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ORIGINAL RESEARCH

Evaluating the Therapeutic Efficiency and Efficacy of Blood Purification for Treating Severe Acute Pancreatitis: A Single-Center Data Based on Propensity Score Matching

Hongwei Huang[1], Jiacheng Mo[2], Gui Jiang[2], Zheng Lu[1]

[1]Intensive Care Unit, Guangxi Hospital Division of the First Affiliated Hospital, Sun Yat-Sen University, Nanning, Guangxi, 530022, People's Republic of China; [2]Intensive care unit, The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, Guangxi, 530021, People's Republic of China

Correspondence: Zheng Lu, Intensive Care Unit, Guangxi Hospital Division of the First Affiliated Hospital, Sun Yat-sen University, Nanning, Guangxi, 530022, People's Republic of China, Email iculuzheng@163.com

Purpose: To evaluate the long-term efficacy and cost-efficiency of blood purification (BP) in severe acute pancreatitis (SAP) through single-center data.

Patients and Methods: A total of 155 SAP patients were collected and followed up for 6 months. The participants were divided into control (49 cases) and BP group (106 cases) according to whether they received BP treatment or not. The primary outcomes were 6-month mortality, length of hospital stay, and hospitalization costs. Propensity score matching (PSM) analysis was performed based on various factors such as gender, age, etiology, SOFA score, JSS score, and creatinine value on day 1.

Results: There were significant differences in all baseline data between BP and control groups ($p<0.05$). However, there was a significant difference in the mortality, length of hospital stay, hospital costs and infection aggravation rate the in outcome data for 6-months (all $p<0.05$). BP was not considered a death factor in any adjusted models, with p-values ranging from 0.81 to 0.93. The results of subgroup analysis after PSM showed that BP mode had no significant impact on prognostic indicators, but the length of ICU stay and total costs were significantly increased (all $p<0.001$). There was no significant difference in mortality among the cases that did not require early intervention after 6 months ($p=0.487$). However, the patients in BP group had longer ICU stays ($p=0.001$) and higher hospitalization costs ($p<0.001$) compared to the control group.

Conclusion: The utilization of BP therapy did not decrease the 6-month mortality in SAP patients. Additionally, BP therapy has a significant impact on the duration of ICU stay or hospitalization expenses. However, the effectiveness and cost-efficiency of this therapy are unsatisfactory, and early intervention does not enhance survival benefits. Furthermore, there was no substantial variation in survival benefits between continuous veno-venous hemofiltration (CVVH) alone and compound BP.

Keywords: severe acute pancreatitis, blood purification, long-term efficacy, cost-efficiency

Introduction

Acute pancreatitis (AP) is an inflammatory reaction induced by the state of the pancreas caused by factors such as gallstones, alcohol, hyperlipidemia, etc. Globally, the incidence of severe acute pancreatitis is 34/100,000, and it increases constantly.[1,2] Severe acute pancreatitis (SAP) is the common acute abdominal diseases. It refers to the dysfunction of one or more organs other than the pancreas for more than 48 hours.[3] It is characterized by rapid progression, development of multiple complications, and high mortality rates. Despite the recent advances in the treatment of SAP, the mortality rate due to multiple organ dysfunction syndrome (MODS), and secondary infections is still high (20%–40%).[4] Surviving patients suffer from various secondary diseases which affect their quality of life. For example, 40% of the patients experience an abnormal glucose tolerance or type 3 diabetes after the acute phase,[5] 25% experience an impairment of the pancreatic exocrine function,[6] 50% of the patients with necrotizing pancreatitis

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experienced mobility impairment one year after the onset, and 18% of patients experienced recurrence, while 8% developed chronic pancreatitis.[7]

Blood purification (BP), is a non-surgical treatment method that is vital in the treatment of SAP patients. It can effectively lower the concentration of inflammatory mediators in pancreatitis patients, shorten hospital stay, and reduce mortality rate.[8–10] However, due to the differences in study design, enrollment population, BP parameters, as well as the lack of clinical trials that investigate the effects of BP on the long-term survival and quality of life of SAP patients, there is still much debate regarding the use of this technology in inflammatory diseases, particularly pancreatitis, and sepsis.

In a previous meta-analysis,[11] we reported that high-volume hemofiltration (HVHF) had a better efficacy/utility ratio than the control group and was linked to decreased mortality rates, lower hospital stays, and expenses. The variations in the baseline of the included studies and the statistical definition of the time of death, however, limited the reliability of this conclusion. Furthermore, a previous study[12] based on a database demonstrated that although BP is beneficial for stabilizing hemodynamics, it has no impact on the short-term and long-term mortality rates of patients. Therefore, this study collected case data of SAP patients treated at Guangxi Zhuang Autonomous Region People's Hospital from 2013 to 2022 and used propensity score matching (PSM) methods to control for group differences. The 6-month mortality rate, length of hospital stay, and hospital costs were the main outcome indicators, aiming to evaluate whether BP treatment could bring long-term benefits to SAP patients and determine the cost-efficiency, as well as assessing the influence of the mode and intervention timing on patient outcome indicators.

