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Influencing factor analysis and clinical efficacy of early intervention in severe acute pancreatitis with persistent organ failure

Minchun Bu[1,2,6], Yun Zhang[1,3,6], Xiaochun Xie[4,6], Kaiming Li[5], Gang Li[2]✉, Zhihui Tong[2] & Weiqin Li[1,2]✉

This study aims to analyze the risk factors requiring early intervention in severe acute pancreatitis (SAP) patients with persistent organ failure and evaluate the clinical outcomes following treatment. This was a retrospective observational study. Inverse probability treatment weighting using propensity score methods was employed to balance baseline characteristics. Univariate and multivariate logistic regression analyses were performed to identify risk factors associated with early intervention. Smooth curve fitting was applied to explore potential relationships between variables and intervention timing. Threshold effect analysis was conducted to identify the optimal inflection point in nonlinear relationship. A total of 310 patients were included in this study. Compared to the standard treatment group (n = 162), the early intervention group (n = 148) had a higher proportion of multiple organ failure (77.1% vs. 63.6%, *P* = 0.021) and higher mortality (27.7% vs. 16.0%, *P* = 0.013), but early intervention was not significantly associated with adverse outcome (OR 1.52, 95% CI 0.71–3.26, *P* = 0.283). Risk factors associated with early intervention included computed tomography severity index, SOFA score, intra-abdominal pressure (IAP), and remifentanil equivalents. Among these, the SOFA score showed a negative linear relationship with intervention timing, while distinct threshold effects were observed between IAP, remifentanil equivalents, and intervention timing. One week after intervention, most patients showed improved organ function, along with reduced requirements for sedation and analgesia, as well as decreased C-reactive protein level levels and IAP (all *P* < 0.05). SAP patients requiring early intervention tended to have higher disease severity. Although early intervention can improve short-term organ function, reduce IAP, and lower analgesic requirements, its impact on reducing mortality remains uncertain.

Keywords Severe acute pancreatitis, Organ failure, Acute necrotic collection, Early intervention, Retrospective study

Abbreviations

ANC	Acute necrotic collection
CI	Confidence interva
CRP	C-reactive protein
CTSI	CT severity index
IAP	Intra-abdominal pressure
LRT	Likelihood ratio test

[1]Medical College of Yangzhou University, Yangzhou 225000, Jiangsu Province, People's Republic of China. [2]Department of Critical Care Medicine, Center of Severe Acute Pancreatitis (CSAP), Jinling Hospital, Medical School of Nanjing University, No. 305 Zhongshan East Road, Nanjing 210000, Jiangsu Province, People's Republic of China. [3]The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou, Jiangsu, China. [4]Department of Critical Care Medicine, Nanjing Drum Tower Hospital, Nanjing, Jiangsu, China. [5]Jinling Clinical Medical College, Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China. [6]Minchun Bu, Yun Zhang and Xiaochun Xie contributed equally to this work. ✉email: nju8icu@126.com; ctgchina@medbit.cn

IPTW	Inverse probability of treatment weighting
IPN	Infected pancreatic necrosis
MOF	Multiple organ failure
MODS	Multi-organ dysfunction syndrome
OF	Organ failure
OR	Odds ratio
POF	Persistent organ failure
PCD	Percutaneous catheter drainage
RCT	Randomized controlled trial
SAP	Severe acute pancreatitis
SOFA	Sequential Organ Failure Assessment

Severe acute pancreatitis (SAP) is one of the most critical illnesses in the digestive system[1]. Globally, its incidence varies depending on regional and population factors, but it has generally exhibited an increasing trend in recent years[1,2]. Pathologically, SAP is characterized by pancreatic hemorrhage and necrosis, which often trigger systemic inflammatory response syndrome and multiple organ failure (MOF)[3,4]. If organ failure (OF) persists without remission, mortality rates can exceed 30%[3]; therefore, early and accurate assessment of disease severity, coupled with prompt and effective interventions, is pivotal in the comprehensive management of SAP.

Pancreatic necrosis in SAP primarily results from enzymatic autodigestion of pancreatic tissue and microcirculatory disturbances[3]. Morphologically, it manifests as an accumulation of inactive necrotic tissues, which may include pancreatic parenchyma, peripancreatic tissues, exudates, and inflammatory cells[5,6]. Within the first 4 weeks of disease onset, this condition is termed acute necrotic collection (ANC)[6]. Previous basic studies have demonstrated that pancreatic tissue damage in early SAP activates both the immune system and pro-inflammatory responses. Concurrently, the systemic release of inflammatory mediators (e.g., cytokines and chemokines) contributes to remote organ injury and dysfunction via circulatory dissemination[2,7,8]. Furthermore, clinical evidence indicates that the incidence of OF in SAP patients with ANC exceeds 30%[9–11].

Current guidelines recommend invasive intervention for ANC when infection is confirmed, while advocating for delayed intervention until necrosis liquefaction and encapsulation (typically ≥ 4 weeks post-onset) to avoid the early-stage hyper-inflammatory state in SAP and reduce post-procedural complications[5,6]. Although some studies also suggest that early ANC intervention may be considered in patients with persistent organ failure (POF) unresponsive to conservative therapy, potentially indicating occult early-stage infection, optimal timing continues to be debated[6,12].

A single pilot study found that early intervention in SAP patients with POF may improve organ function and reduce mortality[13]. Therefore, this study aimed to summarize the clinical characteristics of SAP patients with POF and ANC, explore the potential relationship between some key indicators and the timing of intervention, as well as the specific effect of different intervention timing on OF and clinical outcomes.

