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Bilateral paravertebral block reduces complications after pancreatectomy in retrospective cohort analysis

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To investigate the effects of paravertebral block (PVB) on postoperative pancreatic fistula (POPF) and major complications in adult pancreatic surgery. All data of patients who underwent pancreatic surgery at Changhai hospital between January 2017 and June 2021 were retrieved. According to whether they received PVB or not, the patients were divided into the PVB and non-PVB groups. POPF-related factors were balanced by covariate balancing propensity score (CBPS) based inverse probability weighting. After that, the POPF and postoperative major complications between the two groups were compared. Another propensity score matching, multivariate logistic regression and instrumental variable regression were employed for sensitivity analysis. Results of sensitivity analysis were expressed as relative risk (RR) or odd ratio (OR) and 95% confidence interval (CI). A total of 3360 patients were included in the study, with 374 patients in PVB group and 2986 patients in non-PVB group. After CBPS, there was no significant difference in incidence (5.7% VS 6.2%, *P* = 0.785) between the groups (PVB VS non-PVB). Postoperative nasogastric tube retention time (2d VS 3d, *P* < 0.001), and length of hospital stay (11d VS 12d, *P* = 0.031) were significantly reduced in the PVB group. delayed gastric emptying (DGE) (RR 0.476; 95% CI 0.262–0.863; *P* = 0.014) and postpancreatectomy hemorrhage (PPH) (RR 0.426; 95% CI 0.287–0.630; *P* < 0.001) were reduced more than 50% in PVB group. PVB did not increase the risk of POPF, but reduced DGE and PPH by more than 50%, and improved postoperative recovery after pancreatectomy.

Keywords Paravertebral block, Pancreatectomy, Postoperative pancreatic fistula, Delayed gastric emptying, Postoperative hemorrhage, Enhanced recovery after surgery

Pancreatic cancer is the fourth leading cause of cancer death in the US[1]. Surgery is vital in obtaining the curative effect for pancreatic cancer[2]. However, pancreatic postoperative complications still reach 40–50%, even with minimally invasive surgery in recent years, and various improvements surgeons have made for surgery and perioperative protocols[3]. The incidence of postoperative pancreatic fistula (POPF) is as high as 3.8–14.6%[4,5], which is the most common complication and is associated with a significant reduction in long-term survival[6].

Increasing evidence has shown that ultrasound-guided paravertebral block (PVB) technique provides an alternative for epidural analgesia, and even bilateral PVB can be provided for pain relief for upper laparotomy[7,8]. However, Several factors have potential risks for POPF in anesthesia management, including hypotension, intraoperative fluid balancing and inotrope use[9,10]. In a large retrospective study, one-shot bilateral PVB injections showed a very low technical complication rate of only 0.7%, with symptomatic bradycardia and hypotension being the most common complications[11], which may increase the demand for intraoperative inotrope use and fluid volume. Therefore, there is a potential risk of increased POPF in bilateral PVB.

Several studies have reported the impact of PVB on surgical outcomes[12,13]. A small prospective study of bilateral PVB included only 53 patients and found that when compared to thoracic epidural catheters, thoracic paravertebral catheters offered equivalent analgesia and fewer modality-related adverse events in patients

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who underwent open pancreaticoduodenectomy[8]. But thesmall sample size limited the assessment of the postoperative complications. Therefore, to the best of our knowledge, there have been no bilateral PVB studies on POPF and major postoperative complications in pancreatic surgery.

Our study aimed to explore the evidence of the relationship between bilateral PVB and POPF and postoperative complications after pancreatic surgery. This study provides evidence for the optimal choice of anesthesia management in pancreatic surgery.

Results

A total of 4299 patients underwent pancreatic surgery, of which 4131 patients were included in the study. A total of 3360 patients met the inclusion criteria. The enrolled patients were divided into general anesthesia combined with a bilateral PVB (PVB group, n = 374 cases) and general anesthesia not combined with a PVB (non-PVB group, n = 2986 cases) (Fig. 1). In the non-PVB group, 96 patients received general anesthesia alone, whereas 2890 patients underwent general anesthesia combined with transversus abdominis plane (TAP) block. Both the PVB and non-PVB groups received postoperative multimodal intravenous patient-controlled analgesia. The characteristic data of the two groups are presented in Table 1. There were significant differences in age, preoperative jaundice, pancreatic tumor texture, operation method, and surgical approach ($P < 0.05$), and SMDs of operation and surgical approach were over 0.30. After CBPS, the bias in the characteristic data was adjusted (Table 1).

After CBPS, there was no significant difference in the incidence of POPF between the PVB and non-PVB groups (5.7% vs. 6.2%, $P = 0.774$). There was no significant difference in the incidence of BL between the PVB and non-PVB groups (20.4% vs. 22.3%, $P = 0.449$) (Table 2).