Material and Methods

Subjects and Selection Criteria

Patients who were admitted in to the hospital between January 2013 and May 2022 and fulfilled the diagnostic standards for SAP were included in this study. These patients were followed up for 6 months after they were discharged from the hospital. This study complies with the Declaration of Helsinki and was approved by the Ethics Committee of Guangxi Hospital Division of the First Affiliated Hospital, Sun Yat-sen University (approval number: KY-KJT-2023-184). The patients provided written consent to their participation for this study.

The inclusion criteria were as follows: (1) Meets 2012 Atlanta SAP diagnostic criteria;[3] (2) Age ≥18 years old; (3) The presence of organ dysfunction was defined as an Acute Physiology and Chronic Health Evaluation (APACHE) II score ≥8 and Sequential Organ Failure Assessment (SOFA) score >2 and lasting for more than 48 hours. To improve the specificity of assessing pancreatitis, a new severity score (Japanese Severity Score (JSS) for AP) was introduced.[13] The inclusion criteria for this study are: APACHE II score ≥8, SOFA score >2, and JSS score ≥3 and lasting for more than 48 hours.

The exclusion criteria were as follows: (1) Surgical debridement and drainage, endoscopic retrograde cholangiopancreatography (ERCP) and other interventional procedures performed prior to hospital admission; (2) Patients with malignant tumor, Child-Pugh C chronic liver failure, chronic renal failure requiring maintenance BP, chronic pancreatitis, and other underlying diseases with life expectancy less than 3 months; (3) Unknown status on whether BP was performed during the treatment in other hospitals; (4) Pancreatitis with pseudo-cyst in the previous year; (5) The duration of treatment in other hospitals is more than one week.

Grouping

The grouping information was shown in Figure 1. The criteria for intervention in cases of high blood pressure were based on the 2012 KDOQI standard.[14] In patients who did not meet the absolute or relative indication for kidney replacement, early intervention in the form of blood purification was carried out 48 hours after onset. Absolute indicators for intervention included plasma urea nitrogen levels exceeding 36mmol/L, uremic encephalopathy, uremic pericarditis, nerve and muscle damage caused by uremia, serum potassium levels exceeding 6.5mmol/L, serum magnesium levels exceeding 4mmol/L, acidosis with a pH level below 7.15, 24-hour urine output less than 200mL or anuria, cerebral edema, and pulmonary edema caused by fluid overload. Additionally, serum creatinine levels greater than 353.5mmol/L and increased by more than three times from baseline were also considered absolute indicators. Relative indicators

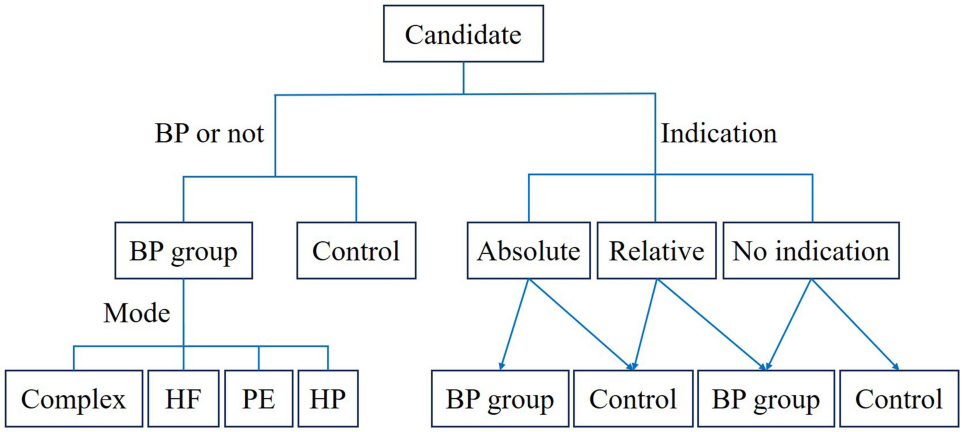

Figure 1 Groups and subgroups.
Abbreviations: BP, blood purification; Complex, two or more modes; HF, hemofiltration; PE, plasma exchange; HP, hemoperfusion.

included serum creatinine levels between 176.8–353.5mmol/L with more than a two-fold increase from baseline and urine output less than 0.5mL/kgh for more than 12 hours. The intervention was not required if none of the above extreme or relative indicators were present in a patient.

Outcomes Measures

The primary objectives of this study were to evaluate the 6-month all-cause mortality rate, length of hospital stay, and hospitalization costs. The secondary objectives included assessing the length of ICU stay and the incidence of local pancreatic complications such as pancreatic pseudocyst, local and peripheral pancreatic infections, and pancreatic hemorrhage. Additionally, the study aimed to determine the incidence of systemic complications, such as bleeding in the abdominal cavity, digestive tract, chest, or other viscera, and new or worsened infections during the disease. The surgical intervention rate was also evaluated, including laparotomy or interventional hemostasis, CT-guided cyst puncture and drainage, vascular interventional hemostasis or thrombectomy, extracorporeal membrane oxygenation support, and ERCP. Finally, organ function scores on day 7 after treatment were also examined.

Statistical Analysis

Statistical Software Package for Social Sciences (SPSS), version 25 Stata/MP 17.0, and R studio 4.0 were utilized in the analysis. The data was reported in the form of mean ± standard deviation (SD) for the normally distributed data and median and quartile ranges for non-normal distributed data. Usage rates were indicated for count data. The first step in the data analysis was to directly compare the outcomes across the two groups (Control group and BP treatment group). The multivariate logistic regression analysis was conducted to determine whether blood pressure was a risk factor of resultant deaths. Finally, demographic data and factors that affected the outcome of death at admission were used as the baseline data for PSM. The Chi-square method, *t*-test, and rank sum tests were employed. The significance level was set at $p<0.05$ for a two-sided test.