Materials and methods

Study population

The study retrospectively analyzed the clinical database of the Severe Acute Pancreatitis Treatment Center at Jinling Hospital, encompassing patients consecutively admitted from January 2015 to December 2022. All patients underwent contrast-enhanced computed tomography scans to confirm the diagnosis of ANC and evaluate the CT severity index (CTSI)[5,6]. Percutaneous catheter drainage (PCD) is the initial step of the "step-up" treatment strategy for ANC recommended by the guidelines[12]. The primary indications for intervention included: suspected or confirmed infected pancreatic necrosis (IPN), gastric outlet obstruction, intra-abdominal hemorrhage, disconnected pancreatic duct syndrome, etc.[6,12,13]. Based on the treatment approach, patients were further categorized into the standard treatment group (receiving conservative treatment or undergoing PCD after 4 weeks of disease onset as needed) and the early intervention group (undergoing PCD within 4 weeks of disease onset).

Inclusion criteria were as follows: (1) meeting the revised Atlanta classification criteria for acute pancreatitis[14]; (2) presence of pancreatic or peripancreatic necrosis; (3) admission within 14 days of disease onset; (4) presence of POF at day 14 post-onset or prior to intervention; (5) age 18–75 years.

Exclusion criteria included: (1) history of malignancies, immunosuppressant use, or significant comorbidities (including New York Heart Association class III/IV heart failure, active myocardial ischemia, history of cirrhosis, chronic kidney disease stage ≥ 3, or chronic obstructive pulmonary disease requiring home oxygen therapy); (2) acute pancreatitis during pregnancy, recurrent acute pancreatitis, or chronic pancreatitis; (3) underwent debridement of pancreatic necrotic tissue before admission; (4) incomplete clinical data.

The study protocol was approved by the Ethics Committee of Jinling Hospital (Approval No.: 2019-JLAPDMC-011) and conducted in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Organ function assessment

To accurately assess organ function, the Sequential Organ Failure Assessment (SOFA) scoring system[15] was adopted in this study. According to this system, a single organ function score of ≥ 2 was defined as OF, while failure of two or more organ systems is defined as MOF. OF lasting for ≥ 48 h was termed POF.

The assessment of neurological function was conducted using theGlasgow Coma Scale[16]. However, the subjective nature of this scale, particularly under sedation and analgesia, poses significant challenges. To address this limitation, the current study meticulously documented the dosages of sedative and analgesic agents required to achieve target sedation levels, serving as a supplementary objective measure to enhance the reliability of

neurological function assessment. Analgesic assessment was conducted by calculating the daily cumulative dose of analgesic drugs and converting it to remifentanil equivalent[17]. Sedation assessment involved determining whether sedative drugs were administered and the type of sedative drug used.

Abdominal organ function was a key component of the assessment. Intra-abdominal pressure (IAP), a critical indicator for evaluating gastrointestinal function, was measured via standardized protocol: patients were positioned supine with zeroing of the transducer at the mid-axillary line. 25 mL of sterile saline was instilled into the bladder via a Foley catheter. Measurements were recorded at end-expiration after a 30-s equilibration period[18].

Data collection

Since most patients underwent intervention after 14 days of disease onset, laboratory indicators and organ function assessments were based on data collected on day 14 post-onset. For patients who received interventions within 14 days of onset, data were extracted from the day preceding the intervention.

To further explore the effect of different intervention timing on organ function and clinical indicators from a temporal perspective, this study analyzed changes in IAP, C-reactive protein (CRP) levels, SOFA scores, and remifentanil equivalents at three post-intervention intervals (days 1, 3, and 7). The change values were defined as the differences between the indicators before and after intervention, with values greater than 0 indicating improvement or alleviation compared to pre-intervention, and values less than 0 indicating worsening or aggravation.

Clinical outcomes consisted of the incidence of major complications (all classified as Grade ≥ 3 per CTCAE criteria[19]), the rate of laparotomy, total hospital length of stay, and in-hospital mortality.

Statistical analysis

Data were analyzed using SPSS software (version 27.0) and EmpowerStats software (version 4.2). The independent samples *t*-test or Mann–Whitney *U* test was used to compare continuous variables between groups. Categorical variables were analyzed with the χ^2 test or Fisher's exact test. The inverse probability of treatment weighting (IPTW) was applied using propensity score methods to balance baseline covariates between groups[20]. A logistic regression model was used to estimate propensity scores for the probability of belonging to the early intervention group based on the following independent variables: age, gender, etiology, comorbidities, and other clinical indicators with statistically significant differences. The logistic regression model was also employed to screen for variables associated with in-hospital mortality and the need for early intervention. Smooth curve fitting was first employed to explore potential non-linear relationships and identify candidate inflection points at which the trend direction or magnitude shifted. To determine the optimal inflection point, we performed a systematic grid search across the clinically relevant range of the exposure variable. For each candidate inflection point, a piecewise linear regression model was fitted. The likelihood ratio test (LRT) was used to compare the segmented model against the linear model (under the null hypothesis of no inflection point). The inflection point with the most statistically significant LRT result (lowest *p*-value) and the largest improvement in model fit (ΔAIC > 2) was then selected as optimal. All statistical tests were two-sided, and a *p*-value < 0.05 was considered statistically significant.

