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ORIGINAL RESEARCH

Effect of the Step-Jump Approach in Infected Pancreatic Necrosis: A Propensity Score-Matched Study

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Purpose: The effects of the step-jump approach on the survival and prognosis of infected pancreatic necrosis (IPN) patients have not yet been determined.

Patients and Methods: Between November 2018 and June 2023, 188 patients were included in this study. There were 144 patients in the step-up group (the SU group) and 44 in the step-jump group (the SJ group). In the SU group, patients successfully treated with percutaneous catheter drainage (PCD) alone were classified into the SU-1 group (n=101), while those requiring additional surgery after PCD were categorized into the SU-2 group (n=43). In the SJ group, patients who underwent minimally invasive necrosectomy (MIN) without PCD were assigned to the SJ-1 group (n=34), whereas those who initially underwent PCD followed by immediate open surgery were placed in the SJ-2 group (n=10). Propensity score matching (PSM) was used to mitigate bias.

Results: After PSM, a total of 34 pairs were successfully matched. A comparison of the SU group with the SJ-1 group (upfront MIN without PCD) revealed similar mortality rates (P=0.239); however, the incidences of multiple drug-resistant organisms (MDROs) (P=0.029) and surgical complications (P<0.001) were significantly lower in the SJ-1 group. After comparing the SU-2 and SJ-2 groups (patients who underwent direct open necrosectomy without MIN after PCD failure), the incidences of surgical complications and MDRO in the SJ-2 group were significantly lower (P<0.05).

Conclusion: Compared with the step-up approach, the step-jump approach is safer and more effective and can significantly reduce the incidence of MDRO and surgical complications.

Keywords: infected pancreatic necrosis, step-up approach, step-jump approach, propensity score match

Introduction

Acute pancreatitis (AP) is a common and fatal disease worldwide with an incidence of approximately 34/100,000.[1] Approximately 20% of patients with AP develop pancreatic or peripancreatic necrosis, and nearly 30% of them ultimately develop infected pancreatic necrosis (IPN).[2,3] As a common complication in the later course of AP, IPN is characterized by a poor prognosis and a high mortality rate of up to 30%, which often leads to severe complications such as intraabdominal hemorrhage, gastrointestinal fistula, and bleeding.[4–6] The step-up approach, which includes percutaneous catheter drainage (PCD), minimally invasive necrosectomy (MIN), and open necrosectomy (OPN), is regarded as the gold standard of treatment for confirmed or suspected IPN and has been accepted and recommended by most of the relevant guidelines.[7,8]

The step-up approach is advocated because of its minimal surgical trauma and ability to cure nearly one-third of IPN patients without surgery.[9] Although the results from the PANTER trial[9,10] confirmed the safety and superiority of the step-

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up approach over the OPN approach in terms of reducing mortality and incidence of complications, a "one-size-fits-all" treatment may have undesirable consequences because of the complexity and heterogeneity of IPN. Excessive attention to the step-up approach may lead to missed surgical opportunities or even death. Therefore, Miao et al proposed that the step-jump approach, an innovation over the traditional step-up approach, should be adopted for early intervention.[11] Considering the strong heterogeneity and varying circumstances of the disease, personalized critical care and highly individualized therapeutic strategies should be applied to IPN treatment.[12,13] For patients requiring surgical intervention, upfront OPN or MIN without PCD may also achieve the desired clinical outcomes. In the present study, we aimed to evaluate the effect of the step-jump approach in two dimensions: (1) direct MIN without PCD and (2) direct OPN after PCD failure. In addition, we explored specific scenario where the step-jump approach should be considered as the primary choice.

Materials and Methods

Patient Enrollment and Study Design

A retrospective analysis was conducted using the clinical data of IPN patients admitted to our tertiary referral center between November 2018 and June 2023. The inclusion criteria were as follows: (1) patients conforming to the diagnostic criteria for IPN; (2) those with complete clinical data; (3) aged between 18 and 80 years. The exclusion criteria were as follows: (1) acute exacerbation of chronic pancreatitis; (2) complications with severe systemic disease; (3) coexistence of immunosuppressive factors, such as immunosuppressants or acquired immune deficiency syndrome.

Procedures

In our center, the selection of appropriate surgical methods involves considering doctors' opinions, evidence-based medicine, and patients' preferences. For IPN patients, surgical intervention is preferably performed after 4 weeks.[14] Conversely, PCD is administered to patients with infected or symptomatic necrotic collections during the early period.[7] The step-up approach is primarily applicable to patients with the following characteristics: (1) for walled-off necrosis (WON) with poor liquefaction, PCD allows for egress of necrosis and alleviation of infection symptoms; (2) for WON with great liquefaction and maturity, PCD alone has the potential to cure IPN patients; (3) the puncture route is feasible and safe under ultrasound guidance. In contrast, patients with the following characteristics receive the step-jump therapy: (1) presence of a large amount of dry necrotic tissue, insufficient liquefaction, and no significant relief after conservative treatment or PCD; (2) delays in treatment due to multiple referrals after failing to receive standardized step-up treatment in base hospitals; (3) patients' preference for surgery to achieve definite and one-time removal of lesions.

All procedures were performed by three experienced pancreatic surgeons who had completed at least 50 laparoscopic or open pancreatic necrosectomy surgeries. The step-up approach is the most common modality for the treatment of IPN following PCD→MIN→OPN. The preferred path for PCD (step-1) is either the median or retroperitoneal approach under the guidance of ultrasound.[15] Clinical improvement was defined as resolution of SIRS/sepsis, or resolution of one or more organ failures in patients without SIRS/sepsis and >25% decrease in the size of the necrotic collection on CT 72 h after intervention. Deterioration of these parameters by other infectious causes was excluded.[16] Clinical failure was defined as the absence of clinical improvement or clinical deterioration.[16] Therefore, if clinical failure occurred 72 h after PCD, a CT scan would be made to assess the drain's position and any additional possible collections. If the drain was correctly positioned and no additional collections were found, the patient proceeded to the next step.[17] MIN (step-2), such as laparoscopic pancreatic necrosectomy (LPN), minimal access lesser omentum sac pancreatic necrosectomy (MALOSPN), minimal access retroperitoneal pancreatic necrosectomy (MARPN) or videoscopic assisted retroperitoneal debridement (VARD), would then be considered. PCD is preferred if residual infection occurs within the abdominal cavity, even after MIN. Finally, if there was clinical failure even after MIN or any life-threatening complications suddenly occurred, OPN (step-3) would be used as the last rescue measure in the step-up approach.