Results

Baseline and Outcomes of Patients

The total of 463 cases were identified at the baseline. And a total of 155 participants were retained after the establishment of the exclusion and inclusion criteria. The gender distribution was unbalanced, with 111 males and 44 females. The median age of the participants was 47 years, with a range of 24–87 years. The Etiology of SAP included biliary (62 cases), alcohol (23 cases), hyperlipidemia (40 cases), and others (30 cases). Twenty-one patients of all the eligible participants had a history of pancreatitis in the previous year, 50 patients were diagnosed with hypertension, 26 were diagnosed with type 2 diabetes, 25 were obese, 2 had benign tumors, 8 had chronic kidney disease that did not require dialysis, 2 had chronic underlying

lung disease, and 3 had compensatory liver disease. Furthermore, 11 cases had an underlying heart disease without heart failure.

Among 155 patients, 106 were administered BP at least once (BP group), while the remaining 49 were in the control group. Apart from comorbidities, the baseline data of the BP group and the control group were statistically different, as illustrated in Table 1. BP group had significantly higher 6-month mortality, longer hospital stays, higher hospitalization costs, and a higher rate of infection aggravation rate (all $p<0.05$) than the control group in terms of outcome indicators.

Analysis of Death-Influencing Factors

Among 155 patients in the study, 104 were classified as survivors and 51 as non-survivors. The risk factors between the death group and the survival group were screened prior to establishing the mortality model. The variables with statistical differences between the two groups are displayed in Table 2. Following the exclusion of the statistically significant factors, a multivariate regression analysis was performed to identify mortality risk factors using the backward method and the significance level set at $p=0.05$. Model correction is implemented by additional influence factors to the basis of the previous model. Model 1 included patient baseline data and BP treatment. Blood cell classification examination and

Table 1 The Baseline and Outcomes of Control and BP Groups

Variables	Control Group (n=49)	BP Group (n=106)	*p*-value
Baseline			
Gender (male)	27(55%)	84(79%)	0.002[a]
Age (years)	58(IQR39–72)	45(IQR35–64)	0.020[b]
Etiology			
Biliary	30	32	0.003[c]
Alcohol	8	15	
Hyperlipidemia	10	30	
Others	1	29	
Comorbidities			
Hypertension	8	42	0.254[d]
Type 2 diabetes	12	14	
Chronic kidney disease	3	5	
Heart disease	5	6	
Others	21	39	
1st creatinine (umol/L)	88(IQR67–137)	179.5(IQR83–340)	<0.001[b]
1st BUN (mmol/L)	7.2(IQR5.3–9.3)	10.5(6.2–16.1)	0.002[b]
1st NLR	12.97(IQR8.05–23.07)	9.07(IQR4.64–16.48)	0.04[b]
1st hematocrite	42.0(IQR36.7–49.3)	38.8(IQR26.4–46.3)	0.012[b]
1st dysfunctional organs	1(IQR1–2)	2(IQR1–3)	<0.001[b]
1st JSS score	5(IQR4–5)	6(IQR5–7)	<0.001[b]
1st APACHE II score	10(IQR8–13)	13(IQR9–18)	0.002[b]
1st SOFA score	3(IQR2–4)	5(IQR3–9)	<0.001[b]
Outcome			
6-month mortality	7(14.28%)	44(44.51%)	0.001[a]
Length of hospital stay (days)	15(IQR12–21)	20.5(IQR12–33)	0.017[b]
Hospitalization costs (US $)	8,715(IQR5,535–16,170)	18,840(IQR14,415–35,700)	0.001[b]
Local complication rate	36.7%	41.5%	0.059[c]
Infection aggravation rate	28.6%	60.3%	0.001[b]
Surgical intervention rate	26.54%	022.64%	0.172[c]
7th SOFA score[d]	3(IQR2–4)	3(IQR2–7)	0.173[b]
7th JSS score[e]	2(IQR2–4)	3(IQR2–4)	0.140[b]

Notes: [a]Chi-square test; [b]Wilcoxon rank sum test; [c]Multigroup Chi-square test; [d]*t*-test; [e]the SOFA and JSS score of the seventh day after admission.

Abbreviations: BUN, blood urea nitrogen; NLR, neutrophil to lymphocyte ratio.