Following CBPS, the PVB group had a shorter postoperative gastric tube retention time [median (IQR), 2 (2,3) d vs. 3 (2,4) d, $P < 0.001$] and postoperative fasting time [median (IQR), 3 (3,4) d vs. 3 (3,5) d, $P < 0.001$] than the non-PVB group. There was a lower incidence of postoperative DGE [3.3% vs. 6.6%, $P = 0.015$] and PPH [7.8% vs. 16.7%, $P < 0.001$] in the PVB group. Additionally, the PVB group had a shorter length of hospital stay than the control group [median (IQR), 11d (9,16) vs. 12d (10,17), $P = 0.031$] (Table 2). There was no difference in the mortality rates between the two groups at 30 and 90 days after surgery (Table 2).

In the PVB group, the RR of DGE was 0.469 (95% CI 0.259–0.849, $P = 0.015$) before matching and 0.476 (95% CI 0.262–0.863, $P = 0.014$) after matching. In the PVB group, the RR of postoperative hemorrhage was 0.390 (95% CI 0.260–0.583, $P < 0.001$) before CBPS and 0.426 (95% CI 0.287–0.630, $P < 0.001$) after CBPS (Fig. 2).

All three sensitivity analyses were performed on POPF, postoperative bleeding, and DGE. Among the three sensitivity studies, the 1:1 PSM and multivariate regression analysis supported the conclusion of three

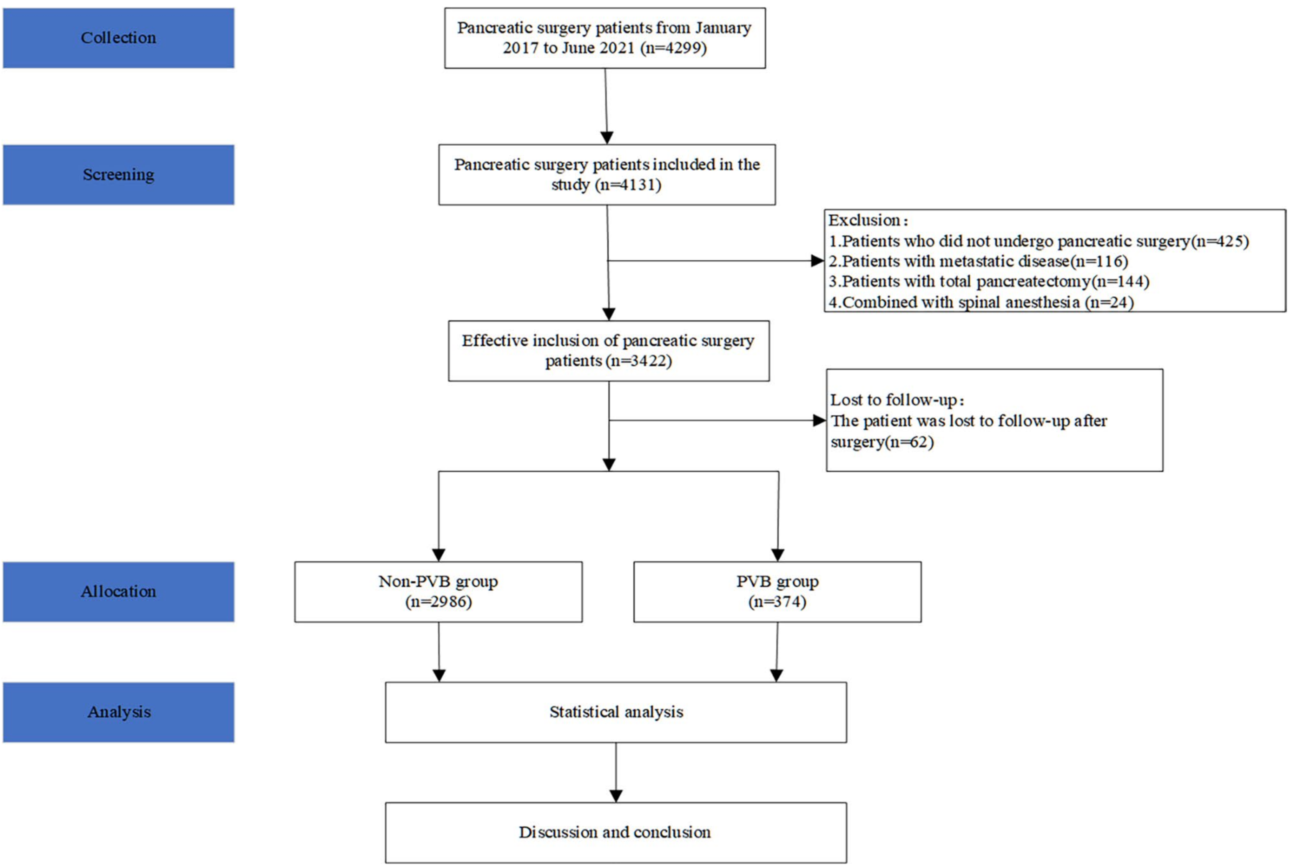

Fig. 1. Flowchart of the patient allocation. PVB: Paravertebral block.