The step-jump approach represents an upgrade from the traditional step-up approach and is implemented in two situations: (1) patients undergo MIN directly, bypassing PCD; (2) patients initially undergo PCD followed by direct transition to OPN as the final strategy because of the poor efficacy of PCD. In addition, the type of intervention approach and choice of incision depend on the exact distribution of pancreatic necrosis on CT scans or the former path of the PCD.

After surgical debridement of the necrotic tissue, dual-modality drains were left in the cavity to allow egress of necrosis and fluid, as well as for irrigation or flushing. All patients underwent contrast-enhanced CT within 48 h after admission to determine the location and extent of necrosis and to calculate the modified computed tomography severity index (MCTSI). Lactic acid concentration was evaluated using arterial blood gas analysis within 24 h of admission to our hospital. The detailed treatment strategies are presented in Figure 1.

Classification of Infected Pancreatic Necrosis

Based on years of practice, the clinical experience of our medical center, and the classification system introduced by Baroud et al,[18,19] we developed a new system that classifies IPNs into four types according to necrotic tissue collection sites on CT. (1) Type I (central type): necrotic tissue is limited to the lesser omental sac and its surrounding spaces. (2) Type II (peripheral type): necrotic tissue is limited to the bilateral renal colon and pelvic areas. Three subtypes are derived from this type according to the infection site: IIa, IIb, and IIc. In type IIa and IIb patients, necrotic tissue is localized to the left and right kidney-colon spaces, respectively. In type IIc patients, necrotic tissue is limited to the pelvic–rectal region. (3) Type III (mixed type): necrotic tissue often spreads through various pathways and gaps in the abdominal cavity, leading to widespread infection and necrosis, which can be regarded as the coexistence of type I and type II lesions; the central and peripheral infection foci may be interconnected. (4) Type IV (isolated type): the necrotic tissue is limited to the middle part of the anterior pararenal space, retroperitoneal cavity, and upper segment of the