Table 2 Death-Influencing Variables

Variables	Survivors (n=104)	Non-Survivors (n=51)	*p*-value
Kidney disease	0(0%)	8(15.69%)	<0.001[a]
Obesity	22(21.15%)	3(5.88%)	0.011[a]
Pancreatitis	19(18.27%)	2(3.92%)	0.013[a]
Age (years)	44.5(IQR34.5–66)	50(IQR38–75)	0.05[b]
BP treatment	62	44	<0.01[c]
Etiology			
Biliary	42	20	0.028[d]
Alcohol	17	5	
Hyperlipidemia	30	8	
Others	15	18	
Department			
ICUi	30	20	0.012[d]
ICUii	27	17	
EICU	30	20	
GI Medicine	17	17	
Min-Lym (10^9/L)	0.73(IQR0.58–1.03)	0.46(IQR0.29–0.75)	<0.01[b]
Max-NLR	21.34(IQR16.24–34.53)	43.69(IQR19.06–88.24)	<0.01[b]
Min-Albumin (g/L)	26.17±4.05	24.08±3.9	<0.01[e]
Min-Calcium (mol/L)	1.745(IQR1.61–1.845)	1.63(IQR1.43–1.82)	0.016[b]
Min-Platelet (10^9/L)	152(IQR99–181)	65.1(IQR33–115)	<0.01[b]
Max-BUN (mmol/L)	10(IQR7–13.7)	17(IQR12–28)	<0.01[b]
Min-Crea (umol/L)	51.5(IQR41.94–70)	125(IQR67.0–211)	<0.01[b]
Max-Crea (umol/L)	112.5(IQR79.0–205.5)	317(IQR174.0–502.0)	<0.01[b]
Max-Bilirubin (umol/L)	34(IQR20.5–59.0)	55.4(IQR33.9–149.0)	<0.01[b]
Min-Hematocrite	27(IQR22–32)	18.1(IQR16–25)	<0.01[b]
1st APACH II score	10(IQR8–13.5)	16(IQR12–23)	<0.01[b]
1st SOAF score	4(IQR3–6)	7(IQR5–11)	<0.01[b]
1st JSS score	4(IQR4–5)	6(IQR5–7)	<0.01[b]
Number of 1st dysfunctional organs	2(IQR1–2)	3(IQR2–5)	<0.01[b]
Max-APACH II	12(IQR10–15)	20(IQR17–29)	<0.01[b]
Max-SOFA	8(IQR5–10)	14(IQR11–17)	<0.01[b]
Max-JSS	5(IQR4–6)	7(IQR6–8)	<0.01[b]
Number of largest dysfunctional organs	3(IQR3–5)	6(IQR5–7)	<0.01[b]

Notes: [a]Fisher exact test; [b]Wilcoxon rank sum test; [c]Chi-square test; [d]Multigroup Chi-square test; [e]*t*-test.
Abbreviations: NLR, neutrophil lymphocyte ratio; Crea, creatinine.

blood biochemical examination were added in Model 2. The APACHE II score, SOFA score, JSS score, and number of dysfunctional organs on the first day of admission were added to Model 3. Based on this, the maximum APACHE II score, SOFA score, JSS score, and number of dysfunctional organs were all added to Model 3. However, on this basis, Models 4, 5, 6, and 7 only added the maximum APACHE II score, SOFA score, JSS score, and number of dysfunctional organs respectively. Information about the variables included in each model, the R^2, and the variance inflation factor (VIF) were shown in Table 3.

Despite Model 3 having the largest R^2 value, it encompassed all variables that differed between groups, leading to a VIF value surpassing 5. Upon conducting a collinearity analysis, it was determined that APACH II score, SOFA score, JSS score, the maximum number of dysfunctional organs, and the first-day number of damaged organs displayed collinearity. Consequently, variables with collinearity were incorporated into Models 4, 5, 6, and 7.

The results demonstrated that the chosen variables remained consistent across all models, with obesity, age, max-creatinine, min-platelet, max-neutrophil to lymphocyte ratio (NLR), max-APACHE II score, max-SOFA score, max-JSS score, and max-number of dysfunctional organs emerging as critical determinants of mortality. Notably, the exclusion of

Table 3 Models of Multiple Factors Logistic Regression About Mortality

Model	Factors and β value	Constant	R^2	VIF
Model 1	Age 1.03, BP 4.87	0.01	21.21	2.2
Model 2	Max-creatinine 1.02, max-NLR 1.02, min-platelet 0.98	0.22	75.08	1.61
Model 3	Max-creatinine 1.02, 1st dysfunctional organs 0.56, max-APACH II score 1.15, max-number of dysfunctional organs 1.93, max-SOFA score 1.34	0.0001	96.36	7.92
Model 4	Max-creatinine 1.02, max-NLR 1.02, max-APACH II score 1.17	0.002	80.91	2.7
Model 5	Min-calcium 0.03, age 1.04, max-SOFA score 1.63	0.11	88.41	7.61
Model 6	Max-creatinine1.01, max-NLR 1.02, min-platelet 0.99, max-JSS score 2.44	0.0085	87.81	3.61
Model 7	Max-creatinine 1.02, max-NLR 1.02, min-platelet 0.98, max-number of dysfunctional organs 2.19	0.22	75.08	1.61

BP as a risk factor for mortality in all models, except for the initial one, is noteworthy, given its large *p*-value (ranging from 0.81 to 0.93), suggesting that it did not influence the survival of patients.

According to the LR Chi-square value and VIF, the optimal model was Model 6, and the regression equation was as follows: Y=0.0085+0.99X1+1.01X2+1.02X3+2.44X4. Y represented the risk of death, while X1, X2, X3, and X4 represented min-platelet, max-creatinine, max-NLR, and max-JSS score, respectively.

The predictive value of the continuous variables for death was expressed using the local regression lowess smooth curve, as shown in Figure 2.