Parameters	Before CBPS PVB (n = 374)	Non-PVB (n = 2986)	P	SMD	After CBPS PVB (n = 369.5)	Non-PVB (n = 2612.0)	*P*	SMD
Gender, n (male%)	227(60.7)	1709(57.2)	0.222	0.070	216.4 (58.6)	1494.5 (57.2)	0.662	0.027
Age, mean(SD),y	58.5 ± 11.7	60.0 ± 12.2	0.025*	0.125	59.9 ± 11.9	60.0 ± 12.2	0.840	0.013
BMI, mean(SD),kg/m^2	22.7 ± 2.9	22.7 ± 3.1	0.864	0.010	22.7 ± 2.9	22.7 ± 3.1	0.836	0.012
ASA			0.464	0.063			0.532	0.062
Ⅰ, n (%)	13(3.5)	72(2.4)			12.0(3.3)	63.0(2.4)		
Ⅱ, n (%)	336(89.8)	2716(91.0)			329.8(89.3)	2375.5(90.9)		
Ⅲ, n (%)	25(6.7)	198(6.6)			27.7(7.5)	173.5(6.6)		
Hypertension, n (%)	111(29.7)	942(31.5)	0.479	0.041	120.7(32.7)	824.5(31.6)	0.703	0.024
Diabetes, n (%)	83(22.2)	619(20.7)	0.501	0.036	93.6(25.3)	541.8(20.7)	0.075	0.109
Biliary stented, n (%)	22(5.9)	186(6.2)	0.909	0.015	18.3(5.0)	162.7(6.2)	0.315	0.055
Preoperative jaundice, n (%)	145(38.8)	964(32.3)	0.014*	0.136	112.4(30.4)	840.6(32.2)	0.494	0.038
Preoperative Chemotherapy, n (%)	153(5.1)	22(5.9)	0.618	0.015	172.8(5.1)	188.8(5.7)	0.664	0.024
Pancreatic texture			0.049*	0.139			0.685	0.053
Hard, n (%)	72(19.3)	743(24.9)			85.6(23.2)	652.3(25.0)		
Medium, n (%)	124(33.2)	885(29.6)			117.0(31.6)	772.7(29.6)		
Soft, n (%)	178(47.6)	1358(45.5)			166.9(45.2)	1187.0(45.4)		
Anesthesia time, median(IQR), h	3.7(3.1,4.3)	3.6(2.9,4.2)	0.052	0.053	3.7(3.1,4.3)	3.6(2.9,4.2)	0.366	0.050
Operation time, median(IQR),h	3.0(2.3,3.4)	2.9(2.3,3.5)	0.429	0.003	3.0(2.3,3.4)	2.9(2.3,3.5)	0.919	0.006
Operation method			< 0.001*	0.306			0.895	0.025
PD, n (%)	201(53.7)	1683(56.4)			211.8(57.3)	1473.3(56.4)		
PP, n (%)	76(20.3)	1303(43.6)			102.9(27.9)	756.7(29.0)		
Other, n (%)	97(25.9)	442(14.8)			54.8(14.8)	382.0(14.6)		
Surgical approach			< 0.001*	0.313			0.234	0.205
Laparoscopic assistance, n (%)	5(1.3)	165(5.5)			19.2(5.2)	146.1(5.6)		
Open surgery, n (%)	369(98.7)	2761(92.5)			350.3(94.8)	2412.6(92.4)		
Laparoscopic conversion-open surgery, n (%)	0(0.0)	9(0.3)			0.0(0.0)	9.0(0.3)		
Da Vinci robot assisted surgery, n (%)	0(0.0)	51(1.7)			0.0(0.0)	45.2(1.7)		
Intraoperative vascular anastomosis, n (%)	55(14.7)	489(16.4)	0.456	0.046	57.1(15.4)	427.9(16.4)	0.668	0.025

Table 1. Charateristic data of patients undergoing pancreatic surgery before and after CBPS. **P* value was less than 0.05, with statistical significance. CBPS: Covariate balancing propensity score; SMD:Standardized mean difference; PVB: Paravertebral block; Non-PVB: Non-Paravertebral block; BMI: Body mass index; ASA: American Society of Anesthesiologists physical status classification; PD:Pancreatoduodenectomy; PP: Partial pancreatectomy; n: numbers; y: years; h:hours.

complications in CBPS matching. The lasso results for the selection of risk factors in POPF multivariate regression were illustrated in supplementary Fig. 1. In instrumental variable regression analysis, the results supported the conclusion of CBPS matching that PVB reduced postoperative bleeding and DGE. PVB was negatively correlated with POPF. In all three instrumental variable regressions, the first-stage F-statistics were well above the conventional weak-instrument threshold of 10 (POPF: $F = 33.06$, $p < 0.001$; PPH: $F = 27.76$, $p < 0.001$; DGE: $F = 30.09$, $p < 0.001$), confirming that the instrument is fully satisfying the relevance assumption. The ORs or RRs of the three sensitivity analyses, along with the 95% CI and *P* values, were displayed in the forest plot (Fig. 3).