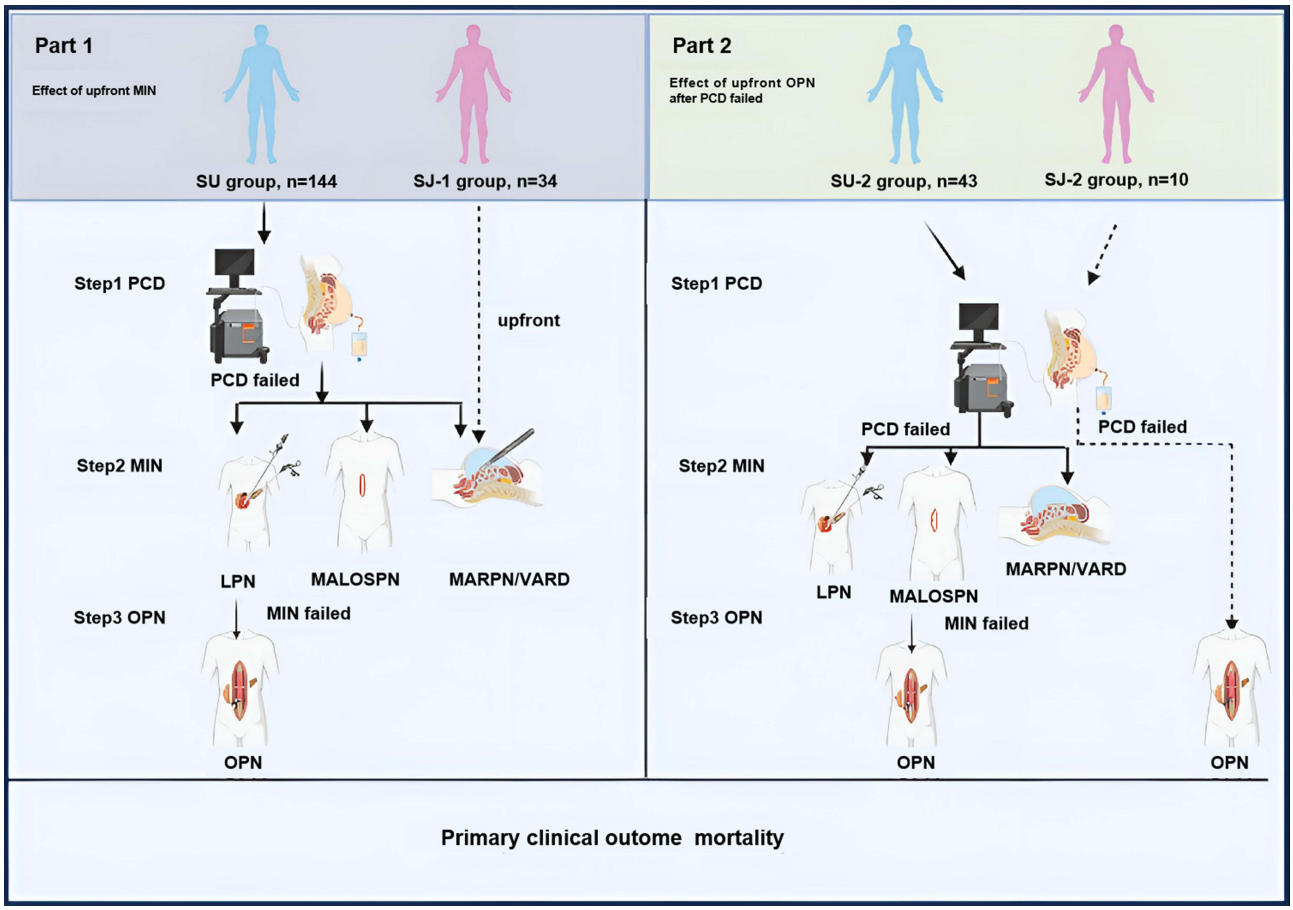

Figure 1 Treatment flowcharts for patients in the step-up (SU) and step-jump (SJ) groups This study comprises two main parts. According to the treatment strategies used in our hospital, 188 patients were enrolled in this study, including 144 patients in the SU and 44 in the SJ groups. Part 1: We aimed to evaluate the effects of omitting PCD by comparing the SU and SJ-1 groups (patients in the SJ-1 group received MIN directly). Part 2: We assessed the effects of direct OPN after PCD failure. Therefore, we selected 43 patients from the SU group who underwent further treatment after PCD failure (SU-2 group). Ten patients in the SJ group received OPN directly after PCD failure and were assigned to the SJ-2 group.

mesenteric root, and the infection site is deep in isolation.[20,21] Table 1 shows the suggested intervention approaches for each type of IPN based on the classification system mentioned above.

Data Collection and Propensity Score Matching

Baseline data including demographic data, etiology, body mass index (BMI), severity, MCTSI score, Ranson score, laboratory test results, and IPN classification were collected. The data used to evaluate the clinical outcomes included in-hospital mortality, total hospital stay, cost, number of debridements, incidence of organ failure, surgical complications, positive bacterial culture results, and residual infection.

Propensity score matching (PSM) was performed to evaluate the differences in baseline variables between the SU group and SJ-1 group. After comparing the baseline data of the two groups, we found that BMI, MCTSI, percentage of neutrophils, hemoglobin level, IPN classification, and referral rate were significantly different between the two groups. Therefore, we conducted PSM to mitigate the selection bias and ensure that the data were comparable. We considered the Ranson score, MCTSI, and neutrophil percentage as predictors, setting the matching tolerance to 0.05, performing 1:1 matching, and yielding 34 pairs.

Observation Outcomes

The primary outcome of this study was in-hospital mortality rate. The secondary outcomes of this study were the occurrence of organ failure, number of patients with postoperative complications, presence of residual infection, positive bacterial culture results, number of debridements, and total length and cost of hospital stay. The relevant observables used in this study are listed in Table 2.

Statistical Analysis

The distribution of variables was examined using the Kolmogorov—Smirnov test. Continuous normally distributed variables are presented as the means ± standard deviations and were evaluated using *a t* test. Continuously skewed variables are expressed as medians with interquartile ranges, and the Mann–Whitney *U*-test was used for the difference tests. Categorical variables were compared using the chi-squared test or Fisher's exact test. A two-sided P value < 0.05 indicated a statistically significant difference. These analyses were performed using SPSS software (version 22.0; SPSS, Chicago, IL, USA).

Table 1 Locations and Suggested Intervention for Every Type of IPN

IPN type	Detailed Locations in CT Scanning	Surgical Intervention Pathways
Type I	Lesser omental sac and its peripheral space	PCD/LPN
Type II		PCD, MIAPN, VARD, LPN
Type IIa	Left kidney-colon space	
Type IIb	Right kidney-colon space	
Type IIc	Pelvic-rectal space	
Type III	Mixed type of type I and type II	Diversified types of intervention including OPN
Type IV	1. Central part of anterior pararenal space, and medium vessels-included retroperitoneal spaces (abdominal aorta and its branches, inferior vena cava) 2. Upper mesentery root 3. Adjacent to duodenum 4. Neck and head of pancreas 5. Retropancreatic and introduodenal segments of common bile duct	Diversified types of intervention including OPN

Abbreviations: IPN, Infected pancreatic necrosis; LPN, Laparoscopic pancreatic necrosectomy; MIAPN, Minimal incision access pancreatic necrosectomy; OPN, Open pancreatic necrosectomy; PCD, Percutaneous catheter drainage; VARD, Video-assisted retroperitoneal debridement.

Table 2 Definitions for Observational Indicators

Infected pancreatic necrosis	Fulfillment of either of the following two criteria: (1) extraluminal gas in the pancreatic and/or peri-pancreatic tissues on contrast-enhanced computed tomography (CECT); (2) positive bacterial or fungal culture results with fine needle aspiration (FNA) or other invasive procedures.
Respiratory failure	PaO2/FiO2 <300 or need for mechanical ventilation
Renal failure	Creatinine level is more than 177 umol/L after rehydration.
Circulatory failure	Systolic blood pressure is less than 90 mm Hg despite adequate fluid resuscitation
Organ failure	Marshall score of ≥ 2.
Multiple organ failure	Existence of at least 2 organ failure
New-onset organ failure	First onset of organ failure requiring intervention at any time in a 24-hour period
Post-operative residual infection	Presentation of residual infected necrotic tissues in the abdominal or retroperitoneal spaces after active surgical treatment, and it usually occurs 2 or 3 months after SAP.

Results

Characteristics and Treatment of IPN Patients

In total, 188 IPN patients were assessed for eligibility (Figure 2). The patients had a mean age of 44.6±13.1 years, with 117 and 71 being male and female, respectively. In terms of etiology, there were 74 cases of biliary pancreatitis, 65 cases of hyperlipidemic pancreatitis, 20 cases of alcoholic pancreatitis, and 29 cases of pancreatitis of other etiologies including traumatic pancreatitis, autoimmune pancreatitis, and other unknown etiologies. Of the 188 IPN patients, 144 and 44 were in the SU and SJ groups, respectively. Patients cured with PCD alone were assigned to the SU-1 group (n=101), while patients who received a step-up strategy after PCD failure were assigned to the SU-2 group (n=43).