Results

Baseline characteristics and clinical outcomes

The flowchart of this study is shown in Fig. 1. Briefly, a total of 310 patients were included, with 148 in the early intervention group and 162 in the standard treatment group. Within the early intervention group, 15 patients underwent PCD within 14 days of symptom onset. Table 1 and Table S1 summarize the baseline demographic and clinical characteristics of the two groups before and after IPTW adjustment, while Figure S1 illustrates the differences in variable distribution before and after IPTW. The proportion of MOF was significantly higher in the early intervention group (77.1% vs. 63.6%, $P = 0.021$). Additionally, the early intervention group demonstrated higher demands for sedation and analgesia, elevated IAP, and higher CTSI (all $P < 0.05$). Regarding clinical outcomes (Table 2), the early intervention group had a higher incidence of major complications ($P < 0.001$), a longer hospital stay ($P < 0.001$), a higher proportion of laparotomy ($P = 0.044$), and increased mortality (27.7% vs. 16.0%, $P = 0.013$). Compared to patients receiving delayed intervention in the standard therapy group, the early intervention group demonstrated a significantly higher proportion of endoscopic necrosectomy and open necrosectomy (Table S2). However, no significant association was observed between early intervention and in-hospital mortality (Odds Ratio [OR] 1.52, 95% Confidence Interval [CI] 0.71 to 3.26, $P = 0.283$) (Table S3).

Heterogeneity between subgroups based on intervention timing

The early intervention group was further divided into two subgroups based on the timing of PCD relative to disease onset: one subgroup undergoing PCD within 3 weeks of symptom onset (n = 92) and the other undergoing PCD between three and 4 weeks after symptom onset (n = 56). Patients who underwent PCD within 3 weeks exhibited significantly higher SOFA score ($P < 0.001$), greater sedation requirements ($P < 0.001$), higher analgesic doses ($P = 0.002$), elevated IAP ($P < 0.001$), and increased CRP levels ($P = 0.002$). However, no significant differences were observed in CTSI or the distribution of OF between the two subgroups (Table 3). Regarding clinical outcomes, the mortality rate was significantly higher in the subgroup receiving PCD within 3 weeks (33.7% vs. 17.9%, $P = 0.037$).

Risk factors for early intervention in SAP patients with POF

Multivariable logistic regression analysis revealed that patients with higher CTSI ($P < 0.001$), elevated SOFA scores ($P < 0.001$), increased IAP ($P = 0.040$), and greater analgesic doses ($P = 0.045$) faced a significantly elevated