Discussion

It have been reported that hypotension was one of the complications of PVB, with an incidence rate between 3.6 and 4.6%[14]. Additional volume and vasoactive drug treatment may be required for hypotension, which may potentially increase the incidence of POPF. However, in this study, except for a slight increase in the colloid crystal ratio, PVB did not significantly increase the total fluid volume and three commonly used vasoactive drug (supplementary table 1, supplementary Fig. 2). Previous studies also suggested that the increase in volume and vasoactive drugs with PVB is not a problematic issue[11,15]. Additionally, a recent study reported that intraoperative fluid balance within the range of −8.47 to 13.56 mL/kg/h did not increase the risk of POPF[16]. Nearly 75% of the patients with PVB in this study received fluid administration below the upper limit of the range. Therefore, the systemic hemodynamic effect of PVB had a relatively small potential impact on POPF, and the data supported the conclusion that PVB did not affect the occurrence of POPF.

Although the intraoperative blood loss between the two groups was very similar, the intraoperative blood transfusion rate in the PVB group decreased remarkable (supplementary table 1). It is unclear why PVB can reduce intraoperative blood transfusions. In previous guidelines, a strict intraoperative transfusion strategy requires hemodynamic stability[17,18]. According to previous research and clinical practice[19,20], it might be inferred

Parameters	Before CBPS				After CBPS			
	PVB (n = 374)	Non-PVB (n = 2986)	P	SMD	PVB (n = 369.5)	Non-PVB (n = 2612.0)	*P*	SMD
Postoperative infection			0.674	0.050			0.822	0.037
Incision, n (%)	10(2.7)	101(3.4)			11.6(3.2)	88.4(3.4)		
Abdominal cavity, n (%)	40(10.7)	292(9.8)			32.5(8.8)	255.3(9.8)		
CCE	6(1.6)	43(1.4)	0.983	0.013	6.4(1.7)	37.5(1.4)	0.672	0.024
Arrhythmias, n (%)	2(0.5)	27(0.9)	0.765	0.087	1.2(.3)	24.5(0.9)	0.284	0.076
AMI, n (%)	0(0.0)	4(0.1)	1.000	0.052	0.0(0.0)	3.5(0.1)	0.452	0.052
AHF, n (%)	2(0.5)	5(0.2)	0.178	0.069	0.0(0.0)	6.1(0.2)	0.320	0.068
Cardiac arrest, n (%)	3(0.8)	4(0.1)	0.034*	0.069	0.0(0.0)	6.1(0.2)	0.320	0.068
Stroke, n (%)	0(0.0)	1(0.0)	1.000	0.026	0.0(0.0)	0.9(0.0)	0.707	0.026
Coma, n (%)	0(0.0)	4(0.0)	1.000	0.052	0.0(0.0)	3.5(0.1)	0.452	0.052
PCs, n (%)	14(3.7)	98(3.3)	0.646	0.025	14.6(4.0)	85.7(3.3)	0.547	0.036
Reoperation, n (%)	4(1.1)	61(2.0)	0.236	0.079	3.4(.9)	53.4(2.0)	0.115	0.094
AKI, n (%)	10(2.7)	91(3.0)	0.872	0.022	12.5(3.4)	79.7(3.1)	0.759	0.019
PPH, n (%)	27(7.2)	497(16.6)	< 0.001*	0.294	29.0 (7.8)	435.2 (16.7)	< 0.001*	0.271
DGE, n (%)	12 (3.2)	197(6.6)	0.015*	0.157	12.0 (3.3)	172.4(6.6)	0.014*	0.155
BL, n (%)	73(19.5)	665(22.3)	0.226	0.068	75.4(20.4)	581.6(22.3)	0.449	0.045
POPF			0.611				0.774	0.057
Grade B, n (%)	20(5.3)	176(5.9)	0.758	0.024	20.6(5.6)	154.0(5.9)	0.820	0.014
Grade C, n (%)	1(0.3)	8(0.3)	1.000	< 0.001	0.5(0.1)	7.0(0.3)	0.556	0.027
Nasogastric tube retention time, median (IQR),d	2(2,3)	3(2,4)	0.033*	0.181	2(2,3)	3(2,4)	< 0.001*	0.206
Postoperative fasting time, median (IQR),d	3(3,4)	3(3,5)	0.037*	0.145	3(3,4)	3(3,5)	< 0.001*	0.182
PONV, n (%)	27(7.2)	196(6.6)	0.659	0.026	25.8(7.0)	171.4(6.6)	0.771	0.025
Length of hospital stay, median(IQR),d	11(9,16)	12(10,17)	0.010*	0.130	11(9,16)	12(10,17)	0.031*	0.124
Length of ICU stay, median(IQR),d	2(1,3)	1(0,3)	0.006*	0.014	2(1,3)	1(0,3)	0.651	0.020
Mortality in 30 days , n (%)	4(1.1)	22(0.7)	0.704	0.035	4.5(1.2)	19.2(0.7)	0.347	0.050
Mortality in 90 days, n (%)	4(1.1)	28(0.9)	1.000	0.013	4.5(1.2)	24.5(0.9)	0.614	0.028

Table 2. Postoperative major complications and Continuous data of postoperative outcomes before and after CBPS. **P* value was less than 0.05, with statistical significance. CBPS: Covariate balancing propensity score; SMD:Standardized mean difference; PVB: Paravertebral block; Non-PVB: Non-Paravertebral block; PCs: Pulmonary complications; AKI: Acute kidney injury; PPH:Postopancreatectomy hemorrhage; DGE: Delayed gastric emptying; CCE: Cardio-cerebrovascular events; AMI: Acute myocardial infarction; AHF: Acute heart failure; BL: Biochemical leakage; POPF: Postoperative pancreatic fistula; PONV: Postoperative nausea and vomiting.

that milder hypotension and more stable hemodynamic manifestations delivered by PVB may have aided in the implementation of the rigorous blood transfusion strategy at the cutting-edge of blood transfusion criteria.