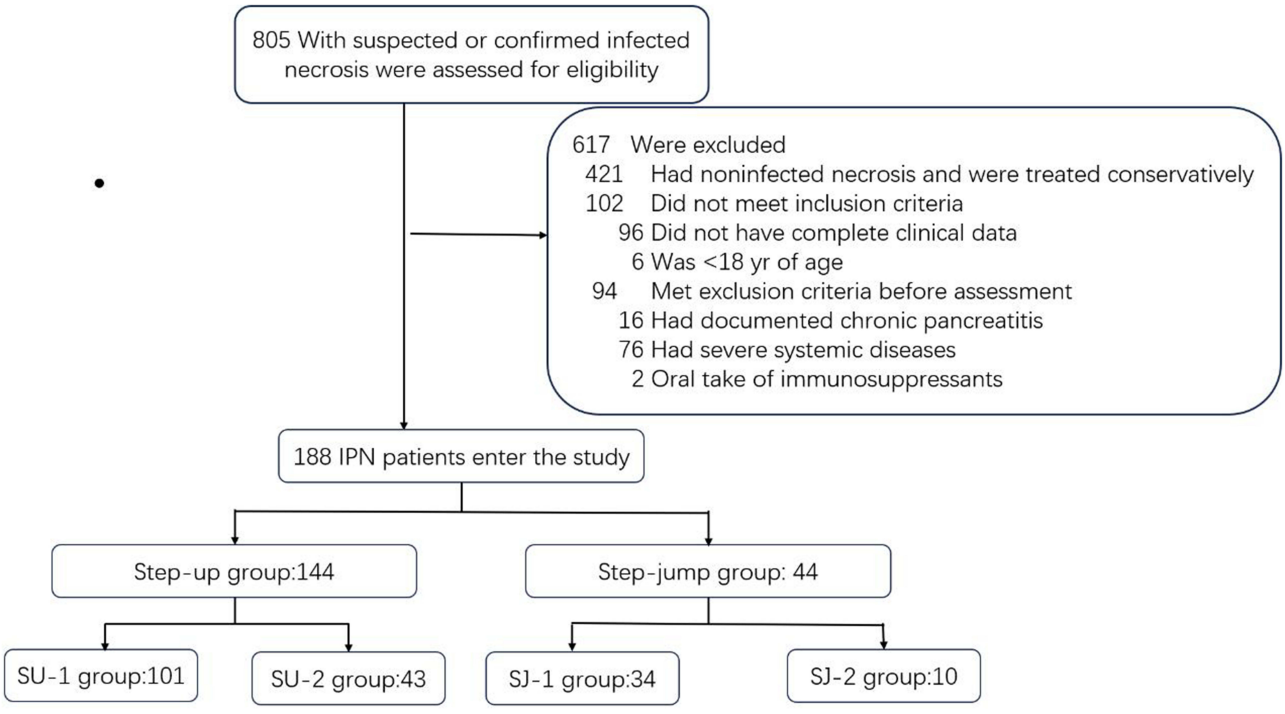

Figure 2 Flowchart for patient selection.
Abbreviations: IPN, infected pancreatic necrosis; SU, Step-up approach; SJ, Step-jump approach.

Patients treated with MIN without PCD were allocated to the SJ-1 group (n=34), while those who underwent OPN after PCD failure were allocated to the SJ-2 group (n=10).

There were no significant differences in age, sex, etiology, preoperative comorbidities, severity, Ranson score, length of ICU stay before intervention, white blood cell count, neutrophil count, albumin level, lactic acid concentration, or procalcitonin level at admission between the SJ-1 and SU groups ($P>0.05$). Before PSM, patients in the SJ-1 group had poor nutritional status and more extensive pancreatic necrosis. They exhibited lower BMI (23.3±4.5 vs 25.5±4.5, $P=0.010$), lower hemoglobin level (105.0[90.0,127.5] vs 120.0[104.0,153.0], $P=0.006$), lower percentage of neutrophil (79.5[72.0,82.2] vs 85.4[80.2,89.4], $P<0.001$), higher MCTSI scores (8[8, 10] vs 8[6, 8], $P<0.001$), elevated referral rates (76.5% [26/34] vs 51.4% [74/144], $P=0.008$), and proportion of type III IPN (85.3% [29/34] vs 54.8% [79/144], $P<0.001$) (Table 3).

Table 3 Patient Baseline Data Comparison Before PSM

Characteristics	SU Group (n=144)	SJ-1 Group (n=34)	*P value*
Age (years)	45.0±13.3	43.9±13.2	0.628
Sex [n (%)]			0.543
Male	85 (59.0)	22 (64.7)	
Female	59 (41.0)	12 (35.3)	
BMI (Kg/m^2)	25.5±4.5	23.3±4.5	0.010*
Etiology [n (%)]			0.662
Gallstones	55 (38.2)	15 (44.1)	
Hyperlipidemia	53 (36.8)	10 (29.4)	
Alcoholic	14 (9.7)	4 (11.8)	
Others	22 (15.3)	5 (14.7)	
Degree of severity [n (%)]			0.145
MSAP	62 (43.1)	10 (29.4)	
SAP	82 (56.9)	24 (70.6)	
ICU stay before intervention [n (%)]			0.226
Yes	54 (37.5)	9 (26.5)	
No	90 (62.5)	25 (73.5)	
Comorbidities [n (%)]			0.774
Hypertension	29 (20.1)	6 (17.6)	
Coronary diseases	6 (4.2)	2 (5.9)	
Diabetes	26 (18.1)	5 (14.7)	
Others	17 (11.8)	5 (14.7)	
MCTSI score	8 (6,8)	8 (8,10)	0.000*
Ranson score	2 (1,3)	2.5 (2,3.25)	0.297

(*Continued*)

Table 3 (Continued).