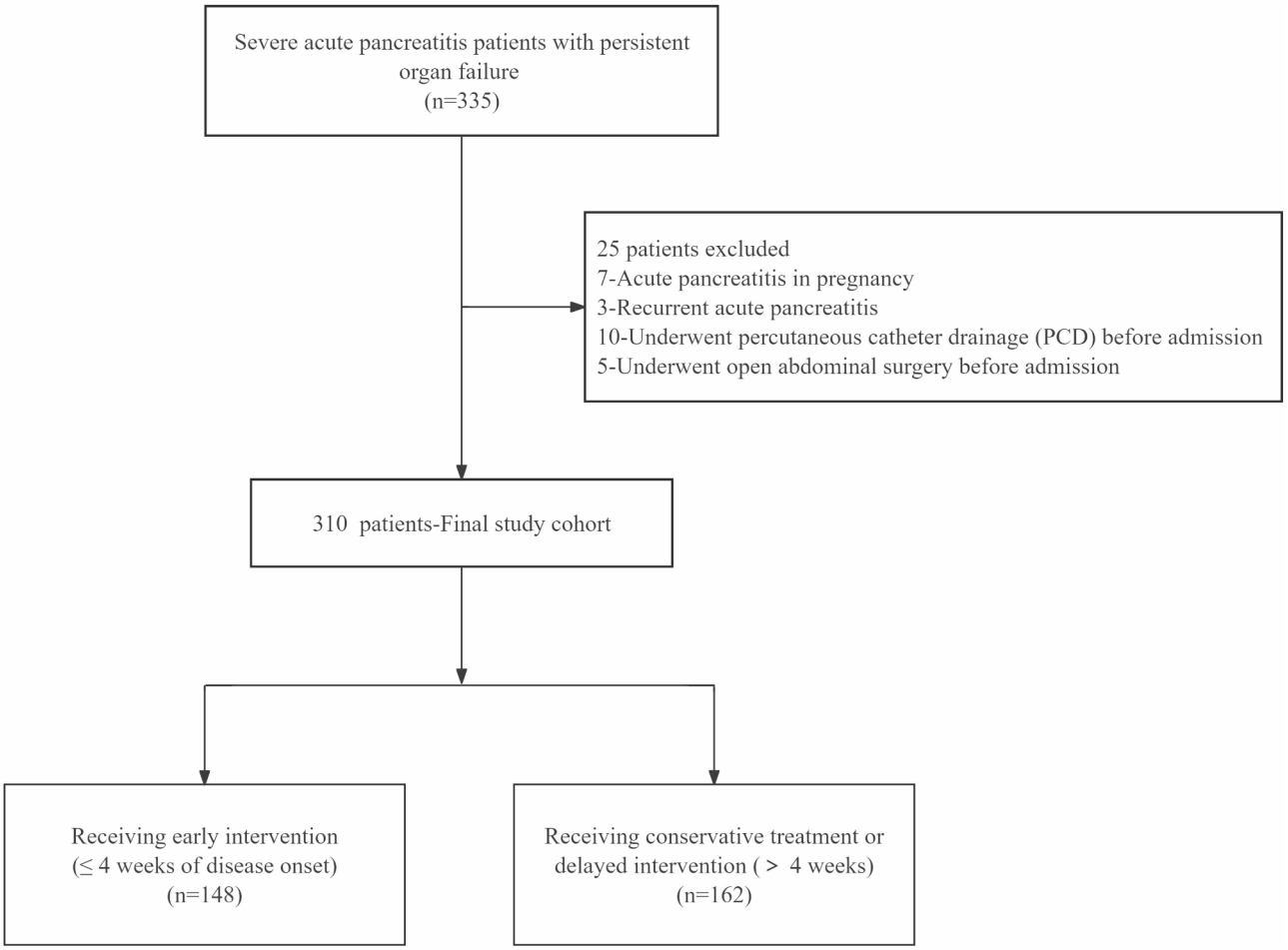


Fig. 1. The flow chart of study design.

risk of requiring early intervention (Table S4). Based on smooth curve fitting (Fig. 2), the SOFA score exhibited a negative linear relationship with the timing of early intervention (adjusted odds ratio [adjOR] − 0.570, 95% CI − 0.867 to − 0.273, $P < 0.001$). Non-linear associations were observed between IAP and intervention timing, as well as between remifentanil equivalent and intervention timing. Threshold effect analysis (Table S5) indicated that for IAP levels ≥ 13 mmHg (adjOR − 0.842, 95% CI − 1.161 to − 0.523, $P < 0.001$), higher IAP was associated with earlier intervention timing. Similarly, for remifentanil equivalents between 0 and 3 mg (adjOR − 2.642, 95% CI − 3.621 to − 1.663, $P < 0.001$), higher analgesic doses correlated with earlier intervention timing. Despite the absence of a significant linear relationship for remifentanil equivalents > 3 mg, the fitted curve trend suggested that these patients all received intervention at earlier timing (Fig. 2).

Clinical effects of early intervention

Comparison of organ function and key clinical indicators pre-intervention and on day 7 post-intervention revealed that patients receiving intervention within 3 weeks of symptom onset, improvements in respiratory function, hemodynamic stability, and consciousness were observed, along with reduced sedation/analgesia requirements, lower CRP levels, and decreased IAP (Table S6). In contrast, patients undergoing intervention between 3 and 4 weeks after onset demonstrated improvement in renal function and consciousness, as well as reductions in IAP and CRP levels (Table S7).

Smooth curve fitting visualized potential relationships between the changes in CRP levels, IAP levels, SOFA scores, and remifentanil equivalents at three post-intervention time points and intervention timing (Figs. S2–S5). The results of threshold effect analysis (Table S8) revealed that earlier intervention timing was associated with a greater reduction in IAP levels at day 7 post-intervention (adjOR − 0.140, 95% CI − 0.244 to − 0.036, $P = 0.009$). Additionally, among patients receiving intervention within 3 weeks of symptom onset, significant reductions in SOFA scores were observed on day 3 post-intervention (adjOR − 0.139, 95% CI − 0.234 to − 0.044, $P = 0.004$) and day 7 post-intervention (adjOR − 0.162, 95% CI − 0.292 to − 0.032, $P = 0.016$), along with markedly reduced analgesic doses at day 7 post-intervention (adjOR − 0.178, 95% CI − 0.284 to − 0.072, $P = 0.001$).

Indicators	Unweighted cohort			Weighted cohort		
	Early intervention (n = 148)	Standard therapy (n = 162)	*P*	Early intervention (n = 291)	Standard therapy (n = 322)	*P*
Age (year)	46.0 (36.0–54.0)	42.5 (32.5–53.0)	0.161	46.0 (36.0–54.0)	45.0 (34.0–54.0)	0.343
Sex			0.131			0.997
Male	101 (68.2)	123 (75.9)		207 (71.1)	229 (71.1)	
Female	47 (31.8)	39 (24.1)		84 (28.9)	93 (28.9)	
Etiology			0.765			0.076
Biliary	65 (43.9)	61 (37.7)		130 (44.7)	123 (38.2)	
Hypertriglyceridemia	79 (53.4)	96 (59.3)		150 (51.5)	192 (59.6)	
Alcoholic	3 (2.0)	4 (2.4)		10 (3.4)	5 (1.6)	
Other causes	1 (0.7)	1 (0.6)		1 (0.4)	2 (0.6)	
Comorbidities			0.362			0.688
Hypertension	47 (31.8)	45 (27.7)		86 (29.6)	90 (27.9)	
Diabetic	37 (25.0)	34 (20.9)		71 (24.4)	77 (23.9)	
Hyperlipidemia	68 (45.9)	88 (54.3)		138 (47.4)	168 (52.2)	
Organ failure distribution			0.021			0.376
Isolated respiratory failure	28 (18.9)	47 (29.0)		59 (20.3)	82 (25.5)	
Isolated renal failure	5 (3.4)	12 (7.4)		12 (4.1)	9 (2.8)	
Isolated cardiovascular failure	1 (0.6)	0 (0.0)		2 (0.7)	3 (0.9)	
Multiple organ failure	114 (77.1)	103 (63.6)		218 (74.9)	228 (70.8)	
SOFA score	5.0 (3.0–8.5)	4.5 (3.0–8.0)	0.036	5.0 (3.0–8.0)	5.0 (3.0–8.0)	0.116
Sedation			0.010			0.950
No medication	56 (37.8)	89 (54.9)		104 (35.7)	112 (34.8)	
Single medication	53 (35.8)	40 (24.7)		83 (28.6)	92 (28.6)	
Combined medication	39 (26.4)	33 (20.4)		104 (35.7)	118 (36.6)	
Remifentanil equivalent (mg)	4.0 (1.2–9.6)	2.0 (0.8–6.0)	0.006	2.0 (0.0–6.0)	2.0 (0.0–5.0)	0.863
IAP (mmHg)	14.5 (11.0–17.0)	12.0 (7.5–15.0)	< .001	13.0 (10.0–16.0)	13.0 (9.0–16.0)	0.061
CRP (mg/L)	182.9 (131.4–218.6)	156.6 (97.1–215.0)	0.097	164.7 (105.1–228.3)	156.9 (97.1–210.5)	0.124
CTSI	8 (8–10)	6 (6–8)	< .001	8 (6–10)	8 (6–10)	0.261

