Received: 16 March 2021 | Revised: 8 May 2021 | Accepted: 15 June 2021

DOI: 10.1111/aor.14016

SYSTEMATIC REVIEW

Artificial Organs WILEY

High-volume hemofiltration reduces short-term mortality with no influence on the incidence of MODS, hospital stay, and hospitalization cost in patients with severe-acute pancreatitis: A meta-analysis

Hongwei Huang[1] | **Qin Zhou**[2] | **Meng-hua Chen**[1]

[1]Department of Intensive Care Unit, The Second Affiliated Hospital of Guangxi Medical University, Nanning City, China

[2]Department of Medical Record, The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning City, China

Correspondence
Chen Menghua, Department of Intensive Care Unit, The Second Affiliated Hospital of Guangxi Medical University, No. 166, Daxue East Road, Xixiangtang District, Nanning City, Guangxi Province, China.
Email: daffodils0622@163.com

Abstract

This study aimed to investigate the efficiency, safety and cost-efficiency of blood purification (BP) in treating patients with severe-acute pancreatitis (SAP). A literature search was conducted using PubMed, OVID, International Clinical Trials Register (ICTRP), and Cochrane Central Register of Controlled Trials (CENTRAL). A total of 11 prospective studies and 6 retrospective studies, which reported the mortality of 1279 SAP patients, were included for analysis. Decreased short-term mortality and incidence rate of infection were observed in the high-volume hemofiltration (HVHF) group, but not in patients treated with other types of BP. There was no significant difference in the incidence of multiple-organ dysfunction (MODS), duration of hospital stay, or cost of hospitalization between the BP and non-BP groups. The starting time point, substitution fluid flow rate, filter membrane type, hemofilter change interval, anticoagulation, and sustaining times of BP varied across studies. In conclusion, HVHF may reduce the short-term mortality (<4 weeks), not long-term mortality, of SAP patients by decreasing the incidence of infection, while other types of BP did not show a significant beneficial effect. Neither HVHF nor other BP patterns affect the duration of hospital stay, cost of hospitalization, or incidence of MODS in SAP patients.

KEYWORDS

acute pancreatitis, complication, cost of hospitalization, duration of hospital stay, mortality, renal replacement therapy

1 | INTRODUCTION

Acute pancreatitis is an inflammatory condition of the pancreas mainly caused by bile stones or excessive use of alcohol, as proposed by the 2012 Atlanta classification consensus.[1] It can be classified into mild, moderate severe, and severe pancreatitis (SAP). The latter two account for 20%-30% of all patients, who suffer from single or multiple-organ dysfunction

Abbreviations: BP, blood purification; CIs, confidence intervals; CONSORT, consolidated standards of reporting trials; MDs, mean differences; MODS, multiple-organ dysfunction syndrome; ORs, odds ratios; RRs, risk ratio; SAP, severe-acute pancreatitis; SIRS, systemic inflammatory response syndrome; STROBE, strengthening the reporting of observational studies in epidemiology.

and require intensive care. Despite the advances in SAP treatments, the early hospital mortality rate (≤4 weeks) caused by multiple-organ dysfunction syndrome (MODS), infection, and the later hospital mortality rate (≥4 weeks) caused by gastrointestinal tract bleed, fistula, severe malnutrition may be up to 15%-30%.[2]

Blood purification (BP) includes continuous hemofiltration, hemodialysis, hemodiafiltration, plasma exchange, hemoabsorption, etc Many articles have reported the benefits of renal replacement for SAP, especially in decreasing the levels of cytokines and systemic inflammatory response syndrome (SIRS),[3-5] which are highly expressed and considered predictors of poor prognosis in SAP patients. However, most of these trials were small-sample, non-blinded, non-strict random studies. They focused on the efficiency of BP on removing cytokines, but not on the end or long-term outcomes, such as mortality or endocrine/exocrine functions of the pancreas. Also, treatment methods and patient population varied significantly across studies. All the limitations leave the role, efficiency, and safety of BP controversial. None of the guidelines recommend BP for pancreatitis,[1,6] except the one in Japan. Even in the Japan guideline, BP is only recommended to reduce proinflammatory cytokines in cases with abdominal compartment syndrome or with unstable circulation dynamics and anuria after sufficient initial fluid infusion.[7,8]