Characteristics	SU Group (n=144)	SJ-1 Group (n=34)	*P value*
Tertiary Referral [n (%)]			0.008
Yes	74 (51.4)	26 (76.5)	
No	70 (48.6)	8 (23.5)	
IPN classification [n (%)]			0.000*
I	24 (16.7)	2 (5.9)	
II	33 (22.9)	1 (2.9)	
III	79 (54.8)	29 (85.3)	
IV	8 (5.6)	2 (5.9)	
WBC counts ($\times 10^9$/L)	13.4±6.5	12.8±8.3	0.657
Percentage of neutrophils (%)	85.4 (80.2,89.4)	79.5 (72.0,82.2)	0.000*
Hb (g/L)	120.0 (104.0,153.0)	105.0 (90.0,127.5)	0.006*
ALB(g/L)	32.4±5.9	32.2±5.6	0.834
Neutrophil count ($\times 10^9$/L)	10.4 (7.2, 14.8)	8.1 (5.1, 12.2)	0.130
PCT (ng/mL)	0.7 (0.2,3.9)	0.4 (0.2,1.9)	0.333
Lactic acid (mmol/L)	1.5 (1.1,2.4)	1.0 (0.7, 2.4)	0.105

Note: *P<0.05.
Abbreviations: BMI, Body mass index; IPN, Infected pancreatic necrosis; MSAP, Moderate severe acute pancreatitis; SAP, Severe acute pancreatitis; MCTSI, Modified computer tomography severity index; WBC, White blood cell count; Hb, Hemoglobin; Alb, Albumin; CRP, C-reactive protein; PCT, Procalcitonin.

Regarding clinical outcomes, patients in the SJ-1 subgroup had higher hospital costs (129,573.0 [72,145.5, 184,057.2] vs 71,824.4 [42,937.8, 123,029.5], P=0.001) and longer hospital stays (31.0 [18.0, 41.5] vs 20.5 [14.0, 36.0], P=0.032). There were no differences in the number of debridements, number of positive bacterial cultures, number of multiple drug-resistant organisms (MDRO), residual infection, organ failure, surgical complications, or mortality (P>0.05). (Table 4)

In the SU group, 101 patients were treated successfully with PCD (SU-1 group), while 43 (29.9%) patients underwent MIN or OPN due to PCD failure (SU-2 group), including 26 patients with LPN; two, MALOSPN; six, MARPN; one, VARD; and eight, OPN. In the SJ group, 26 patients underwent LPN; six, MALOSPN+MARPN; and two, VARD directly without undergoing PCD. Ten patients (22.7%) underwent OPN as the final rescue treatment after PCD failure.

Clinical Outcomes for IPN Patients After PSM

After PSM, 34 pairs of patients were included in the study, and the baseline variables of the two patient groups were comparable (Table 5). The mortality rates between the two groups were not statistically different (0% [0/34] vs 8.8% [3/34], P=0.239). Regarding secondary outcomes, there were no significant differences in the total hospital stay, incidence of organ failure, number of debridements, and residual infection (P>0.05). Patients in the SJ-1 group had higher costs before PSM; however, these differences were no longer evident after PSM (129,573.0 [72,145.5,184,057.2] vs 90,565.5 [49,336.8, 178,133.7], P=0.280). The MDRO rate was lower in the SJ-1 group (35.3% [12/34] vs 61.8% [21/34], P=0.029). Furthermore, the incidence of surgical complications in the SJ-1 group was lower, especially for new-onset organ failure, gastrointestinal fistula, gastrointestinal bleeding, and venous thrombosis (0% [0/34] vs 5.9% [2/34]; 0% [0/34] vs 11.8% [4/34]; 2.9% [1/34] vs 5.9% [2/34]; 0% [0/34] vs 2.9% [1/34], P<0.001) (Table 6).

Table 4 Patient Clinical Outcomes Before PSM

Characteristics	SU group (n=144)	SJ-1 group (n=34)	*P value*
Mortality	12 (8.3)	0 (0)	0.081
Total hospital stay (days)	20.5 (14.0,36.0)	31.0 (18.0,41.5)	0.032*
Total hospital cost (yuan)	71,824.4 (42,937.8,123,029.5)	129,573.0 (72,145.5,184,057.2)	0.001*
Organ failure [n (%)]			0.529
Respiratory failure	4 (2.8)	0 (0)	
Renal failure	5 (3.5)	0 (0)	
Circulatory failure	9 (6.3)	3 (8.8)	
MOF	2 (1.4)	0 (0)	
Positive bacterial culture [n (%)]			0.071
Blood drainage	30 (20.8)	7 (20.6)	
Catheter-drainage infection	92 (63.9)	24 (70.6)	
MDRO [n (%)]			0.386
Yes	40 (27.8)	12 (35.3)	
No	104 (72.2)	22 (64.7)	
Numbers of debridement [n (%)]			0.298
Once	32 (22.2)	28 (82.4)	
Twice or more	11 (7.6)	6 (17.6)	
Residual infection [n (%)]			0.077
Yes	41 (28.5)	15 (44.1)	
No	103 (71.5)	19 (55.9)	
Surgical complication [n (%)]			0.160
Intraabdominal hemorrhage	7 (4.9)	3 (8.8)	
New-onset organ failure	11 (7.6)	0 (0)	
Gastrointestinal bleeding	3 (2.1)	1 (2.9)	
Gastrointestinal fistula	6 (4.2)	0 (0)	
Venous thrombosis	2 (1.4)	0 (0)	

Note: *$P<0.05$.
Abbreviations: ICU, Intensive care unit; MDRO, Multiple drug resistant organism; MOF, Multiple organ failure; PSM, propensity score match.