Table 1. The baseline data of patients in the two groups. *Continuous variables were presented as median (interquartile range); categorical variables as n (%). SOFA, Sequential Organ Failure Assessment; IAP, intra-abdominal pressure; CRP, C-reactive protein; CTSI, computed tomography severity index.

Indicators	Unweighted cohort			Weighted cohort		
	Early intervention (n = 148)	Standard therapy (n = 162)	*P*	Early intervention (n = 291)	Standard therapy (n = 322)	*P*
Complication						
Infected pancreatic necrosis	140 (94.6)	56 (34.6)	< .001	225 (77.3)	165 (51.2)	< .001
Intestinal fistula	45 (30.4)	14 (8.6)	< .001	58 (19.9)	59 (18.3)	0.613
Intra-abdominal hemorrhage	73 (49.3)	10 (6.2)	< .001	111 (38.1)	72 (22.4)	< .001
Pancreatic fistula	34 (22.9)	10 (6.2)	< .001	56 (19.2)	53 (16.5)	0.386
Laparotomy	51 (34.5)	39 (24.1)	0.044	65 (22.3)	50 (15.5)	0.031
Length of hospital stay (d)	45.0 (29.5–71.0)	17.0 (11.0–23.0)	< .001	36.0 (22.0–64.0)	25.0 (15.0–41.0)	< .001
In-hospital mortality	41 (27.5)	26 (16.1)	0.013	70 (24.1)	59 (18.3)	0.082

Table 2. Clinical outcomes in the two groups. *Continuous variables were presented as median (interquartile range); categorical variables as n (%).

Discussion

This retrospective study described the clinical characteristics of SAP patients with ANC and POF, and compared the effects of different intervention timing on organ function and clinical outcomes. The findings demonstrated that early intervention significantly improved organ function and attenuated systemic inflammatory status in this population, with the majority of patients achieving survival. Additionally, smooth curve fitting visualized potential non-linear relationships between key clinical indicators and intervention timing, providing evidence to guide early identification of SAP patients requiring therapeutic escalation.

The current dominant view maintains that IPN is the most common indication for intervention in patients with SAP, and that conservative treatment should be adopted as much as possible until full liquefaction and

Indicators	Receiving intervention within three weeks (n = 92)	Receiving intervention during three to four weeks (n = 56)	*P*
SOFA score	6.0 (3.0–12.0)	4.0 (2.0–10.0)	< .001
Organ failure distribution			0.214
Isolated respiratory failure	13 (14.1)	15 (26.8)	
Isolated renal failure	3 (3.2)	2 (3.6)	
Isolated cardiovascular failure	1 (0.1)	0 (0.0)	
Multiple organ failure	75 (81.6)	39 (69.6)	
Sedation			< .001
No medication	21 (22.8)	35 (62.5)	
Single medication	47 (51.1)	16 (28.6)	
Combined medication	24 (26.1)	5 (8.9)	
Remifentanil equivalent (mg)	2.4 (0.8–9.6)	1.2 (0.0–6.0)	0.002
IAP (mmHg)	15.0 (9.0–27.0)	12.0 (6.0–20.0)	< .001
CRP (mg/L)	179.5 (28.4–329.5)	131.0 (17.1–269.5)	0.002
CTSI	10 (6–10)	8 (6–10)	0.154
Complication			
Infected pancreatic necrosis	88 (95.7)	52 (92.9)	0.477
Intestinal fistula	27 (29.3)	18 (32.1)	0.720
Intra-abdominal hemorrhage	50 (54.3)	23 (41.1)	0.117
Pancreatic fistula	23 (25.0)	11 (19.6)	0.452
Laparotomy	30 (32.6)	21 (37.5)	0.544
Length of hospital stay (d)	43.5 (10.0–242.0)	50.5 (13.0–160.0)	0.430
In-hospital mortality	31 (33.7)	10 (17.9)	0.037

Table 3. Comparison of clinical characteristics and outcomes between subgroups derived from the early intervention group (unweighted sample) stratified by intervention timing. *Continuous variables were presented as median (interquartile range); categorical variables as n (%). SOFA, Sequential Organ Failure Assessment; IAP, intra-abdominal pressure; CRP, C-reactive protein; CTSI, computed tomography severity index.