Since 2010, three meta-analyses on the efficiency of BP have been published,[9-11] which were focused on different outcomes and shared differences inclusion criteria. For example, the included studies with the outcomes ranged from laboratory parameters to APACHE-II score, included study's numbers shifted from two to nine. There are still some limitations observed in these articles. Such as some studies included in the first meta-analysis[9] (2013), BP was given to both experimental and control groups. The second meta-analysis[10] (2019) included only one study to evaluate a single outcome. The third one[11] (2020) included nine studies, five of which reported mortality data. One of the five studies reported the mortality in the BP group but not in the control group, and the remaining four studies used APACHII grade for mortality analysis. One of them recruited patients with no organ dysfunction which cannot be considered as SAP. In conclusion, although the studies have played an important role in evaluating the efficiency of BP on SAP, it is still necessary to reexamine the role of BP in SAP from different aspects, especially considering the end-point outcomes, and also paying attention to its possible side effects, cost-efficiency. In the current meta-analysis, we take the end-point result, mortality, as main outcome to evaluate the efficacy of BP in treating patients with SAP, and adopt incidence of MODS and complications as secondary outcomes to evaluate its safety. Along with that we also pay attention to the length of stay in hospital and cost of hospitalization in order to analyze its cost-efficiency rate. At the same time, to reduce data loss and publication bias, in addition to random control trials, controlled studies and retrospective studies also are collected, which reported mortality in both BP and controlled groups. The studies are divided into different subgroups to analyze the influences of varied factors such as BP parameters and study design.

2 | MATERIALS AND METHODS

2.1 | Literature search

Literature search was conducted on January 5, 2021 using PubMed, OVID, International Clinical Trials Register (ICTRP), and Cochrane Central Register of Controlled Trials (CENTRAL). The following searching strategies were used:

1. "pancreatitis" OR "pancreas inflammation" [Title/Abstract]
2. "extracorporeal blood therapy" [Title/Abstract] OR "renal replacement therapy" [Title/Abstract]
3. "hemofiltration" [Title/Abstract] OR "hemopurification" [Title/Abstract] OR "hemodialysis" [Title/Abstract] OR "hemodiafiltration" [Title/Abstract] OR "hemoabsorption" [Title/Abstract] OR "plasma exchange"
4. 2 AND 3
5. 1 AND 4

2.2 | Inclusion and exclusion criteria

The inclusion criteria were as follows: (a) SAP was diagnosed according to the Atlanta classification or its subsequent revised versions,[1] (b) two groups of patients were included: the standard treatment group and the BP group, (c) mortality was reported in both groups. The exclusion criteria were as follows: (a) studies that were irrelevant to our objective, (b) case report, (c) studies in which the desired data were not reported, (d) studies in which the same population was reanalyzed by updated studies, (e) studies including patients with malignant tumor, chronic liver dysfunction, chronic kidney dysfunction, chronic pancreatitis.

2.3 | Study selection

A total of 204 studies were identified using the searching strategies. Among them, 185 studies were excluded (Figure 1), leaving 11 prospective studies[4,12-21] and 6 retrospective studies[22-27] for analysis. Studies by Wang et al and Alekasandrova et al[19,27] had two subgroups, which could be considered as two independent studies. Therefore, a total of 19 studies were analyzed. The characteristics of these studies are summarized in Table 1

2.4 | Data collection

The included studies were classified into two groups: the prospective group and the retrospective group. According to consensus of renal replacement therapy, generally speaking, effluent flow rate greater or equal to 40 mL per kilogram of body weight per hour can be classified as high-volume hemofiltration. Because the dose of RRT verified in large range, it is hard to do subgroup according different dose and blood purification patterns, so we simply put all other blood purification patterns do not fulfill the definition of HVHF into one group named non-HVHF.[28] The following data were collected from all studies: study characteristics (ie, country, sample size, study interval, study design), population characteristics (ie, sex, etiology), BP methods (ie, HVHF, normal CVVH, plasma exchange), the time when the treatment started, and the outcomes, such as mortality rate, duration of ICU or hospital stay, incidence of MODS, incidence of complications (ie, bleeding, infection), and surgical intervention rate.

