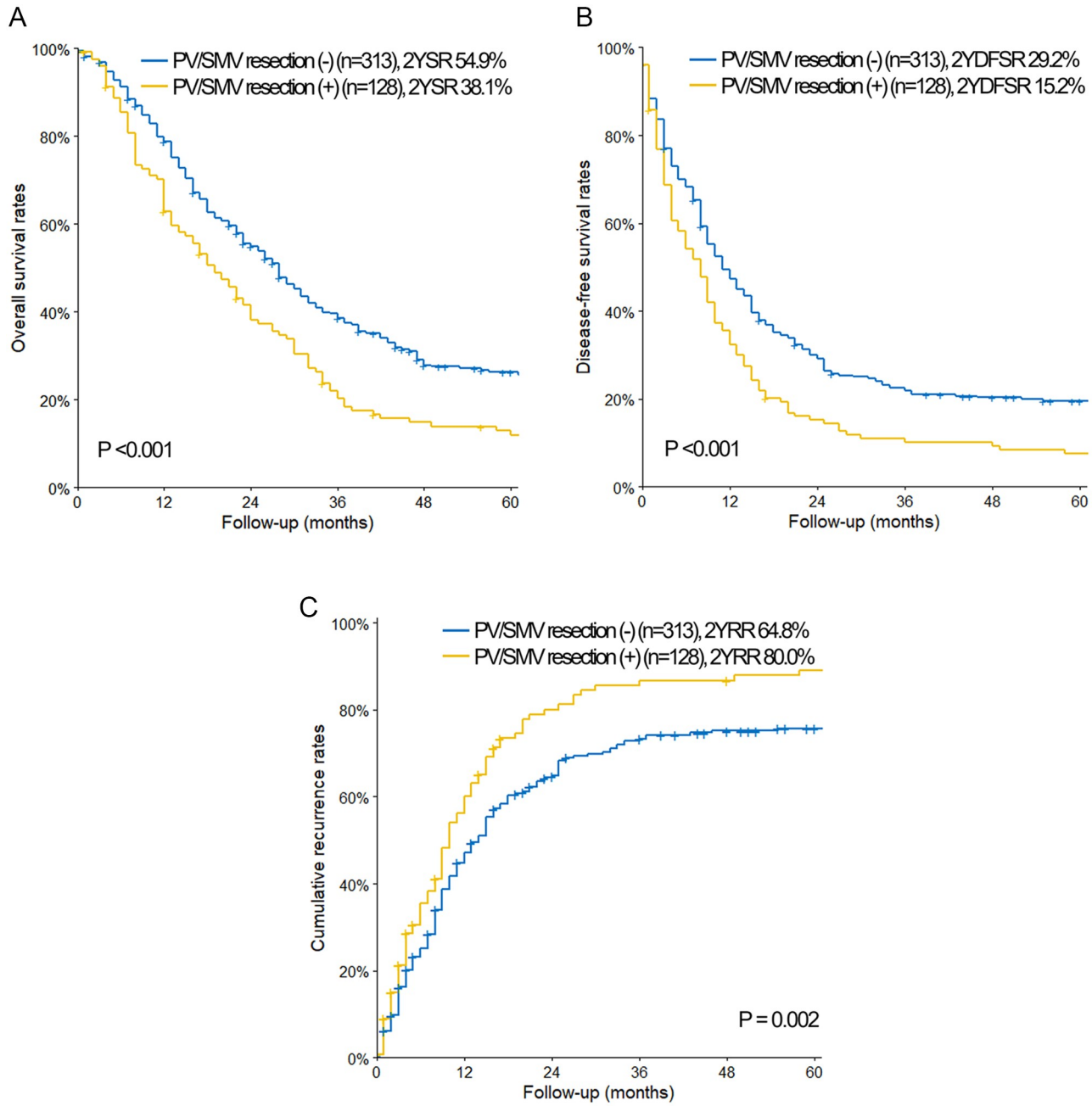

Figure 3. Comparison of overall survival (A), disease-free survival (B), and cumulative recurrence rate (C) between patients who underwent PV/SMV resection and those who did not.