Effect of the Step-Jump Approach in Patients with PCD Failure

Owing to the widespread acceptance of the step-up strategy and the lack of consensus or guidelines for direct minimally invasive interventions, PCD is often used as the first step in IPN intervention in clinical practice. However, PCD may fail to control the progression of infection symptoms, leading to the gradual deterioration of clinical symptoms in specific patients. Therefore, it is crucial to adopt timely and effective strategies to prevent PCD failure. To assess the effects of the step-jump approach in patients with PCD failure, we categorized the SU-2 group and SJ-2 groups for new data collection

Table 5 Patient Baseline Data Comparison After PSM

Characteristics	SU group (n=34)	SJ-1 group (n=34)	*P value*
Age (years)	44.7±13.0	43.9±13.2	0.803
Sex [n (%)]			0.618
Male	20 (58.8)	22 (64.7)	
Female	14 (41.2)	12 (35.3	
BMI (Kg/m^2)	24.7±3.3	23.3±4.5	0.135
Etiology [n (%)]			0.503
Gallstones	15 (44.1)	15 (44.1)	
Hyperlipidemia	14 (41.2)	10 (29.4)	
Alcoholic	1 (2.9)	4 (11.8)	
Others	4 (11.8)	5 (14.7)	
Degree of severity [n (%)]			0.582
MSAP	8 (23.5)	10 (29.4)	
SAP	26 (76.5)	24 (70.6)	
ICU stay before intervention [n (%)]			0.078
Yes	16 (47.1)	9 (26.5)	
No	18 (53.0)	25 (73.5)	
Comorbidities [n (%)]			0.147
Hypertension	9 (26.5)	6 (17.6)	
Coronary diseases	3 (8.8)	2 (5.9)	
Diabetes	10 (29.4)	5 (14.7)	
Others	3 (8.8)	5 (14.7)	
MCTSI score	8 (8,10)	8 (8,10)	0.694
Ranson score	1 (1,3)	2.5(2,3.25)	0.072
Tertiary Referral [n (%)]			0.189
Yes	21 (59.1)	26 (76.5)	
No	13 (40.9)	8 (23.5)	
IPN classification [n (%)]			0.082
I	2 (5.9)	2 (5.9)	
II	4 (11.8)	1 (2.9)	
III	27 (79.4)	29 (85.3)	
IV	1 (2.9)	2 (5.9)	
WBC counts (×109/L)	13.4±5.5	12.8±8.3	0.740
Percentage of neutrophils (%)	86.8 (80.4,89.6)	79.5(72.0,82.2)	0.115

(*Continued*)

Table 5 (Continued).

Characteristics	SU group (n=34)	SJ-1 group (n=34)	*P value*
Hb (g/L)	115.5 (102.5,153.0)	105.0(90.0,127.5)	0.134
ALB(g/L)	31.2±6.3	32.2±5.6	0.485
Neutrophil count (×109/L)	9.8 (7.6, 16.0)	8.1 (5.1, 12.2)	0.181
PCT (ng/mL)	0.7 (0.3,6.1)	0.4 (0.2,1.9)	0.120
Lactic acid (mmol/L)	1.5 (1.1,2.2)	1.0 (0.7,2.4)	0.216

Abbreviations: BMI, Body mass index; IPN, Infected pancreatic necrosis; MSAP, Moderate severe acute pancreatitis; SAP, Severe acute pancreatitis; MCTSI, Modified computer tomography severity index; WBC, White blood cell count; Hb, Hemoglobin; Alb, Albumin; CRP, C-reactive protein; PCT, Procalcitonin.

Table 6 Patient Clinical Outcomes After PSM

Characteristics	SU group (n=34)	SJ-1 group (n=34)	*P value*
Mortality	3 (8.8)	0 (0)	0.239
Total hospital stay (days)	21.5 (15.8,45.8)	31.0 (18.0,41.5)	0.361
Total hospital cost (yuan)	90,565.5 (49,336.8,178,133.7)	129,573.0 (72,145.5,184,057.2)	0.280
Organ failure [n (%)]			0.474
Respiratory failure	1 (2.9)	0 (0)	
Renal failure	0 (0)	0 (0)	
Circulatory failure	5 (14.7)	3(8.8)	
MOF	1 (2.9)	0 (0)	
Positive bacterial culture [n (%)]			0.170
Blood drainage	10 (29.4)	7 (20.6)	
Catheter-drainage infection	21 (61.8)	24 (70.6)	
MDRO [n (%)]			0.029*
Yes	21 (61.8)	12 (35.3)	
No	13(38.2)	22 (64.7)	
Numbers of debridement [n (%)]			0.283
Once	31 (91.2)	28 (82.4)	
Twice or more	3 (8.8)	6 (17.6)	
Residual infection [n (%)]			0.209
Yes	10 (29.4)	15 (44.1)	
No	24 (70.6)	19 (55.9)	

(*Continued*)

Table 6 (Continued).

Characteristics	SU group (n=34)	SJ-1 group (n=34)	*P value*
Surgical complication [n (%)]			0.000*
Intraabdominal hemorrhage	2 (5.9)	3 (8.8)	
New-onset organ failure	2 (5.9)	0 (0)	
Gastrointestinal bleeding	2 (5.9)	1 (2.9)	
Gastrointestinal fistula	4 (11.8)	0 (0)	
Venous thrombosis	1 (2.9)	0 (0)	

Note: *$P<0.05$.
Abbreviations: ICU, Intensive care unit; MDRO, Multiple drug resistant organism; MOF, Multiple organ failure; PSM, Propensity score match.

methods. A total of 53 patients were included in this study: 43 in the SU-2 group and 10 in the SJ-2 group. No significant differences were observed between the baseline data of the two groups (Table 7). The clinical mortality rates were similar between the two groups (20.0% [2/10] vs 14.0% [6/43], $P=0.636$). In terms of secondary clinical outcomes, the overall incidence of surgical complications was lower in the SJ-2 subgroup ($P=0.012$), especially new-onset organ failure (0% [0/10] vs 7.0% [3/43]), gastrointestinal fistula (10.0% [1/10] vs 11.6% [5/43]), and venous thrombosis (0% [0/13] vs 2.3% [1/43]) (Table 8). In addition, the MDRO infection rate was lower in the SJ-2 subgroup (20.0% [2/10] vs 41.9% [18/43], $P<0.001$).