2.5 | Statistical analysis

Data were synthesized using the Review Manager (the Cochrane Collaboration, version 5.4, UK). The STATA software (version 10.0, STATA Corporation, Texas, USA) was used to perform meta-regression analysis and to detect publication bias. The mean difference (MD) and 95% confidence interval (CI) were calculated for continuous data. The odds ratio (OR) and 95% CI were used to describe dichotomous data. When continuous data were reported as median and range, the mean and standard deviation were calculated using the method reported previously. The I^2 was used to evaluate the heterogeneity across studies. When I^2 was >50%, meta-regression was used to determine the source of heterogeneity. The random-effect model was used at the same time, otherwise, the fixed-effect model was adopted. The sensitivity analysis was performed to assess the strength and reliability of the results by excluding one study in turn. The subgroup analysis was conducted based on hemofiltration methods and study design. The publication bias of randomized studies was assessed by funnel plot. The Beggar's and Egger's tests were used to detect publication bias using the STATA software if needed. Retrospective and observational studies were evaluated by the Newcastle-Ottawa scale.

3 | RESULTS

3.1 | Study characteristics and quality assessment

The characteristics of 19 studies and 1279 patients are summarized in Table 1. the Jadad scale[29] and the Newcastle–Ottawa Scale (NOS)[30] were applied to assess the methodological quality of randomized clinical trials (RCTs) and other prospective studies, respectively. The Jadad scale consists of three methodological items: randomization (0-2 points), blinding (0-2 points), and dropouts and withdrawals (0-1 point). RCT that achieves a Jadad score of 3 or more are of moderate to high quality. For NOS evaluation, three methodological items should be concerned: sample selection, design of the control and comparability, and outcome assessment. Studies that acquire an NOS score of six or more are of moderate-to-high quality. Disagreement happening during the selection process was discussed and resolved by participants. The quality of randomized studies was relatively low, except for the one published by Wang et al[19] Three

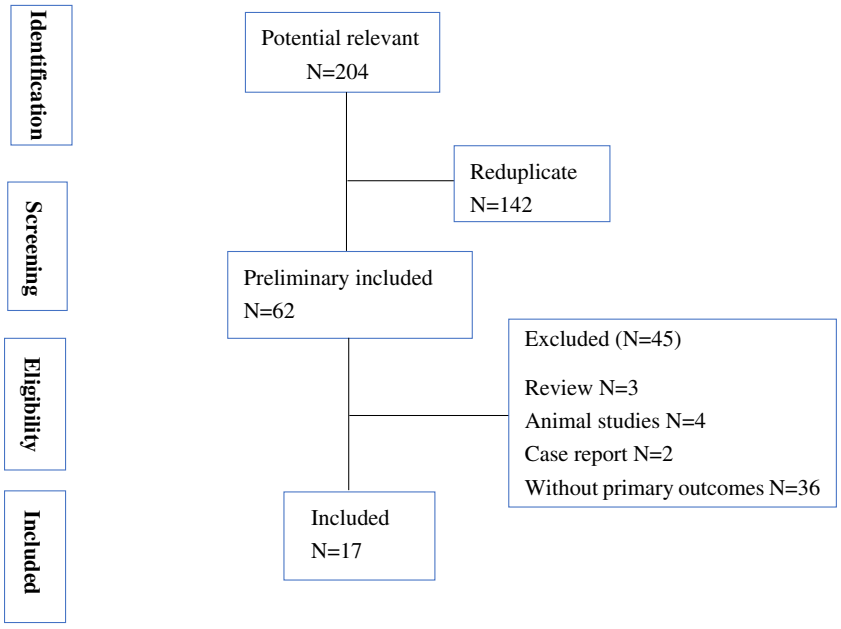

FIGURE 1 Proceeding of study selection [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Characteristics of included studies and SAP patients