PSM Verification of Outcomes Indicators Between Control and BP Groups

Twenty-seven variables were recorded during the admission period. These include hematocrit, total white blood cell count, NLR, platelet count, CRP, PCT, blood urea nitrogen (BUN), creatinine value, bilirubin, serum calcium, amylase, BE value, and various other laboratory markers, as well as JSS score, SOFA score, and other pertinent factors. However, the only variables that showed statistical significance between the control and BP groups were creatinine, BUN, NLR, hematocrit, dysfunctional organs, JSS score, APACHE II score, and SOFA score (all $p<0.001$) (Table 1).

In the univariate logistic regression analysis (with a significance level of $p<0.05$), K^+, hematocrit, platelet count, lactate dehydrogenase, NLR, BUN, creatinine, activated partial prothrombin time, SOFA, JSS, APACHE II, and the number of dysfunctional organs emerged as the most prominent variables. Further multivariate regression analysis using the backward regression method identified the SOFA score and creatinine value on the first day as the primary influencing factors for mortality (with a significance level of $p<0.05$).

PSM was conducted based on the baseline data of patients, including gender, age, etiology, SOFA score at admission, JSS score, and creatinine. The distribution of baseline variables and outcome indicators after matching between the two groups were presented in Table 4. The 6-month mortality, length of hospital stay, local complication, systemic complication, new or worsening infection, surgical intervention, 7-day SOFA and JSS scores in the BP group did not show any improvement compared with the control group (all $p>0.05$), however, the length of ICU stay and total costs were significantly increased (all $p<0.001$), and the incidence of local complications in the BP group was high.

Effect of BP Mode on Outcomes

A total of 105 patients with acute liver failure were included in the study, 11 patients of them received hemoperfusion alone, 50 received continuous veno-venous hemofiltration (CVVH) alone, and 44 received sequential CVVH after hemoperfusion. One patient who received plasma exchange was excluded from the analysis. Direct comparisons revealed that the 28-day mortality of the hemoperfusion group was lower than that of the other groups (0%, 42.0%, and 22.7%, respectively), but the 6-month mortality rate was the same. However, the baseline comparison showed that the initial SOFA score and JSS score of patients in this group were lower than those in other groups. Therefore, the three groups were matched 1:1:1 using the R method. After matching, there was one case in the hemoperfusion group which is eligible for analysis. Hence, only CVVH alone and sequential CVVH after hemoperfusion were compared. The baseline and outcome indicators after the matching of the two groups are shown in Table 5. There were no statistical significant differences in all outcome indicators (all $p>0.05$).