specificity of 75%, with an overall accuracy of 81%[9]. However, as the TVI increased, its sensitivity and accuracy decreased significantly in this study, thereby raising the question of its clinical utility. The sensitivity of radiological prediction is also important for surgeons planning PV/SMV resection to achieve R0 resection in patients with suspicious preoperative vessel involvement. Additionally, a previous meta-analysis reported a wide range of true pathologic PV/SMV involvement, varying from 17% to 78%[5], highlighting the discrepancies between pre/intraoperative assessment and pathological confirmations of PV/SMV invasion. Recently, with the increasing use of neoadjuvant therapy, differentiating between PV/SMV invasion and changes due to fibrosis or inflammation based solely on imaging findings has become increasingly challenging[23]. Therefore, it is necessary to develop a practical model that can accurately predict vessel involvement based on the previously reported model[9], rather than relying solely on TVI assessments.

Another potential approach is the integration of radiomics. CT-based radiomics has been shown to improve the predictive accuracy of PV/SMV involvement and margin status. A recent Chinese study developed a radiomics-based risk model that combined radiomics features with venous deformity to estimate

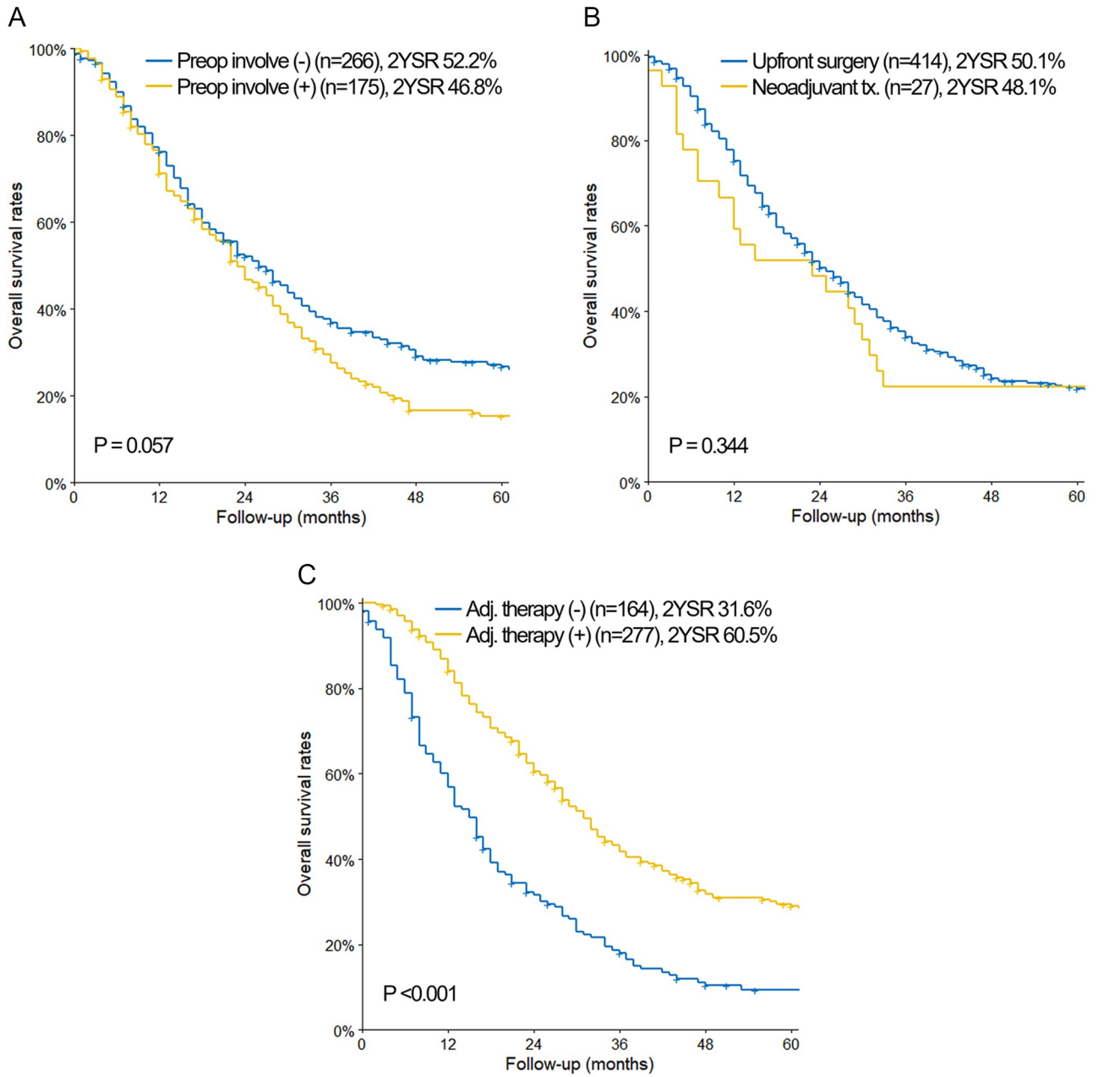

Figure 4. Comparison of overall survival according to preoperative PV/SMV involvement (A), neoadjuvant therapy (B), and adjuvant therapy (C).

PV/SMV involvement, achieving an area under the curve of 0.928, which was significantly higher than conventional imaging assessments[10]. Furthermore, according to Bian et al., a radiomics score derived from CT imaging was also significantly associated with the pathologic PV/SMV margin, with an area under the curve of 0.750[24]. Incorporating such radiomics models could enhance the identification of patients who require PV/SMV resection, thereby improving clinical decision-making. Moreover, the intraoperative decision-making process remains crucial for determining the necessity of PV/SMV resection, even in patients with a low likelihood of preoperative radiological PV/SMV involvement. During surgery, careful dissection should be attempted first, and PV/SMV resection should be considered if dissection is not feasible or if vessel involvement is definitively confirmed preoperatively. Additionally, intraoperative frozen biopsy can also provide valuable information to assist in deciding whether PV/SMV resection is necessary, allowing surgeons to evaluate the TVI in real-time and make more informed decisions to achieve an optimal surgical extent.

Despite significant advancements in surgical techniques and improvements in perioperative care, PD remains associated with considerable morbidity, ranging from 30% to 50%[22]. Besides the complexity of the operation itself, combined PV/SMV resection can raise concerns about an increased rate of complications. However, our study found that complication rate did not differ between patients undergoing PV/SMV resection and those