Study	Country	Sample	Time interval	Design	Sex (F/M)	Etiology (B/A/O)	BP pattern	Score
Gao N (2018)[4]	China	92	2017-2017	Controlled trial	46/46	16/30/46	HVHF	2[a]
Guo H (2016)[12]	China	64	2008-2015	Randomized	20/44	NR	HVHF	2[a]
Zhu Y (2011)[13]	China	75	2006-2009	Controlled trial	31/44	57/8/10	HVHF	8[b]
Gong D (2010)[14]	China	12	2004-2006	Controlled trial	0/12	NR	HVHF	7[b]
Sun S (2015)[15]	China	20	2010-2013	Randomized	5/15	Hyperlipidemic	HVHF	3[a]
Abuliniti A (2018)[16]	China	40	2011-2013	Controlled trial	15/25	20/1/19	HVHF	8[b]
Guo H (2016)[12]	China	61	2008-2010	Controlled trial	22/39	35/13/13	HVHF	8[b]
Yang ZH (2004)[18]	China	37	2000-2003	Randomized	15/22	17/12/8	CVVH	2[a]
Wang GL(2017-1)[19]	China	125	2004-2015	Randomized	57/68	16/30/46	CVVH	3[a]
Wang GL(2017-2)[19]	China	130	2004-2015	Randomized	56/64	43/24/53	CVVH	3[a]
Yang C (2010)[20]	China	51	2000-2003	Randomized	NR	NR	CVVH	2[a]
Xia L (2012)[21]	China	60	2005-2011	Randomized	21/39	NR	HVHF	2[a]
Pupelis G (2012)[22]	Latvia	130	2004-2006	Retrospective study	35/95	NR	CVVH	7[b]
Abe R (2010)[23]	Japan	94	around1996	Retrospective study	NR	NR	low-CHDF	7[b]
Zhang XJ (2014)[24]	China	38	2008-2012	Retrospective study	15/23	20/6/12	CVVH	7[b]
Chen JH (2004)[25]	China	29	1992-2003	Retrospective study	NR	Hyperlipidemic	PE	7[b]
Sun BR (2019)[26]	China	75	2015-2019	Retrospective study	19/56	09/9/27	CVVH	7[b]
Alekasandrova (2012-1)[27]	Russia	66	NR	Retrospective study	NR	NR	CVVH	6[b]
Alekasandrova (2012-2)[27]	Russia	41	NR	Retrospective study	NR	NR	CVVH	6[b]

Abbreviations: B/A/O, biliary/alcoholic/others; BP, blood purification; CHDF, continuous hemodiafiltration; CVVH, normal or low continuous venous-venous hemofiltration; F/M, male/female; HVHF, high volume hemofiltration; NR, not reported; PE, plasma exchange.

[a]Randomized clinical trial (RCT), and the Jadad scale points.

[b]The Newcastle–Ottawa Scale (NOS) scale.

TABLE 2 Pooled results of primary outcome

Pooled result	Statistical method	Number of studies	MD/OR	95% CI	*P* value	Heterogeneity *P*	Heterogeneity I^2 (%)
Mortality							
Subgroup							
HVHF	Peto, Fixed	8	2.55	1.47,4.44	.0009	.94	0
Non-HVHF	Peto, Fixed	8	1.12	0.73,1.73	.6	.1	42
Prospective	Peto, Fixed	12	2.26	1.48,3.46	.0002	.81	0
Retrospective	Peto, Fixed	7	1.12	0.69,1.82	.64	.01	63
Short-term	Peto, Fixed	13	1.76	1.20,2.57	.004	.01	57
Long-term	Peto, Fixed	3	1.99	0.70,5.67	.2	.72	0
Total	Peto, Fixed	19	1.66	1.36,2.01	<.00001	.009	36

prospective studies were scored eight stars, indicating high quality. The retrospective studies were scored between 6 and 7 stars, indicating relative low quality, but still fulfill the requirement of further analysis.

3.2 | Mortality data

All studies used mortality as the primary outcome, and the total mortality is shown in Table 2: OR = 1.66, 95% CI [1.36-2.01], $P = .009$, $I^2 = 36\%$. The results of each subgroup were as follows: the HVHF group: OR = 2.55, 95% CI [1.47-4.44], $P = .0009$, $I^2 = 0\%$; the non-HVHF group: OR = 1.12, 95% CI [0.73-1.73], $P = .60$, $I^2 = 42\%$; prospective studies: OR = 2.26, 95% CI [1.48-3.46], $P = .002$, $I^2 = 0\%$; retrospective studies: OR = 1.12, 95% CI [0.69-1.82], $P = .64$, $I^2 = 63\%$. After excluding the study by Alekasandrova et al,[27] the OR, 95% CI, and P values remained unchanged and I^2 value was 40%. Then, as the study by Abe et al was excluded, there was no significant difference in the values of OR and 95% CI, but the I^2 value was 0%. The short-term mortality is also shown: OR = 1.76, 95% CI [1.20-2.57], $P = .004$, $I^2 = 63\%$. After excluding the study by Alekasandrova et al,[27] the OR, 95% CI, and P values remained unchanged and the I^2 value was 20%. The long-term mortality is as follows: OR = 1.99, 95% CI [0.70-5.76], $P = .20$, $I^2 = 0\%$.