encapsulation of necrotic tissue prior to drainage[6,12,21]. However, some IPN patients may develop sepsis or even multiple organ dysfunction syndrome (MODS) while waiting for delayed intervention[5,6]. In such cases, surgical intervention remains the primary approach to controlling infection, but the optimal timing and clinical safety of this procedure remain controversial[6,21]. A single-center retrospective study[22] involving 78 early-intervention patients reported an OF incidence of 57.7% and an overall mortality rate of 26.9%. In the POINTER study[21], while the early-intervention group showed no advantage over the delayed-intervention group in the composite endpoint of mortality and major complications, the overall study population exhibited a lower incidence of OF (20.2%) and lower CTSI, suggesting heterogeneity compared to our cohort. Furthermore, the POINTER study stratified patients based on different drainage strategies following suspected or confirmed IPN, whereas our study focused more on on assessing organ function status to guide the selection of drainage strategies. Currently, some studies also have confirmed the safety and potential clinical benefits of early-stage invasive interventions within the first 4 weeks of disease onset in SAP patients with POF[13,23]. Therefore, the aforementioned evidence indicates that there is significant heterogeneity among SAP patients, and different subgroups may be suitable for distinct treatment modalities. Although IPTW achieved balance in baseline covariates in our study, this statistical adjustment may not fully reflect real-world clinical heterogeneity. The elevated mortality observed in the early intervention group was likely attributable to higher incidence of major complications, underscoring the imperative to integrate rigorous complication management protocols into early intervention strategies.

Multiple studies have demonstrated that POF in the early stage of SAP may serve as an intervention indicator, given its potential association with early infection[6,24,25]. Our study demonstrated a high incidence of IPN in the early intervention group (94.6%), consistent with prior research findings (91% occurrence rate)[26], further supporting a possible link between POF and infection. Additionally, the early intervention group exhibited significantly higher SOFA scores, with SOFA scores negatively correlated with intervention timing (i.e., elevated SOFA scores were associated with earlier interventions), indicating that organ functional status may hold predictive value in guiding intervention timing. A multicenter observational study demonstrated that necrotizing soft tissue infection patients with unresolved organ dysfunction within 14 days of onset had poor prognoses, while the modified SOFA score was an important basis for selecting patients for intervention treatment[27].

In this study, the need for early intervention was also associated with intra-abdominal hypertension (IAH), the extent of pancreatic necrosis exudation, and the use of high-dose analgesics. In SAP, damage-associated molecular patterns released by necrotic tissues exacerbate systemic inflammation through activation of macrophages and neutrophils, while systemic inflammatory response syndrome has been identified as a critical contributor to OF in the early stage of SAP[3,28,29]. Schepers NJ et al. reported that the mortality rate of necrotizing pancreatitis patients with POF reached 43%, 38%, 46%, and 52% for POF durations of < 1 week,

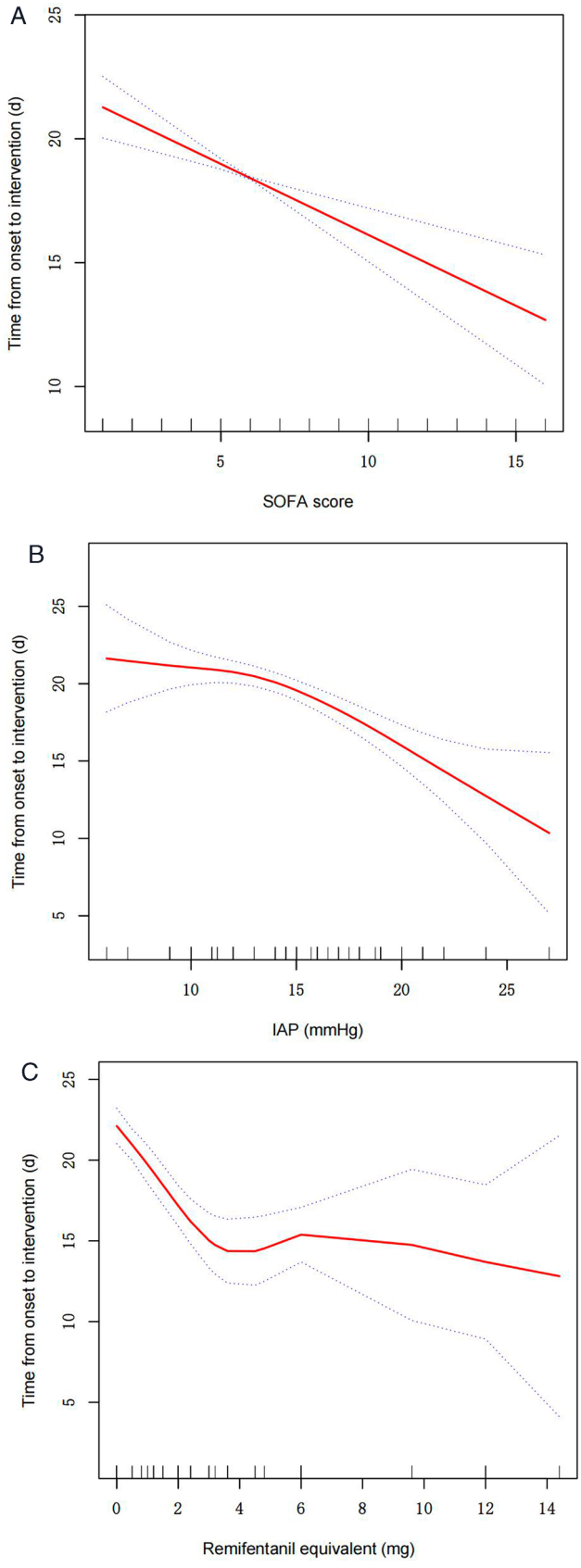
1–2 weeks, 2–3 weeks, and > 3 weeks, respectively[30]. Another study demonstrated significantly higher mortality in patients with POF durations exceeding 2 weeks compared to those with durations < 2 weeks[31]. These findings suggest that early drainage of necrotic tissues containing inflammatory mediators may improve organ failure and clinical outcomes[32]. In the early stage of SAP, pancreatic injury-induced capillary leakage can lead to increased IAP[33]. Current strategies to reduce IAP primarily include gastrointestinal decompression, prokinetic agents, and PCD[34]. Our study revealed a negative correlation between IAP levels and intervention timing when IAP reached ≥ 13 mmHg, likely because conservative treatment alone failed to significantly improve these patients' conditions. Although early relief of abdominal pain (a hallmark symptom of SAP) may reduce patient anxiety and enhance outcomes, prolonged analgesic use carries risks of respiratory depression, gastrointestinal dysfunction, and hepatorenal toxicity[35,36]. Notably, some patients receiving early intervention required lower analgesic doses, potentially attributable to mitigation of MODS and IAH.