Table 7 Baseline Data Comparison of SU-2 and SJ-2 Group

Characteristics	SU-2 group (n=43)	SJ-2 group (n=10)	*P value*
Age (years)	42.9±12.4	39.6±9.5	0.425
Sex [n (%)]			0.096
Male	30 (69.8)	10 (100.0)	
Female	13 (30.2)	0 (0)	
BMI (Kg/m^{2l})	25.6±5.1	25.3±3.6	0.850
Etiology [n (%)]			0.115
Gallstones	15 (34.9)	4(40.0)	
Hyperlipidemia	15(34.9)	2(20.0)	
Alcoholic	6(13.9)	2(20.0)	
Others	7 (16.3)	2(20.0)	
Degree of severity [n (%)]			0.778
MSAP	7 (16.3)	2 (20.0)	
SAP	36 (83.7)	8 (80.0)	

(*Continued*)

Table 7 (Continued).

Characteristics	SU-2 group (n=43)	SJ-2 group (n=10)	*P value*
ICU stay before intervention [n (%)]			0.722
Yes	18 (41.9)	3 (30.0)	
No	25 (58.1)	7 (70.0)	
Comorbidities [n (%)]			0.845
Hypertension	1 (2.3)	1 (10.0)	
Coronary diseases	1 (2.3)	1 (10.0)	
Diabetes	1 (2.3)	1 (10.0)	
Others	3 (7.0)	2 (20.0)	
MCTSI score	8(8,10)	9(7.5,10)	0.623
Ranson score	2 (1,3)	2.5(2,4)	0.635
Tertiary Referral [n (%)]			0.494
Yes	24 (55.8)	7 (70.0)	
No	19 (44.2)	3 (30.0)	
IPN classification [n (%)]			0.080
I	6(14.0)	2(20.0)	
II	2(4.7)	0(0)	
III	28(65.1)	6(60.0)	
IV	7(16.3)	2(20.0)	
WBC counts ($\times 10^9$/L)	11.6(8.6,18.5)	13.4(8.3,19.5)	0.829
Percentage of neutrophils (%)	82.0±7.3	84.3±8.8	0.397
Hb (g/L)	108.0(92.0,136.0)	98.0(83.0,132.5)	0.532
ALB(g/L)	31.7±6.1	33.9±6.1	0.323
Neutrophil count ($\times 10^9$/L)	9.8 (6.8, 16.7)	11.7 (6.8, 16.3)	0.874
PCT (ng/mL)	0.4(0.2,1.4)	0.7(0.4,3.6)	0.814
Lactic acid(mmol/L)	2.0±0.8	1.6±0.5	0.526

Abbreviations: BMI, Body mass index; IPN, Infected pancreatic necrosis; MSAP, Moderate severe acute pancreatitis; SAP, Severe acute pancreatitis; MCTSI, Modified computer tomography severity index; WBC, White blood cell count; Hb, Hemoglobin; Alb, Albumin; CRP, C-reactive protein; PCT, Procalcitonin.

Discussion

The treatment paradigm for IPN has dramatically evolved from the traditional open necrosectomy to the step-up approach, which consists of a sequence of minimally invasive procedures. However, owing to the poor nutritional status of some patients, rapid increases in abdominal pressure, and delayed treatment in grassroots hospitals, their condition can rapidly deteriorate. Immediate and effective intervention is necessary to promptly clear the lesion, drain pus, and alleviate systemic sepsis and cachexia.[13,22] Therefore, Miao proposed the step-jump approach for specific cases of IPN.[11] Our study revealed that the step-jump approach is safer and more effective than the step-up approach. For IPN patients who

Table 8 Clinical Outcomes Comparison for SU-2 and SJ-2 Group

Characteristics	SU-2 group (n=43)	SJ-2 group (n=10)	*P value*
Mortality	6 (14.0)	2 (20.0)	0.636
Total hospital stay (days)	49.0(31.0,67.0)	41.0 (23.5,69.0)	0.562
Total hospital cost (yuan)	126,882.0 (88,411.0,285,300.0)	147,319.1 (96,207.8,379,721.5)	0.413
Organ failure [n (%)]			0.799
Respiratory failure	4 (9.3)	1 (10.0)	
Renal failure	4 (9.3)	1 (10.0)	
Circulatory failure	8 (18.6)	2 (20.0)	
MOF	2 (4.7)	1 (10.0)	
Positive bacterial culture [n (%)]			0.583
Blood drainage	11 (25.6)	3 (30.0)	
Catheter-drainage infection	37 (86.0)	8 (80.0)	
MDRO [n (%)]			0.000*
Yes	18 (41.9)	2 (20.0)	
No	25 (58.1)	8 (80.0)	
Numbers of debridement [n (%)]			0.442
Once	11(25.6)	4 (40.0)	
Twice or more	32 (74.4)	6 (60.0)	
Residual infection [n (%)]			0.455
Yes	29 (67.4)	5 (50.0)	
No	14 (32.6)	5 (50.0)	
Surgical complication [n (%)]			0.012*
Intraabdominal hemorrhage	6 (14.0)	2 (20.0)	
New-onset organ failure	3 (7.0)	0(0)	
Gastrointestinal bleeding	0 (0)	0 (0)	
Gastrointestinal fistula	5(11.6)	1 (10.0)	
Venous thrombosis	1 (2.3)	0 (0)	

Note: *$P<0.05$.
Abbreviations: ICU, Intensive care unit; MDRO, Multiple drug resistant organism; MOF, Multiple organ failure; PSM, Propensity score match.

directly underwent MIN without PCD and those who directly underwent OPN after PCD failure, the step-jump approach showed a great advantage in reducing the incidence of MDRO and surgical complications.