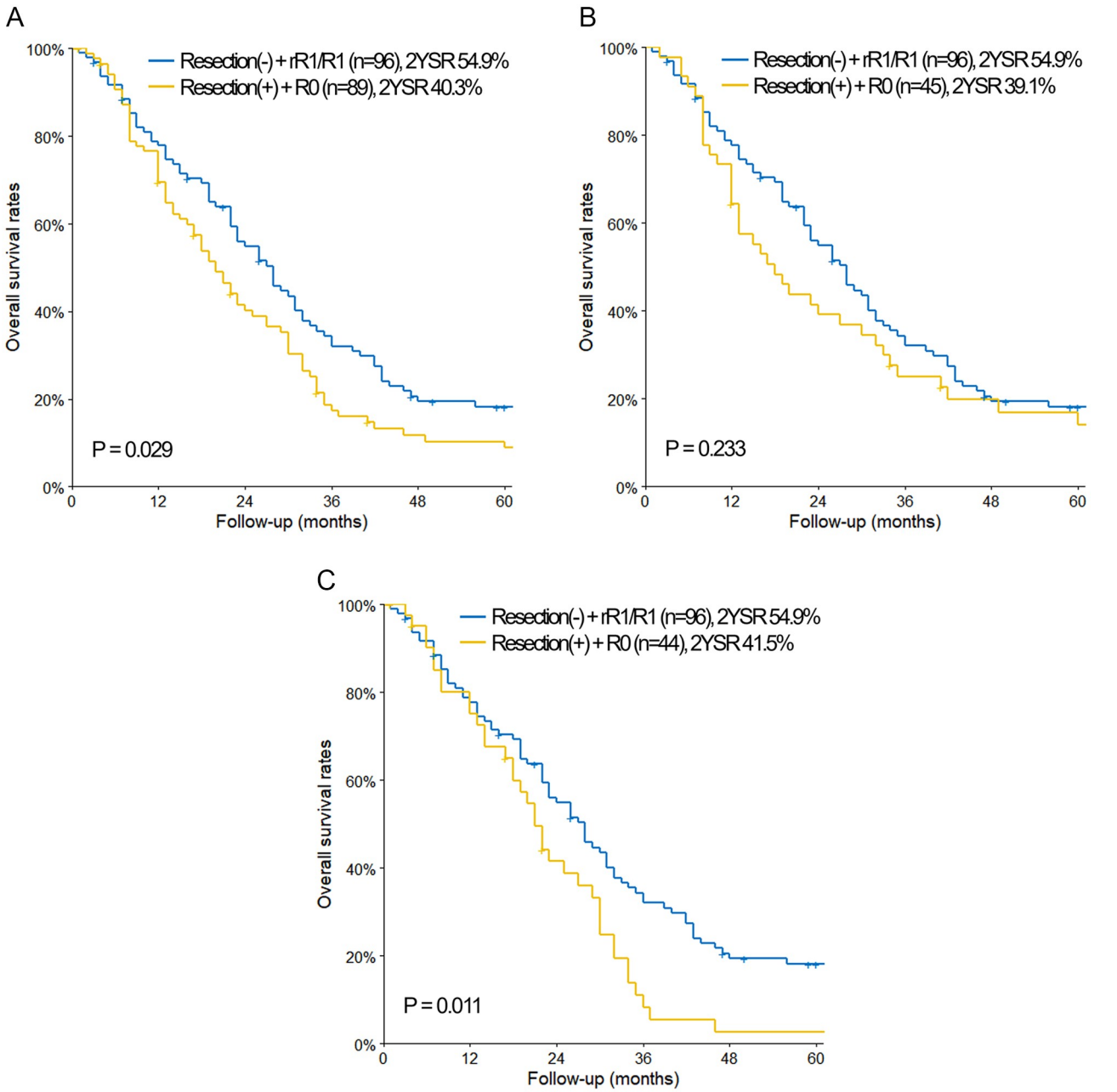

Figure 5. Comparison of overall survival between patients without PV/SMV resection who had rR1/R1 margin and (A) those with PV/SMV resection and R0 margin, (B) those who underwent PV/SMV resection with R0 margin and pathological PV/SMV involvement, and (C) those who underwent PV/SMV resection with R0 margin, but no pathological PV/SMV involvement.

without PV/SMV resection (complication Clavien–Dindo grade 3 or more, 25.8% vs 23.6%, $P = 0.724$). These results are consistent with other studies[7,25–27], indicating that PV/SMV resection can be performed with manageable risks. However, there are studies suggesting contrary results of an elevated risk of complications following combined PV/SMV resection in some patients[5,28,29]. Therefore, further research is essential for safety and technical advancements in PV/SMV resection, including the selection of appropriate grafts and perioperative care, including the standardization of anticoagulation. Moreover, it is crucial to perform vessel resection under well-planned circumstances to minimize complications.

Previous reports have indicated that long-term survival outcomes in patients with PV/SMV resection are satisfactory[12,13]. However, when the survival outcomes of PV/SMV resection are evaluated, making direct comparisons between patients with PV/SMV resection and those without resection is challenging. First, many patients with PV/SMV resection had true pathologic invasion and a higher risk of distant metastasis through the portomesenteric system, leading to a poorer prognosis[6,7]. Additionally, patients who underwent PV/SMV resection were more likely to have advanced disease, such as larger tumor size and more extensive local invasion. Tumor biology, including

Table 2

Cox regression model for the predictors of overall survival of pancreatic cancer following surgical resection.