In addition, this study revealed significant differences between the two intervention timing subgroups in terms of organ function, sedation/analgesic requirements, and inflammatory biomarkers, indicating substantial heterogeneity among SAP patients. While patients undergoing intervention within 3 weeks exhibited more pronounced short-term clinical improvement compared to those treated between 3–4 weeks, the observed disparity in outcomes—specifically the higher in-hospital mortality in the early intervention group—may be attributed to differences in baseline disease severity and procedural risks[26,37]. Early intervention cohorts demonstrated elevated SOFA scores, higher IAP, and more severe systemic inflammatory responses at baseline, suggesting a population with inherently greater clinical complexity. Furthermore, interventions performed during the active inflammatory phase may potentiate endothelial injury due to amplified cytokine cascades, thereby increasing the risk of complications such as secondary infections or delayed organ failure[37–39]. A prospective randomized controlled trial (RCT) reported a 20% incidence of death/major complications in the early intervention group versus 46.7% in the delayed group, concluding that early intervention facilitates timely infection control[13]. As this RCT was a pilot study with a limited sample size (n = 30), future research should expand the sample size and incorporate biomarker-driven stratification through dynamic inflammatory profiling (e.g., interleukin-6 trajectories for systemic inflammation, syndecan-1 levels for endothelial injury)[39,40] to identify subpopulations of SAP patients who derive maximal benefit from early intervention.

Finally, this study has several limitations. First, as a single-center retrospective investigation, it carries inherent selection bias and confounding factors. Despite statistical adjustments, the findings may not fully reflect the clinical characteristics of early-intervention cohorts. Second, potential biases exist in organ function assessments—for instance, failure to exclude biliary etiology in liver function evaluation. Third, excessive subgroup stratification led to reduced sample sizes, which significantly compromised statistical power.

Conclusion

SAP patients requiring early intervention tend to have more severe conditions. Although early intervention may be helpful for improving organ function and reducing systemic inflammatory in SAP patients, there are still differences in long-term clinical outcome, indicating the underlying need of further typing of the population to explore appropriate treatment strategies.


A
Time from onset to intervention (d)
SOFA score
B
Time from onset to intervention (d)
IAP (mmHg)
C
Time from onset to intervention (d)
Remifentanil equivalent (mg)

◀**Fig. 2**. The association between different clinical indicators and the timing of early intervention (The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% confidence interval from the fit). (**A**) The SOFA score is linearly and negatively associated with the timing of clinical intervention. (**B**) A non-linear relationship exists between IAP level and intervention timing. (**C**) A non-linear relationship exists between remifentanil equivalent and intervention timing. SOFA, Sequential Organ Failure Assessment; IAP, intra-abdominal pressure.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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References