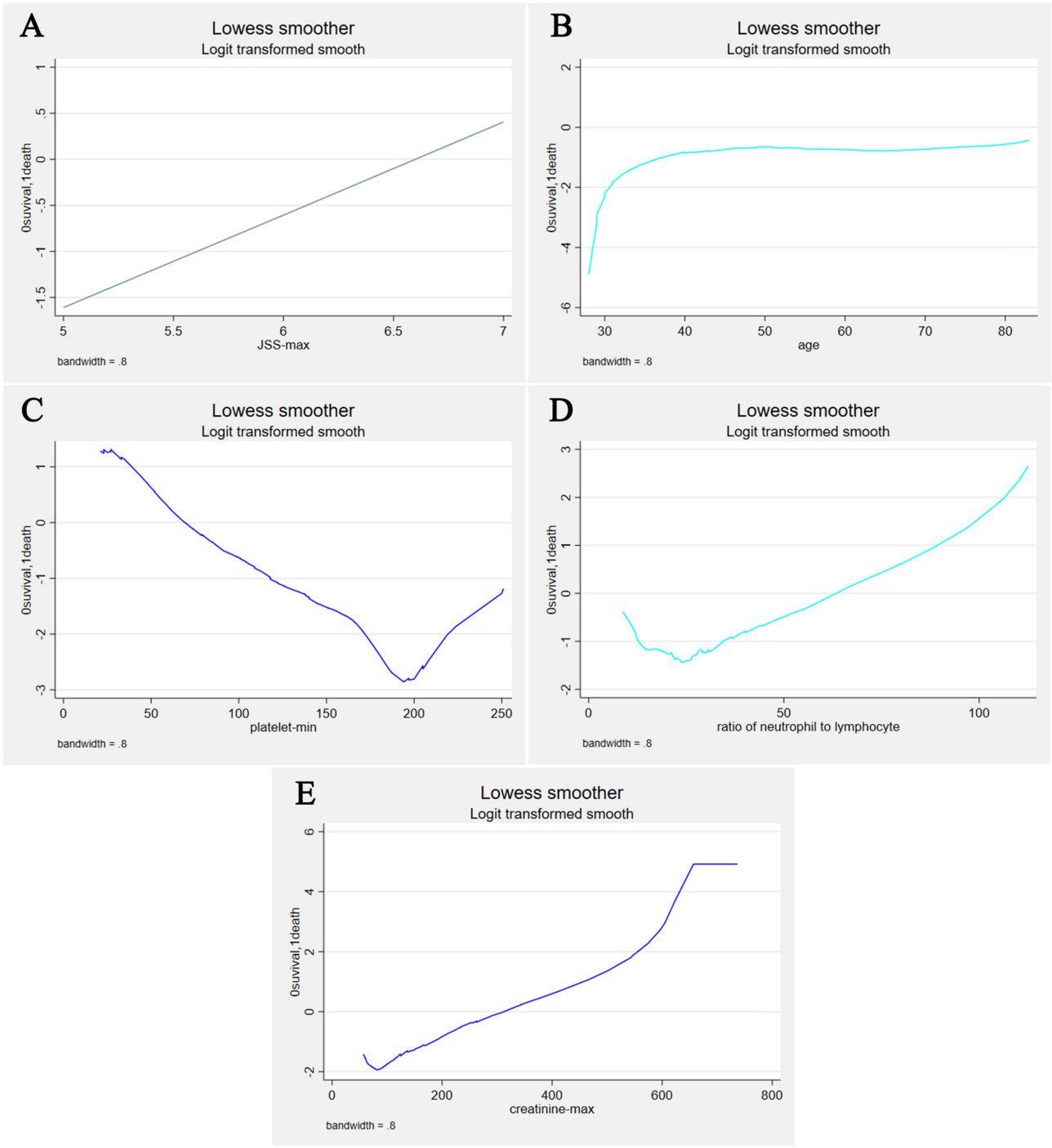

Figure 2 Lowess curve of mortality-related factors. (**A**) Maximum JSS score. (**B**) Age. (**C**) Minimum platelet count. (**D**) Ratio of neutrophils to lymphocytes. (**E**) Maximum creatinine value.

Effect of BP Intervention Time on Outcome Indicators

Among the 155 patients, 83 were assigned to no BP indicators group treatment, out of which 41 patients were treated with BP. The relative indication group consisted of 26 patients. Twenty-one patients who received BP treatment, and the absolute indication group (46 patients), with 44 receiving BP treatment. Given the limited number of patients who did not receive BP treatment in the relative and absolute indication groups and the small sample size after matching, the BP and the control groups for patients without any indication for renal replacement therapy were compared.

Table 4 Baseline Variables and Outcome Indicators After PSM Between Control and BP Groups

Variables	Control Group (n=30)	BP Group (n=30)	*p*-value
Baseline			
Gender (male)	18(60%)	21(70%)	0.430[a]
Age (years)	45(IQR37-66)	54(IQR41-75)	0.180[b]
Etiology			
Biliary	15	18	0.230[c]
Alcohol	7	4	
Hyperlipidemia	7	7	
Others	1	1	
Creatinine[d]	97(IQR67-152)	72(IQR56-136)	0.440[b]
JSS score[d]	4(IQR4-5)	4(IQR4-5)	0.390[b]
SOFA score[d]	3(IQR3-6)	3(IQR2-4)	0.210[b]
Outcome			
6-month mortality	10(50%)	8(40%)	0.652[a]
Length of hospital stay (days)	14.5(IQR12-18)	19(IQR14-26)	0.057[b]
Length of ICU stay (days)	6(IQR3-8)	12(IQR7-19)	<0.001[b]
Total costs (US $)	5.81(IQR3.69–10.78)	12.56(IQR9.61–23.88)	<0.001[b]
Local complication	7,1,0[e]	3,4,1[e]	1.000[a]
Systemic complication	1(3.33%)	3(10%)	0.301[a]
New or worsening infection	9(30%)	15(50%)	0.114[a]
Surgical intervention	4,2,1[f]	2,1,1[f]	0.757[a]
7th SOFA score	3(IQR2-4)	3(IQR2-7)	0.173[b]
7th JSS score	2(IQR2-4)	3(IQR2-4)	0.140[b]

Notes: [a]Chi-square test; [b]Wilcoxon rank sum test; [c]Multigroup Chi-square test; [d]the value of admission; [e]pseudocyst, cyst with infection, cyst with infection and hemorrhage; [f]cyst puncture and drainage, ERCP, exploratory laparotomy, respectively.
Abbreviation: PSM, propensity score matching.

Table 5 Baseline Variables and Outcome Indicators of Model Intervention in Subgroups After PSM

Variables	CVVH (n=20)	Combined (n=20)	*p*-value
Baseline			
Gender (male)	14(70%)	16(80%)	0.757[a]
Age (years)	45(IQR38-67)	56(IQR43-74)	0.330[b]
Etiology			
Biliary	10	11	0.819[c]
Alcohol	14	13	
Hyperlipidemia	5	5	
Others	1	1	
Number of dysfunctional organs	1(IQR1-2)	1(IQR1-2)	1.00[b]
Creatinine[d]	75(IQR62-108)	83(IQR64-136)	0.390[b]
JSS score[d]	4(IQR3.5–5)	4(IQR3-5)	0.980[b]
SOFA score[d]	3(IQR3-5)	3(IQR2-4)	0.900[b]
Outcome			
6-month mortality	10(50%)	8(40%)	0.652[a]
Local complication	9(45%)	9(45%)	0.984[a]
Systemic complication	6(30%)	7(23%)	0.876[a]
New or worsening infection	12(60%)	13(65%)	0.856[a]
Length of hospital stay (days)	21(IQR10, 28)	20(IQR14.5, 34.5)	0.520[b]
Length of ICU stay (days)	12.5(IQR5, 22)	14.5(IQR9, 20.5)	0.163[b]
Total costs (US $)	12.7(IQR10.5, 26.67)	15.96(IQR11.8, 27.83)	0.158[b]

Notes: [a]Chi-square test; [b]Wilcoxon rank sum test; [c]Multigroup Chi-square test; [d]the value of admission.