3.3 | The pooled results of secondary outcomes

Other outcomes related to the safety and cost of BP were also analyzed, including incidence of MODS, incidence of complications (pancreatic abscess in most cases), infection of pancreatic pseudocyst, length of stay in hospital, and cost of hospitalization. The pooled results are given in Table 3.

3.4 | Sensitivity analysis

As the length of stay and cost of hospitalization showed significant heterogeneity, we performed meta-regression analysis to determine the source of heterogeneity. The results showed that study duration and BP methods did not explain the heterogeneity (Table 4). In the subgroup analysis of the mortality in retrospective studies, the OR, 95% CI, and P values remained unchanged after excluding the study by Alekasandrova et al,[27] and the I^2 value was 40%. Then, the study by Abe et al[23] was excluded. The OR and 95% CI had no significantly change, but the I^2 value was 0%. The analysis of the short-term mortality showed that the OR, 95% CI, and P values remained unchanged after excluding the study by Alekasandrova et al,[27] and the I^2 value was 20%. These results suggested that studies by Alekasandrova et al and Abe et al were the major source of heterogeneity.

3.5 | Publication bias

The funnel plot of mortality rate showed that one study was in the significant area, indicating the existence of publication bias. After excluding the study by Alekasandrova et al, no study was found in the significant area. The funnel plot of incidence of MODS, incidence of complications, length of stay in hospital, and cost of hospitalization indicated no publication bias as no study was found in the significant area because tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry, so we did not present the funnel of length of stay in hospital, and cost of hospitalization (Figures 2-4).

4 | DISCUSSION

This meta-analysis aimed to compare the efficacy, safety, and cost of treatment including BP with those of standard therapy without BP in treating patients with SAP. Most of studies included SAP with different incentives, such as alcoholic, biliary or hyperlipidemia or idiopathic, they did not analyze the efficacy of BP to different types of pancreatitis. Our results showed that HVHF, not other BP methods (ie, plasma exchange, standard or low-volume continuous hemofiltration), was significantly associated with decreased mortality, especially short-term mortality and lower incidence of complications in SAP patients. However, HVHF had no effect on the incidence of MODS, length of stay in hospital, or cost of hospitalization.

The mechanism underlying the pathogenesis of SAP remains unclear. The commonly accepted theory is that uncontrolled systemic inflammatory response syndrome (SIRS) leads to the development of multiple-organ failure syndrome and death. Inflammatory cytokines are closely related to the severity of acute pancreatitis, end-organ failure, overall mortality, and duration of hospitalization.[31-33] Blood purification, including hemofiltration, hemodiafiltration, hemodialysis, and plasma exchange, has been shown to reduce the levels of multiple inflammatory mediators,[3-5] and therefore might be effective in treating SAP patients. However, at present, there is no consensus on the efficacy and safety of BP for SAP. Our cross-investigation data (unpublished) showed that BP was often used to treat SAP in China. Consistently, most of the studies included in this meta-analysis were conducted in China. The most commonly used BP method was continuous venous-venous hemofiltration, especially HVHF.

TABLE 3 Pooled results of secondary outcomes

Pooled result	Statistical method	Number of studies	MD/OR	95% CI	*P* value	Heterogeneity *P*	Heterogeneity I^2 (%)
Incidence of MODS							
HVHF	Random	5	1.05	0.86,1.28	.65	.56	0
Non-HVHF	Random	9	0.89	0.73,1.08	.24	.11	39
Prospective Study	Random	9	1.21	0.99,1.48	.06	.21	26
Retrospective	Fixed	6	0.53	0.35,0.80	.003	.95	0
Total	Random	15	0.94	0.85,1.04	.25	.15	22
Incidence of complication							
HVHF	Random	4	1.84	1.05,3.19	.03	.45	0
Non-HVHF	Random	6	1.53	0.87,2.70	.14	.1	46
Prospective	Random	7	2.04	1.27,3.29	.003	.26	22
Retrospective	Fixed	3	1.08	0.58,2.04	.81	.77	0
Total	Random	11	1.62	1.24,2.11	.24	.17	23
Length of stay in hospital							
HVHF	Random	4	0.91	16.12,14.29	.91	<.00001	98
Non-HVHF	Random	6	8.58	−1.21,18.36	.09	<.0001	98
Prospective	Random	7	9.06	3.76,21.89	.17	<.00001	99
Retrospective	Random	2	−10.02	−28.62,8.58	.29	<.00001	94
Total	Random	10	4.7	−1.26,10.66	.12	<.00001	98
Cost of hospitalization							
HVHF	Random	2	2.12	−8.56,4.32	.52	<.00001	93
Non-HVHF	Random	3	−1.15	−4.20,1.90	.46	<.00001	95
Total	Random	5	−1.26	−4.08,1.56	.38	<.00001	93