Additionally, PVB showed impressive performance in terms of postoperative gastrointestinal function. In the PVB group, the retention time of the gastric tube, postoperative fasting time, and length of hospital stay were shortened by one day. The incidence of DGE was reduced by 50%, with a very narrow confidence interval. It has been implicated that the application of PVB in pancreatic surgery can contribute to the enhanced recovery of gastrointestinal function after surgery and shorten the length of hospital stay.

The exact mechanism by which PVB decreased DGE is not clear. But it is well known that opioids carry potential risks of infection and gastrointestinal dysfunction[21,22]. Toll like receptor 4 and opioid receptors were believed to be activated by opioids and have complex crosstalk on immune and gastrointestinal motility[23]. Except that, opioids and acute pain have been reported to reduce peripheral plasma motilin levels and affect gastrointestinal function in the central nervous system[24]. The levels of motilin receptors and plasma motilin are considered to be possibly associated with the occurrence of DGE, especially after duodenectomy[25]. Therefore, the opioid sparing and analgesic effect of PVB previously reported may have played a certain role in reducing postoperative DGE[26]. Extended lymphadenectomy along the common hepatic artery necessarily interrupts both vagal and sympathetic innervation to the antropyloric regions. PVB produces a pharmacologic splanchnic sympathetic blockade, which may re-establish vagal–sympathetic balance and thus represents a plausible mechanism for its protective effect. Postoperative transient pancreatitis has also been implicated in the pathogenesis of DGE. A recent meta-analysis has demonstrated the efficacy of epidural analgesia in the management of acute pancreatitis, suggesting that PVB may likewise possess preventive or therapeutic potential against postoperative pancreatic inflammation[27,28]. Finally, the superior analgesia provided by PVB facilitates early mobilization, which in turn accelerates the restoration of gastrointestinal function and may further contribute to the reduction of DGE.