		Univariate analysis			Multivariate analysis		
	n	HR	95% CI	*P value*	HR	95% CI	*P value*
Age		1.015	1.004–1.026	0.009	1.002	0.989–1.015	0.780
Sex (male)	276	0.980	0.784–1.224	0.858			
Body mass index		0.954	0.920–0.989	0.011	0.960	0.922–1.001	0.053
Preoperative hypertension	183	1.357	1.093–1.684	0.006	1.552	1.231–1.957	<0.001
Preoperative diabetes	178	1.194	0.961–1.484	0.110			
ASA score (vs 1)	64	Ref.		0.307			
2	335	1.160	0.842–1.598	0.363			
3	42	1.421	0.908–2.226	0.125			
Initial CA19-9		1.000	1.000–1.000	0.015	1.000	1.000–1.000	0.859
Preoperative biliary drainage	257	1.112	0.891–1.389	0.347			
Neoadjuvant treatment	27	1.224	0.801–1.870	0.351			
Preoperative PV/SMV involvement	175	1.232	0.991–1.531	0.061			0.647
Contact	85	1.035	0.779–1.376	0.812	0.863	0.632–1.179	0.355
Encasement/invasion	90	1.454	1.117–1.891	0.005	0.923	0.654–1.301	0.646
Operation type (vs PPPD)	222	Ref.		0.127			
Whipple	51	1.385	0.975–1.966	0.069			
PrPD	168	1.178	0.936–1.482	0.162			
Estimated blood loss		1.000	1.000–1.001	<0.001	1.000	1.000–1.000	0.082
PV/SMV resection	128	1.539	1.222–1.938	<0.001	1.343	1.052–1.716	0.018
Pathologic PV/SMV invasion	81	1.579	1.212–2.057	0.001	1.084	0.718–1.635	0.701
PV/SMV margin status (vs R0)	303	Ref.		0.042			0.053
rR1	122	1.099	0.866–1.394	0.439	1.071	0.834–1.376	0.589
R1	12	1.731	0.944–3.174	0.076	1.221	0.651–2.292	0.534
R2	4	4.257	1.578–11.486	0.004	6.024	2.063–17.589	0.001
Pathologic tumor size		1.296	1.166–1.440	<0.001	1.224	0.991–1.513	0.061
T stage (vs T1)	84	Ref.		<0.001			0.025
T2	310	1.745	1.294–2.351	<0.001	1.306	0.867–1.967	0.202
T3, T4	47	2.040	1.334–3.119	0.001	0.804	0.363–1.779	0.590
N stage (vs N0)	133	Ref.		<0.001			<0.001
N1	200	1.414	1.094–1.828	0.008	1.324	1.000–1.753	0.050
N2	108	2.234	1.661–3.078	<0.001	2.217	1.594–3.082	<0.001
Cell differentiation (vs well)	24	Ref.		<0.001		–	<0.001
Moderately	295	1.457	0.900–2.358	0.126	1.778	1.041–3.039	0.035
Poorly	113	2.525	1.522–4.190	<0.001	3.428	1.952–6.023	<0.001
Undifferentiated	9	1.707	0.633–4.603	0.291	4.047	1.41–11.618	0.009
Lymphovascular invasion	295	1.556	1.228–1.971	<0.001	0.966	0.694–1.345	0.839
Perineural invasion	421	2.387	1.269–4.487	0.007	1.260	0.628–2.528	0.515
Complication, CD grade ≥3	107	1.178	0.921–1.507	0.193			
CR-POPF	34	1.022	0.680–1.538	0.915			
PPH grade ≥B	25	1.207	0.776–1.878	0.404			
Adjuvant treatment	277	0.473	0.380–0.590	<0.001	0.398	0.305–0.495	<0.001
Recurrence	295	2.596	1.981–3.403	<0.001	2.310	1.738–3.070	<0.001

ASA, American Society of Anesthesiologists; CA19-9, carbohydrate antigen 19-9; CD, Clavien–Dindo; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; PPPD, pylorus-preserving pancreatoduodenectomy; PrPD, pylorus-resecting pancreatoduodenectomy; PV, portal vein; SMV, superior mesenteric vein.

infiltrative subtypes and microinvasion markers such as lymphovascular invasion and perineural invasion, may also contribute, as tumors requiring PV/SMV resection often exhibit aggressive features such as poor differentiation and deeper infiltration[30]. This suggests that tumors requiring PV/SMV resection may have worse biological behavior, contributing to poorer outcomes in these patients. Despite using multivariate analysis to adjust for these factors, residual confounding may still exist, and such factors could impact the observed survival differences. Therefore, making direct comparisons between patients with and without PV/SMV resection remains inherently challenging. Second, the achievement of an R0 resection was not invariably assured even if the PV/SMV was resected. Kleive *et al* conducted a detailed histopathological mapping of the tumor and its relationship to the margins and concluded that if the tumor infiltrated the vein, the surface of the SMV groove was most likely also involved, whether the vessel was resected or not[31].