Table 6 Baseline Variables and Outcome Indicators of Early Intervention Subgroup After PSM

Variables	Control Group (n=20)	BP Group (n=20)	*p*-value
Baseline			
Gender (male)	12(60%)	14(70%)	0.76[a]
Age (years)	45(IQR38-67)	56(IQR43-74)	0.33[b]
Etiology			
Biliary	13	12	0.82[c]
Alcohol	12	12	
Hyperlipidemia	4	5	
Others	1	1	
Number of dysfunctional organs[d]	1(IQR1-2)	1(IQR1-2)	1[b]
Creatinine[d]	75(IQR62-108)	83(IQR64-136)	0.39[b]
JSS score[d]	4(IQR3.5–5)	4(IQR3-5)	0.98[b]
SOFA score[d]	3(IQR3-5)	3(IQR2-4)	0.9[b]
Outcome			
6-month mortality	1(3.33%)	2(6.66%)	0.487[a]
Length of hospital stay (days)	14.5(IQR12, 18)	19(IQR14, 26)	0.07[b]
Length of ICU stay (days)	6(IQR0-10)	16(IQR8-22)	0.001[b]
Total costs (US $)	6.13(IQR4.21–11.36)	18.77(IQR10.39–26.62)	<0.001[b]
Local complication	9,0[e]	1,3[e]	0.003[a]
Systemic complication	0(0%)	2(6.66%)	0.483[a]
New or worsening infection	9(30%)	13(65%)	0.527[a]
Surgical intervention	2,3,1,0[f]	2,1,0,1[f]	0.735[a]
7th SOFA score	3(IQR2-4)	5(IQR3-7)	0.048[b]
7th JSS score	3(IQR2-4)	3(IQR3-5)	0.236[b]

Notes: [a]Chi-square test; [b]Wilcoxon rank sum test; [c]Multigroup Chi-square test; [d]the value of admission; [e]pseudocyst, cyst with infection, cyst with infection and hemorrhage; [f]cyst puncture and drainage, ERCP, exploratory laparotomy, respectively.

A total of 20 pairs of 40 patients were matched based on gender, age, etiology, the creatinine, JSS and SOFA scores on the first day of hospital admission. Table 6 reveals no significance in the baseline data of patients without indicators, except for age, gender, and etiology (all $p>0.05$).

In patients without indicators, it has been observed that there is no discernible difference in a 6-month mortality rates between the BP group and the control group after matching. However, there is a significant increase in the length of ICU stay and total costs in the BP group. Additionally, the incidence of pseudocyst complicated with infection is higher in the BP group, and the SOFA score is higher after seven days of admission ($p=0.048$). Lastly, the two groups exhibit similar lengths of hospital stay, the intensity of systemic complications, effectiveness of surgical interventions, and JSS scores after the 7 days of hospital admission. These findings are consistent with the original data before dividing subgroups. Statistically significant variables are shown in Table 6.

Discussion

The retrospective case-control study, utilizing the PSM statistical method, concluded that the long-term survival rates of patients treated with BP were not significantly different from those of the control group, which is consistent with our previous study based on the Medical Information Mart for Intensive Care IV (MIMIC IV) database.[12] Regardless, the BP group had longer ICU stays, higher medical costs, and higher incidence of pseudocyst and infection. These findings suggest that BP's efficacy and utility ratio in treating SAP were not superior to those of the control group. Further analysis revealed that even with early intervention, the survival benefit of BP was not better than traditional treatment. Moreover, different treatment modes, such as perfusion, CVVH, and combined mode, did not have an impact on the 6-month mortality rate.

The meta-analysis conducted by Guo et al[10] disclosed that continuous hemofiltration therapy was effective in alleviating SAP within 72 hours after onset of the treatment. This reduced the abdominal pain relief time in SAP patients and it decreased the mortality rates attributable to the SAP. Nonetheless, the results of this study indicated that this treatment had no significant reduction in mortality rates. This increased mortality rate may be attributable to high incidence of local pancreatic infection in the BP group. The findings of this study are consistent with those of other studies that were focused on ICU patients.

The results of this meta-analysis indicate that mortality rates were lower in the group receiving BP compared to the control group. However, upon conducting subgroup analysis, it was found that only the HVHF mode effectively reduced mortality rates by decreasing the occurrence of local pancreatic complications such as abscess and pseudocyst with infection. Other modes of BP did not have any significant impact on mortality rates. In our center, the most commonly used modes for SAP were either hemoperfusion or CVVH and the combination of these two modes in one treatment. Only ten patients met the criteria for HVHF (greater than 40 mL/kg/h[15]). Therefore, our research findings align with the conclusions drawn from the meta-analysis.[11]