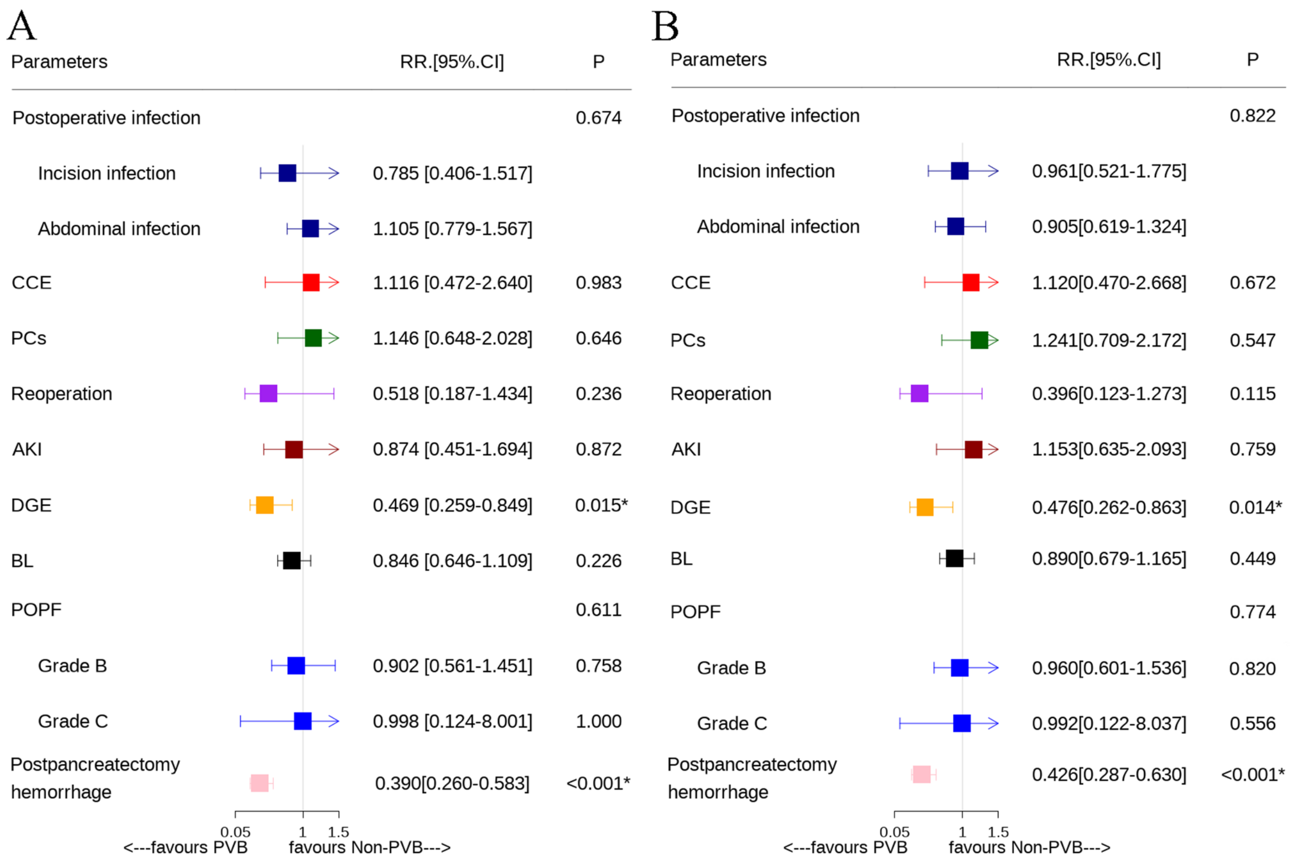

Fig. 2. **A** Relative risk of complications in two group before propensity score matching; **B** Relative risk of complications in two group after propensity score matching; The impact of bilateral PVB on POPF and postoperative complications after pancreatic surgery. PVB: Paravertebral block; POPF: Postoperative pancreatic fistula; RR: Relative risk; CI: Confidence interval; CCE: Cardio-cerebrovascular events; PCs: Pulmonary complications; AKI: Acute kidney injury; DGE: Delayed gastric emptying; BL: Biochemical leak.

It was also impressive that the PVB group showed a decrease of more than 50% in the PPH. Infection and POPF were considered as independent risk factors for PPH, but in this study, PVB did not reduce the incidence of infection or POPF while reducing PPH[29,30]. Moreover, all independent risk factors for PPH identified by our logistic regression (supplementary table 2) were well balanced between groups. There is a few studies on the direct relationship between PVB and PPH, but some of reports on epidural anesthesia which is similar to PVB in nerve root block. A retrospective analysis of the National Surgical Quality Improvement Program (NSQIP) database revealed that, in open abdominal aortic aneurysm repair, combined epidural–general anesthesia was associated with higher odds of receiving a blood transfusion compared with general anesthesia alone (OR 1.63, 95% CI 1.23–2.14; $P=0.001$)[31]. In contrast, another NSQIP retrospective study found no difference in transfusion requirements between epidural anesthesia and transversus abdominis plane block in patients undergoing hepatic resection[32]. A previous nationwide study on perioperative epidural analgesia in liver and pancreatic surgery suggested that postoperative bleeding was not related to epidural analgesia. However, Subgroup analysis further revealed that, compared with conventional analgesia, epidural anesthesia significantly reduced postoperative hemorrhage in patients undergoing pancreaticoduodenectomy (EA: 3.5% vs. non-EA: 5.2%, $p<0.05$). This suggests that regional anesthesia may exert differential effects on postoperative bleeding across distinct surgical procedures. And sepsis as a risk of PPH was reduced in the epidural group in the report[33].

Finally, PVB did not increase overall incidence of other major complications, including AKI, PC, NPPI, CCE, and perioperative mortality for pancreatic surgery. Prior to propensity score weighting, the PVB cohort exhibited a nominally prolonged intensive care unit stay, with this difference achieving statistical significance ($p=0.006$). After adjustment, the disparity was eliminated. Nevertheless, prior investigations have consistently documented more pronounced perioperative hemodynamic fluctuations associated with PVB[11]. Therefore, a clinically relevant safety signal, although presently unconfirmed, cannot be dismissed. The numerical imbalance in mortality, though not statistically significant, further emphasizes the urgent necessity for adequately powered prospective trials specifically designed to clarify the safety profile of PVB in this setting.

There were several limitations in this study. Firstly, this was a retrospective study with retrospective bias. IPW was performed to control intervention bias. CBPS was employed for bias in covariates. CBPS-based stabilized IPW simultaneously balanced the aforementioned bias. A two-stage least-squares instrumental-variable (IV) model was performed for sensitivity analysis to account for unknown bias. Additionally, 1:1 PSM and logistic