The survival benefit of PV/SMV resection was analyzed by comparing patients who achieved an R0 margin with vessel resection and those who achieved an R1 margin without vessel resection. A previous study from our institute demonstrated that patients who achieved R0 margins following PV/SMV resection exhibited better survival than those who did not undergo combined PV/SMV resection with R1 margins[6]. However, the above-mentioned study defined R1 margins based on the 0-mm margin rule, whereas our current study included patients

using revised R1 margins (1-mm margin rule). Furthermore, the potential for short-term and long-term complications from PV/SMV resection, such as PV thrombosis and left-sided portal hypertension due to splenic vein ligation, should not be underestimated[28]. Left-sided portal hypertension and PV thrombosis can lead to varix formation and subsequent bleeding. Recurrent bleeding can significantly worsen the patient's general condition, delaying the initiation and continuation of adjuvant therapy, which may ultimately compromise long-term outcomes. In some cases, massive bleeding may occur, leading to significant morbidity or even mortality. Additionally, hypersplenism contributes to pancytopenia, reducing the patient's tolerance to chemotherapy and increasing the risk of further bleeding. Moreover, compromised liver function due to decreased blood supply from these complications can also affect the overall prognosis and the patient's capacity for the adjuvant therapy. Therefore, PV/SMV resection may be required only in cases where R1 resection is anticipated, advocating for a more conservative surgical approach because PV/SMV resection cannot always guarantee R0 resection, and the rR1 margin was not associated with worse survival outcomes compared to R0 margins.

Pancreatic cancer has a dismal prognosis, with a 5-year OS rate of approximately 12%[32]; however, the effectiveness of FOLFIRINOX and gemcitabine with nab-paclitaxel has been recently revealed in borderline resectable/locally advanced cases, and these regimens have been used as adjuvant therapy regimens[33]. Therefore, effective neoadjuvant therapy and adjuvant therapy are more important these days and provide survival benefits compared to surgical methods. Therefore, patients need to proceed quickly with adjuvant therapy through more conservative surgeries with fewer complications. Neoadjuvant therapy can be considered in patients with definite PV/SMV involvement on preoperative radiological assessments.

This study has some limitations. First, most patients underwent upfront surgery during the study period. Recently, the number of patients receiving neoadjuvant therapy for pancreatic cancer has increased with the widespread use of FOLFIRINOX or gemcitabine with nab-paclitaxel. This trend is particularly notable for borderline resectable pancreatic cancer and even in select resectable cases with PV/SMV abutment. The authors are planning further studies to analyze the clinical implications of PV/SMV involvement and resection in patients receiving neoadjuvant therapy. Second, this was a retrospective study, although we collected data prospectively. The possibility of uncontrolled confounding factors cannot be fully ignored; therefore, further studies with well-controlled designs for these variables are required to strengthen these results. Notably, our institution is currently participating in an ongoing international multicenter randomized controlled trial comparing neoadjuvant FOLFIRINOX with upfront surgery in resectable pancreatic cancer[34]. This trial, which aims to enroll 609 patients, will evaluate outcomes such as OS, disease-free survival, resection rate, and R0 resection rate, with subgroup analyses planned for PV/SMV abutment cases. Third, the number of patients in the subgroups was relatively small to perform a subgroup analysis to draw definitive conclusions, such as comparing survival based on PV/SMV margin status. To address this limitation, future studies should aim to increase the sample size in these subgroups, possibly through multicenter collaboration, to enhance the robustness and generalizability of the findings.

In conclusion, PV/SMV resection could potentially guarantee a higher R0 rate in patients with preoperative vessel involvement. However, this may lead to unnecessary resection in some cases. Furthermore, achieving an R0 margin through PV/SMV resection does not improve survival outcomes compared with those without resection but with positive margins. Therefore, careful evaluation of the need for PV/SMV resection is recommended before and during surgery. It is necessary to proceed with adjuvant therapy immediately after conservative surgery. PV/SMV resection is associated with poor prognosis, suggesting a severe disease status, and an optimal treatment strategy, including neoadjuvant therapy, could be considered.