Numerous studies proved that BP decreases the levels of inflammatory mediators in patients with pancreatitis,[16,17] which is why renal replacement therapy is the commonly used method among SAP patients in China. Nevertheless, the efficacy of inflammatory cytokines reduction on patient survival is still debated in studies of diseases associated with high levels of these cytokines, such as sepsis, pancreatitis, burns, and acute respiratory distress syndrome (ARDS).[18–21] For instance, the EUPHAS trial in 2009 discovered that early use of polymyxin B hemoperfusion (PMX HP) in the treatment of sepsis and septic shock stabilized hemodynamics, and reduced the incidence of multiple organ dysfunction syndrome (MODS), and decreased 28-day mortality in patients with abdominal septic shock caused by Gram-negative bacteria.[22] However, further clinical trials, including the EUPHASII phase clinical trial in 2015 and the EUPHTRATs trial in 2018,[23] revealed that early use of PMX HP does not improve patient outcomes. The trials demonstrated this through various measures. For example, mortality rates at different intervals and changes in SOFA scores. Additionally, there were no significant differences in the dose, rate, and duration of vasopressor use between the treatment and control groups.[24] However, according to a recent study,[25] hemoperfusion combined with prolonged intermittent renal replacement therapy (PIRRT) improved the overall APACHE II scores. It also decreased the inflammatory cascade in AP patients, particularly those with acute kidney injury (AKI), and promoted up the restoration of renal function.

The results of our study indicate that the passing of SAP was associated with various variables, such as age, the highest levels of creatinine and NLR, the lowest platelet count, the most severe JSS, SOFA, and APACHE II scores, as well as the presence of multiple malfunctioning organs. The NLR measures the balance between two important components of the immune system, neutrophils and lymphocytes. Neutrophils activate inflammation and lymphocytes regulate the immune response.[26,27] As a marker of inflammation, the value of NLR indicates the severity and prognosis of the disease, that is, the greater the NLR value, the higher the mortality rate.[26,28–30] In a previous study,[31] it was determined that NLR significantly outperformed other methods in predicting ICU admission and death in patients with AP. This study showed that that the NLR value was lower in the survival group than in the death group, but there was no significant difference between the BP group and the control group, indicating that BP did not reduce the NLR value in patients.

The advancement of technology of the modern intensive care units (ICUs) enabled patients to survive chronic critical states instead of dying in the early stages. This condition is known as persistent inflammation.[32] van der Poll et al[33] revealed the presence of immunosuppression. The leading causes of late death in SAP are peripancreatic tissue and systemic infection caused by immunosuppression.[4] While HVHF has been found to up-regulate the expression of HLA-DR in monocytes and enhance the respiratory burst of neutrophils in some animal experiments,[34,35] few studies focus on the role of regulating the number and function of lymphocytes by BP. Our data indicate that from 51 deceased patients, 34 died from uncontrollable infections. The minimum lymphocyte count in the death group was smaller than that in the survival group [0.46(IQR0.29–0.75) vs 0.73(IQR0.58–1.03), $p<0.001$]. The minimum lymphocyte count in the BP group was also smaller than that in the control group [0.63(IQR0.38–0.95) vs 0.68(IQR0.59–0.92), $p=0.06$]. These findings suggest that BP did not improve the immunosuppression of patients.

Thrombocytopenia has been identified as an autonomous prognosticator of mortality.[36–39] The administration of BP treatment filters, pipelines, and heparin anticoagulation can result in thrombocytopenia.[23] Our findings indicate that the minimum platelet count was significantly lower in the group that succumbed to death compared to the survival group. Moreover, the minimum platelet count in the BP group was also lower than that in the control group, implying that BP has a negative impact on platelet count.

According to our results, the SOFA, APACHE II, and JSS scores were significantly higher in the death group than in the survival group, indicating the effective differentiation capacity of these scores. In predicting mortality in AP patients, a study by Zhou et al[40] demonstrated that SOFA outperformed other laboratory predictors. Furthermore, continuous SOFA scores showed reliability in predicting mortality, and the SOFA assessment effectively predicated late SAP mortality by the 7th day of hospitalization.[41] This is aligns with our findings that revealed the SOFA scores of the BP group were elevated compared to those of the control group seven days post-admission. More recently, Tomescu et al[42] found in the case series that SOFA scores may not accurately predict the severity of SAP. During treatment, although some computational parameters improved, platelet counts did not improve and the overall SOFA score remained the same. It can be seen that the research on the application of SOFA in AP still needs more further research.

The study has several limitations. Firstly, although the PSM method was used, the single-center retrospective case-control design of this study poses limitations that precluded the elimination of the influence of confounding variables. Secondly, the sample size was relatively small, and additional sample size reductions during subgroup analyses could undermine the validity of some findings. Therefore, to assess the effectiveness of BP in SAP and determine which populations may benefit from BP, extensive, randomized, blind, multicenter clinical studies are required.

Conclusion

In summary, our study found no significant impact of BP on NLR, immunosuppression status, organ function score, or mortality in patients with SAP. However, the length of hospital stays and hospitalization costs significantly increased. We also observed an increase in platelet destruction with BP therapy. These may explain why BP does not improve survival rates in SAP patients. However, we should realize that pancreatitis has diverse pathophysiological mechanisms. Taking BP treatment for all SAP patients based on clinical symptom is unsuitable to evaluate its effect, because doctors require precise BP methods.[43] Research on the type of patients who can benefit from BP treatment, the criteria for BP treatment selection, and how BP works to reduce inflammation can substantially improve the therapeutic outcomes. However, it is a major challenge. Furthermore, it is advisable to be prudent during extracorporeal renal support technology in the early stages of AP, particularly in patients who do not require renal replacement therapy.

Data Sharing Statement

All data supporting the findings of this study appear in the submitted manuscript or are available from the corresponding author upon reasonable request.

Disclosure

The authors report no conflicts of interest in this work.

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