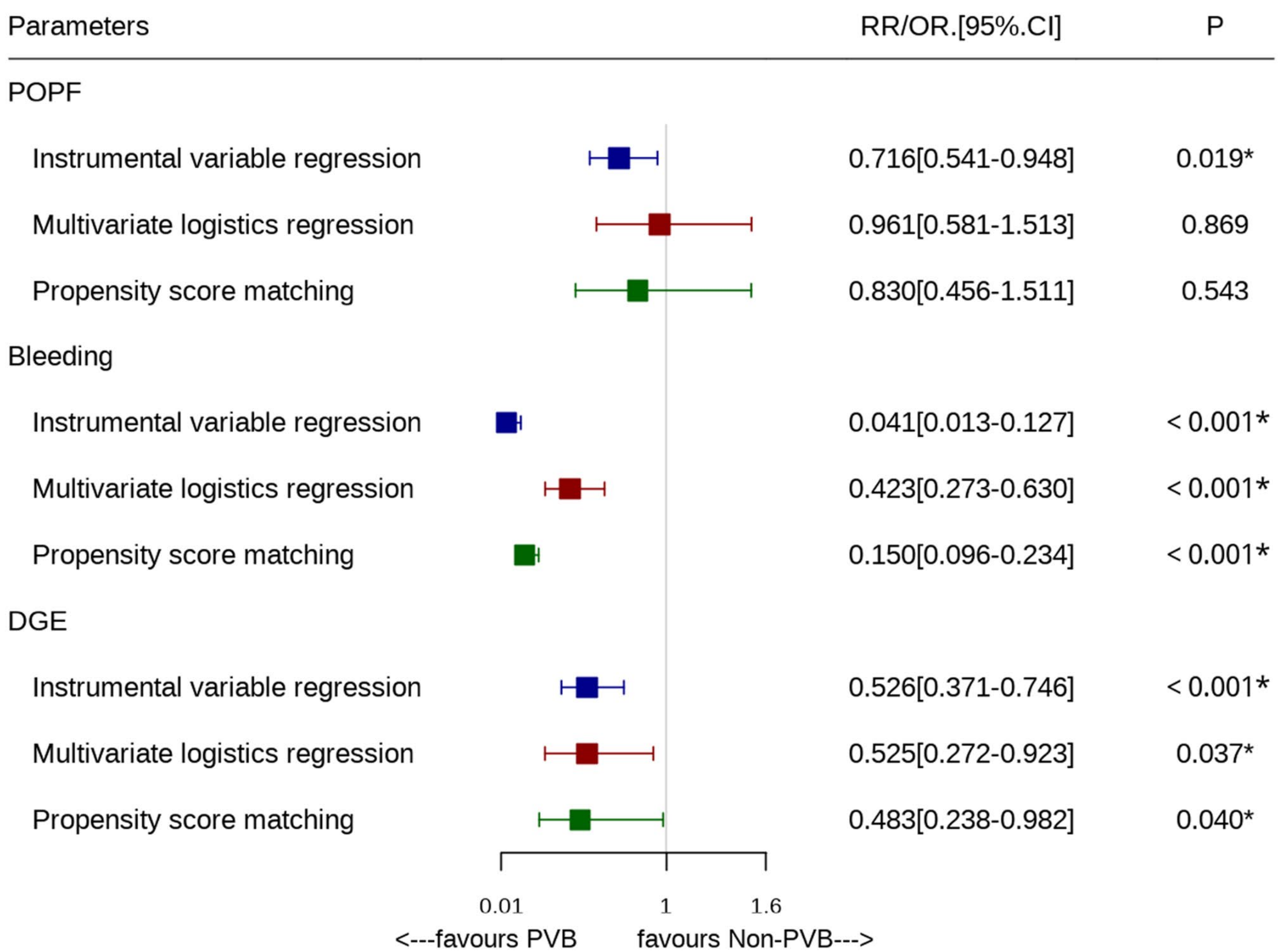

Fig. 3. Three sensitivity analysis results on the relationship between PVB and POPF, PPH and DGE. PVB: Paravertebral block; POPF: Postoperative pancreatic fistula; PPH: Postpancreatectomy hemorrhage; DGE: Delayed gastric emptying; RR: Relative risk in 1:1 propensity score matching; OR: Odds ratio in instrumental variable regression or multivariate logistic regression.

regression were used to verify conclusions. Statistical design was utilized to minimize bias in the study. Although this is a retrospective study, it provides more detailed data for future large-scale randomized controlled studies. Secondly, this was a single-center study, which may have selection bias. However, on the other hand, a single center may reduce the heterogeneity of surgical quality, which is beneficial for studying the impact of anesthesia. Thirdly, the absence of the parameter "time to first ambulation" may still confound the assessment of early postoperative mobilization and DEG outcomes, warranting further validation through prospective large-sample studies.

As an anesthesia technique, PVB not only does not increase postoperative complications in pancreatic surgery, but also has the advantage of reducing surgical complications. It offers several advantages, such as minimizing the need for blood transfusions during surgery, reducing the duration of nasogastric tube placement, shortening the period of postoperative fasting, decreasing the occurrence of PPH and DGE by 50%, and ultimately leading to a shorter hospital stay. PVB is a promising anesthetic management technique for safe and facilitated ERAS in pancreatic surgery.

Methods

This study was approved by the Ethics Committee of Changhai Hospital affiliated to Naval Medical University (NO. CHEC2021-192). Due to the retrospective nature of the study, the Ethics Committee of Changhai Hospital affiliated to Naval Medical University waived the need of obtaining informed consent. The trail was registered at Chinese clinical trial registry (CCTR) on February 7, 2022. The clinical registration number is ChiCTR2200056510 (available at http://www.chictr.org.cn/). All methods were performed in accordance with the relevant guidelines and regulations. After obtaining the ethical approval, the application for obtaining information was then submitted to the electronic information department of the hospital. The data of the first patient enrolled were obtained on March 1, 2022. The data of patients who planned to do pancreatic surgery at Changhai Hospital between January 2017 and June 2021 were retrieved for this study. Patients aged ≥18 years who underwent elective radical surgery for pancreatic cancer and had complete clinical information required for the study were included. Patients with incomplete clinical research data, those who did not undergo pancreatic surgery during the operation, those who underwent total pancreatectomy, and those who received epidural anesthesia were excluded. Patients were divided into two cohorts, the PVB group and the non-PVB group, based on whether they received bilateral PVB. According to the clinical records, the decision to perform PVB was at the discretion of the attending anesthesiologist, subject to the following absolute contraindications: (1) patient refusal or inability to cooperate, (2) pre-operative hemodynamic instability, and (3) local spinal deformity, infection, or any other definitive contraindication to paravertebral puncture. A BMI < 18.5 kg/m^2 was regarded as a relative contraindication. The postoperative 90-day follow-up was conducted in accordance with the visit records of the patient. For patients with incomplete follow-up visit records, telephonic follow-ups were conducted.