The step-jump approach has certain advantages over the step-up approach in terms of reducing the MDRO rate. MDROs are often induced by prolonged hospitalization, excessive antibiotic use, and iterative interventions.[23] The aim of the step-jump approach is to minimize the number of interventions required to reduce the length of hospital stay and hospitalization costs, which can simultaneously reduce the MDRO rate. Wu et al reported that severe AP and multidrug-resistant

Pseudomonas aeruginosa infections were both independent risk factors for mortality.[24] Another study showed that MDR-*Klebsiella pneumoniae* infection was a strong predictor of mortality in AP patients complicated with septic shock.[25] According to our statistics, MDR-*Klebsiella pneumoniae* was the most common pathogen in our center. In addition, several original studies have shown that high levels of CRP, PCT, and neutrophils are predictors of poor prognosis and susceptibility to infection.[26–29] However, none of the above indices were significantly elevated in the SJ group. This could be explained by the fact that these patients crossed the peak of inflammation at the early stage, but the scope of inflammation and necrosis continued to expand, which could partly explain the greater MCTSI in the SJ group.

As mentioned by Cao et al[30,31] and Han et al[32] the "one-step" approach can dramatically shorten the median length of hospital stay compared with step-up laparoscopic-assisted necrosectomy. Additionally, Bang et al reported that upfront endoscopic necrosectomy offers greater advantages over the step-up approach, significantly improving overall patient status and reducing the number of interventions required.[33] However, our results showed that total hospital stay and cost were similar between the two groups. This could be attributed to the fact that many patients in the SJ group were transferred to our center after prolonged infection and multiple interventions at primary hospitals, making them more susceptible to any surgical intervention. In addition, these patients spent more time waiting for PCD to take effect, which partly explains the lack of disparity.

For patients who have experienced PCD failure, direct OPN administration may also lead to the desired outcomes. A retrospective analysis conducted in Finland showed that these indications were associated with mortality. The mortality risk could be greater for patients who do not show clinical improvement despite aggressive treatment.[34] This suggests that patients requiring open surgery were critically ill, with minimal response to MIN. In this context, the decision to perform open surgery should be viewed as an indicator of poor prognosis, rather than the surgery itself being a factor. It is inappropriate to include critically ill patients in the SJ group and compare them directly with the SU group. Therefore, we divided the SJ group into SJ-1 and SJ-2 groups. Cao et al proposed a "one-step" strategy which involves upfront omission of PCD with immediate MIN.[30] Hence, we utilized PSM to compare the outcomes of omitting PCD by comparing the SU group with the SJ-1 group. Subsequently, we conducted a statistical analysis of patients who experienced PCD failure to investigate improved intervention strategies after PCD failure. The new data collection included patient data from the SU-2 and SJ-2 groups to ensure better comparability between the two groups. Patients who do not respond to PCD or MIN may benefit from OPN.

Another pressing issue that requires immediately attention is determining the indications for the step-jump approach. Given the significant heterogeneity of IPN and varying treatment strategies employed at local medical centers, conducting a prospective clinical trial is nearly unfeasible. Several studies have attempted to identify the factors contributing to the failure of the step-up approach. Hollesmans et al reported that multiple organ failure, male sex, an increasing percentage of pancreatic necrosis, and heterogeneity of necrotic tissue collection are negative predictors of successful catheter drainage in IPN patients.[35] Recently, Li et al reported that early spontaneous bleeding, fungal infection, an APACHE II score of 16 points or more, and other factors were found to be independent risk factors for failure of the minimally invasive step-up approach.[36] Similarly, Huang et al developed a risk score model integrating organ failure, percentage of pancreatic necrosis, extrapancreatic necrosis volume, and mean CT density of extrapancreatic necrosis volume to predict patients with greater opportunity for necrosectomy.[37]

Combining the experience of our medical center with those of previous studies,[35,38] we speculate that the step-up approach may be ineffective in several scenarios: (1) There is extensive dry necrotic tissue with inadequate liquefaction, and conservative treatment or PCD does not provide significant relief. (2) The lesion is located deep within the body, lacking suitable intervention pathways, or is adjacent to critical blood vessels and organs, such as in type IV IPNs. (3) Delays in treatment owing to failure to receive standardized step-up approach treatment in primary hospitals, resulting in progression of the condition through multiple referrals. Therefore, a multidisciplinary team comprising gastroenterologists, intensive care physicians, surgeons, radiologists, and endoscopists is essential. This team can develop individualized and integrated therapies for each patient based on comprehensive assessments, including laboratory tests and imaging studies.

The main limitations of this study are as follows: (1) this was a single-center retrospective analysis, where selection bias could only be reduced, not eliminated, even after PSM; (2) owing to the high outpatient referral rate, medical records from their first admission to local hospitals was often unavailable; (3) endoscopic transluminal necrosectomy was not routinely carried out at our center; and (4) the number of patients in both groups after PSM was relatively small (n=34).

Conclusions

The step-jump approach is safer and more effective than the step-up approach. Upfront MIN is recommended for patients with a high probability of PCD failure. For patients with PCD failure, direct OPN instead of MIN may lead to the desired outcomes.

Abbreviations

AP, Acute pancreatitis; BMI, Body mass index; CT, Computed tomography; IPN, Infected pancreatic necrosis; LPN, Laparoscopic pancreatic necrosectomy; MALOSPN, Minimal access lesser omentum sac pancreatic necrosectomy; MARPN, Minimal access retroperitoneal pancreatic necrosectomy; MCTSI, Modified computed tomography severity index; MDRO, Multiple drug-resistant organism; MIN, Minimally invasive necrosectomy; OPN, Open pancreatic necrosectomy; PCD, Percutaneous catheter drainage; PSM, Propensity score match; SJ, Step-jump; SU, Step-up; VARD, Videoscopic assisted retroperitoneal debridement.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Ethical Review Committee of the First Affiliated Hospital of Harbin Medical University (No. 2021GS21). This research conforms to the Declaration of Helsinki. Written informed consent was waived due to the retrospective nature of this study. To ensure the confidentiality of patient data, all personal identifiers have been anonymized from the dataset.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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