Author contributions

HS Kim, SH Shin, IW Han, JS Heo, and H Kim contributed to the study design. HS Kim, H Chae, SY Lim, H Jeong, and SJ Yoon collected data. HS Kim and H Kim analyzed the data and wrote the manuscript in consultation with H Chae, SY Lim, H Jeong, SJ Yoon, SH Shin, IW Han, and JS Heo. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

Ethical approval

This study was approved by the Institutional Review Board of Samsung Medical Center (approval number: 2023-11-123).

Consent

The requirement for written informed consent for this retrospective study was waived by the Institutional Review Board of Samsung Medical Center.

Sources of funding

This research was supported by a grant of the Korean Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2023-KH140182).

Conflicts of interest disclosure

Not applicable.

Presentation

Not applicable.

Research registration unique identifying number (UIN)

This study was registered at the Research Registry (Research Registry Registration Number: reviewregistry10463). https://researchregistry.knack.com/research-registry#home/registrationdetails/668bb41d5bc00c002993b8ad/.

Guarantor

The guarantor for this article is the corresponding author, Hongbeom Kim.

Provenance and peer review

Not applicable.

Data availability statement

Not applicable.

References

[1] Katz MH, Pisters PW, Evans DB, *et al*. Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. J Am Coll Surg 2008;206:833–46.

[2] Tran Cao HS, Balachandran A, Wang H, *et al*. Radiographic tumor-vein interface as a predictor of intraoperative, pathologic, and oncologic outcomes in resectable and borderline resectable pancreatic cancer. J Gastrointest Surg 2014;18:269–78.

[3] National Comprehensive Cancer Network. Pancreatic adenocarcinoma. http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed March 3, 2024 (version 1; 2024).

[4] Murakami Y, Uemura K, Sudo T, *et al*. Benefit of portal or superior mesenteric vein resection with adjuvant chemotherapy for patients with pancreatic head carcinoma. J Surg Oncol 2013;107:414–21.

[5] Giovinazzo F, Turri G, Katz MH, *et al*. Meta-analysis of benefits of portal-superior mesenteric vein resection in pancreatic resection for ductal adenocarcinoma. Br J Surg 2016;103:179–91.

[6] Han S, Choi DW, Choi SH, *et al*. Long-term outcomes following en bloc resection for pancreatic ductal adenocarcinoma of the head with porto-mesenteric venous invasion. Asian J Surg 2021;44:313–20.

[7] Han SS, Park SJ, Kim SH, *et al*. Clinical significance of portal-superior mesenteric vein resection in pancreatoduodenectomy for pancreatic head cancer. Pancreas 2012;41:102–06.

[8] Song A, Liu F, Wu L, *et al*. Histopathologic tumor invasion of superior mesenteric vein/ portal vein is a poor prognostic indicator in patients with pancreatic ductal adenocarcinoma: results from a systematic review and meta-analysis. Oncotarget 2017;8:32600–07.

[9] Kim M, Kang TW, Cha DI, *et al*. Prediction and clinical implications of portal vein/superior mesenteric vein invasion in patients with resected pancreatic head cancer: the significance of preoperative CT parameters. Clin Radiol 2018;73:564–73.

[10] Zhou Y, Wang J, Zhang SL, *et al*. A CT radiomics-based risk score for preoperative estimation of intraoperative superior mesenteric-portal vein involvement in pancreatic ductal adenocarcinoma. Ann Surg Oncol 2023;30:1206–16.

[11] Groen JV, van Manen L, van Roessel S, *et al*. Resection of the portal-superior mesenteric vein in pancreatic cancer: pathological assessment and recurrence patterns. Pancreas 2021;50:1218–29.

[12] Nagakawa Y, Jang JY, Kawai M, *et al*. Surgical outcomes of pancreatectomy with resection of the portal vein and/or superior mesenteric vein and jejunal vein for pancreatic head cancer: a multicenter study. Ann Surg 2023;277:e1081–e1088.