Definitions

POPF: The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula was adopted [34].

Delayed gastric emptying (DGE): The ISGPS defined DGE as the requirement or re-insertion of a nasogastric tube after postoperative day 3 or failure to resume oral diet by postoperative day 7[27].

Postpancreatectomy hemorrhage (PPH): The ISGPS definition was adopted[35].

Acute kidney injury (AKI): Diagnostic criteria for Kidney Disease Improving Global Outcomes (KDIGO) was adopted[36].

Cardiovascular and cerebrovascular events (CCEs) included arrhythmias, acute myocardial infarction (AMI), acute heart failure (AHF), cardiac arrest, stroke, and coma. Postoperative pulmonary complications (PCs) included postoperative pneumonia and pulmonary embolism. Non-pulmonary postoperative infection (NPPI) included incision or abdominal cavity. CCEs, PCs, NPPI and reoperation were all retrieved from medical records.

Primary and secondary outcomes

The primary outcome is the incidence of POPF after exposure. An expected difference of 15% (19% vs 34%) in the frequency of gastrointestinal complications between postoperative PCIA and EDA up to postoperative day 30 was reported by Pratt et al[37]. The Walters Approximate Normal method was used to calculate the required sample size for each group. The sample size was 182 cases, with an expected loss to follow-up rate of 10%, a significance level of $\alpha = 5\%$, and a power of $1\text{-}\beta = 90\%$. A sample size of 200 cases was designed for each group. All eligible sample in the database exceeding the required sample size were included in this study.

The secondary outcomes included major postoperative complications such as DEG, PPH, AKI, CCEs, PCs, NPPI, reoperation, length of hospital stay, and 30-day and 90-day mortality.

Statistical analysis

Missing-data strategy was prespecified and variable-specific. Covariates or outcomes with < 5% missing values were analyzed by complete-case analysis, whereas variables with 5–50% missing were imputed using MICE. Any variable with ≥ 50% missing was omitted from the primary model, and the potential impact of this exclusion was examined in sensitivity analyses. The standard mean difference (SMD) and *p*-values of the characteristic data of the two groups were calculated. For covariate balancing propensity score (CBPS) improving robustness of propensity model, stabilized IPW with CBPS matching was adopted for baseline data balancing[38]. Given that soft pancreatic texture was significantly associated with the development of POPF, pancreatic texture was also balanced between the groups[39]. The "CBPS" package of R was used for the procedure.

Continuous data according to the Kolmogorov–Smirnov test results were represented by mean and standard deviation, while data that did not follow a normal distribution were represented by median and quartiles. Group differences were analyzed using ANOVA or the Mann–Whitney U test. Categorical data were analyzed using the chi-square or exact chi-square statistics. Major postoperative complications were expressed as the relative risk (RR) and 95% confidence interval (CI).

Three sensitivity analyses were employed for the stability of CBPS conclusions. The first one was a 1:1 propensity score matching (PSM), with the same balanced parameters as CBPS and nearest neighbor matching algorithm with a caliper of 0.1. The second was multivariate regression analysis. A total of 28 preoperative and intraoperative parameters were included. If there were more than 280 instances of the events that needed to be analyzed, the principle of "10 events per variable" would be followed. To meet this principle, the number of variables would be reduced by conducting least absolute shrinkage and selection operator (LASSO) regression before performing multivariate regression. Thirdly, a two-stage instrumental regression analysis was performed. Operation date, serving as an instrumental variable, is determined solely by the operating-room scheduling system and is therefore plausibly independent of the pathophysiology underlying post-pancreatectomy complications. It influences paravertebral block (PVB) implementation only through the assigned on-duty anesthesia team and has no direct causal pathway to the surgical procedure itself or to postoperative morbidity, thereby satisfying the exclusion-restriction assumption. Moreover, because the calendar has been empirically validated as a suitable instrumental variable, the actual operation date was accordingly employed as the instrumental variable in this study[40]. PVB was used as the explanatory variable, while other significant parameters of multivariate regression were used as covariates. An F-statistic of more than 10 indicated that the instrument was not weak. Odds ratios (OR) or RR and 95% confidence intervals (CI) were expressed in the results. Statistical software R version 4.2.2 was used for analysis. Statistical protocol was written and approved by the institutional review board before data were accessed.

Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request. Data are located in controlled access data storage at Changhai Hospital.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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