1. Boxhoorn, L. et al. Acute pancreatitis. *Lancet* **396**(10252), 726–734 (2020).
2. Mederos, M. A., Reber, H. A. & Girgis, M. D. Acute pancreatitis: A review. *JAMA* **325**(4), 382–390 (2021).
3. Garg, P. K. & Singh, V. P. Organ failure due to systemic injury in acute pancreatitis. *Gastroenterology* **156**(7), 2008–2023 (2019).
4. Zerem, E. et al. Current trends in acute pancreatitis: Diagnostic and therapeutic challenges. *World J. Gastroenterol.* **29**(18), 2747–2763 (2023).
5. Trikudanathan, G. et al. Current concepts in severe acute and necrotizing pancreatitis: An evidence-based approach. *Gastroenterology* **156**(7), 1994-2007.e3 (2019).
6. Baron, T. H. et al. American Gastroenterological Association clinical practice update: Management of pancreatic necrosis. *Gastroenterology* **158**(1), 67-75.e1 (2020).
7. Liu, T. et al. Accuracy of circulating histones in predicting persistent organ failure and mortality in patients with acute pancreatitis. *Br. J. Surg.* **104**(9), 1215–1225 (2017).
8. Roh, J. S. & Sohn, D. H. Damage-associated molecular patterns in inflammatory diseases. *Immune Netw.* **18**(4), e27 (2018).
9. Maatman, T. K. et al. The continuum of complications in survivors of necrotizing pancreatitis. *Surgery* **168**(6), 1032–1040 (2020).
10. Petrov, M. S. et al. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology* **139**(3), 813–820 (2010).
11. Lytras, D. et al. Persistent early organ failure: defining the high-risk group of patients with severe acute pancreatitis?. *Pancreas* **36**(3), 249–254 (2008).
12. Maurer, L. R. & Fagenholz, P. J. Contemporary surgical management of pancreatic necrosis. *JAMA Surg.* **158**(1), 81–88 (2023).
13. Ke, L. et al. Early on-demand drainage or standard management for acute pancreatitis patients with acute necrotic collections and persistent organ failure: A pilot randomized controlled trial. *J. Hepatobil. Pancreat. Sci.* **28**(4), 387–396 (2021).
14. Dellinger, E. P. et al. Determinant-based classification of acute pancreatitis severity: An international multidisciplinary consultation. *Ann. Surg.* **256**(6), 875–880 (2012).
15. Lambden, S. et al. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. *Crit. Care* **23**(1), 374 (2019).
16. Mehta, R., GP Trainee, Chinthapalli, K., Consultant Neurologist. Glasgow coma scale explained. *BMJ* 2, 365–l1296 (2019).
17. Treillet, E., Laurent, S. & Hadjiat, Y. Practical management of opioid rotation and equianalgesia. *J. Pain Res.* **29**(11), 2587–2601 (2018).
18. Li, L. et al. Optimising the measurement of intra-bladder pressure in patients with predicted severe acute pancreatitis. *Pancreatology* **23**(1), 18–27 (2023).
19. Basch, E. et al. Development of the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). *J. Natl. Cancer Inst.* **106**(9), 244 (2014).
20. Bettega, F. et al. Use and reporting of inverse-probability-of-treatment weighting for multicategory treatments in medical research: A systematic review. *J. Clin. Epidemiol.* **170**, 111338 (2024).
21. Boxhoorn, L. et al. Immediate versus postponed intervention for infected necrotizing pancreatitis. *N. Engl. J. Med.* **385**(15), 1372–1381 (2021).
22. Mukund, A. et al. Safety and efficacy of early image-guided percutaneous interventions in acute severe necrotizing pancreatitis: A single-center retrospective study. *Indian J. Gastroenterol.* **38**(6), 480–487 (2019).
23. Zhang, H. et al. Early versus delayed intervention in necrotizing acute pancreatitis complicated by persistent organ failure. *Hepatobil. Pancreat. Dis. Int.* **21**(1), 63–68 (2022).
24. Gao, L. et al. The clinical outcome from early versus delayed minimally invasive intervention for infected pancreatic necrosis: A systematic review and meta-analysis. *J. Gastroenterol.* **57**(6), 397–406 (2022).
25. Hocke, M. et al. Controversies in EUS-guided treatment of walled-off necrosis. *Endosc. Ultrasound* **11**(6), 442–457 (2022).
26. van Santvoort, H. C. et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N. Engl. J. Med.* **362**(16), 1491–1502 (2010).
27. Bulger, E. M. et al. Impact and progression of organ dysfunction in patients with necrotizing soft tissue infections: A multicenter study. *Surg. Infect. (Larchmt).* **16**(6), 694–701 (2015).
28. Zhou, X. et al. Damage associated molecular patterns and neutrophil extracellular traps in acute pancreatitis. *Front. Cell Infect. Microbiol.* **12**(12), 927193 (2022).
29. Ge, P. et al. Intestinal barrier damage, systemic inflammatory response syndrome, and acute lung injury: A troublesome trio for acute pancreatitis. *Biomed. Pharmacother.* **132**, 110770 (2020).
30. Schepers, N. J. et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. *Gut* **68**(6), 1044–1051 (2019).
31. Huang, P., Lu, D. & Wang, W. Impact of the duration of organ failure on mortality in patients with acute pancreatitis. *Pancreas* **49**(8), e73–e75 (2020).
32. Lu, J. et al. How to identify the indications for early intervention in acute necrotizing pancreatitis patients: A long-term follow-up study. *Front Surg.* **6**(9), 842016 (2022).
33. Jaan, A. et al. Incidence, implications and predictors of abdominal compartment syndrome in acute pancreatitis: A nationwide analysis. *Pancreatology* **24**(3), 370–377 (2024).
34. MancillaAsencio, C. & Berger, F. Z. Intra-abdominal hypertension: A systemic complication of severe acute pancreatitis. *Medicina (Kaunas)* **58**(6), 785 (2022).

35. Cai, W. et al. Pain management in acute pancreatitis: A systematic review and meta-analysis of randomised controlled trials. *Front Med. (Lausanne)* **17**(8), 782151 (2021).
36. Pota, V. et al. Pain in intensive care: A narrative review. *Pain Ther.* **11**(2), 359–367 (2022).
37. Trikudanathan, G. et al. Early (< 4 weeks) versus standard (≥ 4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. *Am. J. Gastroenterol.* **113**(10), 1550–1558 (2018).
38. Hollemans, R. A. et al. Predicting success of catheter drainage in infected necrotizing pancreatitis. *Ann. Surg.* **263**(4), 787–792 (2016).
39. Tang, F. et al. Endothelial dysfunction: Pathophysiology and therapeutic targets for sepsis-induced multiple organ dysfunction syndrome. *Biomed. Pharmacother.* **178**, 117180 (2024).
40. Varga, N. I. et al. IL-6 baseline values and dynamic changes in predicting sepsis mortality: A systematic review and meta-analysis. *Biomolecules* **15**(3), 407 (2025).

Author contributions
MCB, YZ and XCX designed the study. MCB and KML analyzed the data and drafted the manuscript. ZHT guided the overall research process and provided conceptual input. GL and WQL modified the manuscript. All authors have read and approved the final manuscript.

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Declarations

Competing interests
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Correspondence and requests for materials should be addressed to G.L. or W.L.