[13] Hackert T, Klaiber U, Hinz U, *et al*. Portal vein resection in pancreatic cancer surgery: risk of thrombosis and radicality determine survival. Ann Surg 2023;277:e1291–e1298.

[14] Klein F, Berresheim F, Felsenstein M, *et al*. Routine portal vein resection for pancreatic adenocarcinoma shows no benefit in overall survival. Eur J Surg Oncol 2018;44:1094–99.

[15] Jeong J, Choi DW, Choi SH, *et al*. Long-term outcome of portomesenteric vein invasion and prognostic factors in pancreas head adenocarcinoma. ANZ J Surg 2015;85:264–69.

[16] Mathew G, Agha R, Albrecht J, *et al*. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. Int J Surg 2021;96:106165.

[17] Hruban RH, Bishop Pitman M, Klimstra DS. Tumors of the pancreas. In: Atlas Tumor Pathol, 4th Series, Fascicle 6. Armed Forces Institute of Pathology. Armed Force Institute of Pathology; 2007.

[18] The Royal College of Pathologists. Standards and datasets for reporting cancers. Minimum dataset for the histopathological reporting of pancreatic, ampulla of Vater and bile duct carcinoma. Royal College of Pathologists; 2019.

[19] You Y, Choi DW, Heo JS, *et al*. Clinical significance of revised microscopic positive resection margin status in ductal adenocarcinoma of pancreatic head. Ann Surg Treat Res 2019;96:19–26.

[20] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.

[21] Bassi C, Marchegiani G, Dervenis C, *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.

[22] Wente MN, Veit JA, Bassi C, *et al*. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery 2007;142:20–25.

[23] Bolm L, Pisuchpen N, Qadan M, *et al*. Prediction of R status in resections for pancreatic cancer using simplified radiological criteria. Ann Surg 2022;276:215–21.

[24] Bian Y, Jiang H, Ma C, *et al*. Performance of CT-based radiomics in diagnosis of superior mesenteric vein resection margin in patients with pancreatic head cancer. Abdom Radiol (NY) 2020;45:759–73.

[25] Yu XZ, Li J, Fu DL, *et al*. Benefit from synchronous portal-superior mesenteric vein resection during pancreaticoduodenectomy for cancer: a meta-analysis. Eur J Surg Oncol 2014;40:371–78.

[26] Yekebas EF, Bogoevski D, Cataldegirmen G, *et al*. En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels: perioperative outcome and long-term survival in 136 patients. Ann Surg 2008;247:300–09.

[27] Zwart ES, Yilmaz BS, Halimi A, *et al*. Venous resection for pancreatic cancer, a safe and feasible option? A systematic review and meta-analysis. Pancreatology 2022;22:803–09.

[28] Mizuno S, Kato H, Yamaue H, *et al*. Left-sided portal hypertension after pancreaticoduodenectomy with resection of the portal vein/superior mesenteric vein confluence in patients with pancreatic cancer: a project study by the Japanese Society of Hepato-Biliary-Pancreatic Surgery. Ann Surg 2021;274:e36–e44.

[29] Petrucciani N, Debs T, Rosso E, *et al*. Left-sided portal hypertension after pancreatoduodenectomy with resection of the portal/superior mesenteric vein confluence. Results of a systematic review. Surgery 2020;168:434–39.

[30] Delpero JR, Boher JM, Sauvanet A, *et al*. Pancreatic adenocarcinoma with venous involvement: is up-front synchronous portal-superior mesenteric vein resection still justified? A survey of the association Francaise de Chirurgie. Ann Surg Oncol 2015;22:1874–83.

[31] Kleive D, Labori KJ, Line PD, *et al*. Pancreatoduodenectomy with venous resection for ductal adenocarcinoma rarely achieves complete (R0) resection. HPB (Oxford) 2020;22:50–57.

[32] Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–49.

[33] Stoop TF, Theijse RT, Seelen LWF, *et al*. Preoperative chemotherapy, radiotherapy and surgical decision-making in patients with borderline resectable and locally advanced pancreatic cancer. Nat Rev Gastroenterol Hepatol 2024;21:101–24.

[34] ClinicalTrials.gov: NCT05529940. [(accessed on 8 January 2025)]; https://clinicaltrials.gov/study/NCT05529940.