TABLE 4 Meta-regression analysis of secondary outcomes

ES	Coef	SE	*t*	*P* > *t*	[95% CI]	
Year	2.283967	2.247406	1.02	0.356	−3.493174	8.061109
Methods	2.518621	1.505403	−1.67	0.155	−6.388382	1.35114
Nom	2.980012	1.666616	1.79	0.134	−1.304160	7.264184
Cons	1.216123	1.185572	−1.03	0.352	−4.263733	1.831489

Only two studies reported the long-term mortality of SAP patients.[15,16,26] Also, rarely study focused on the recovery of pancreatic function and the cost-efficiency ratio.[34]

A total of 17 studies and 19 comparisons were included in our study. The analysis showed that BP reduced the short-term mortality of SAP patients compared with those treated with standard treatment. The subgroup analysis suggested that HVHF, but not other BP methods (ie, plasma exchange, normal or low-volume hemofiltration), had beneficial effects on SAP patients. Different conclusions were drawn from prospective and retrospective studies because all retrospective investigations adopted normal or low-volume CVVH, which was consistent with the results of the HVHF and non-HVHF subgroups. Moreover, there was diffidence between long-term and short-tern mortality of SAP patients, probably because severe complications that contribute to mortality, such as duodenal fistula and malignant malnutrition, often occur in the late period of SAP, while BP was usually used for patients at the early stage. The sensitivity analysis showed that the studies by Alekasandrova et al and Abe et al were the major source of heterogeneity and publication bias. The study by Alekasandrova et al did not mention whether the enrolled patients had chronic diseases. Also, they defined HVHF as >30 mL/kg/h, which was different from other studies (>40 mL/kg/h). In the study by Abe et al, the control group was admitted to the hospital before 1996, while the study group was admitted after 1996. Also, they did not provide detailed information on BP.

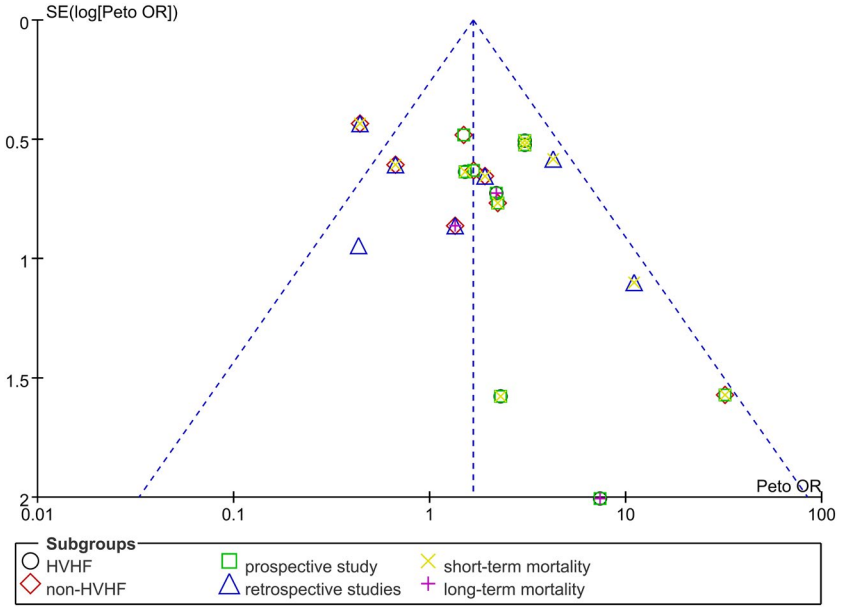

FIGURE 2 Funnel plot of incidence of mortality [Color figure can be viewed at wileyonlinelibrary.com]

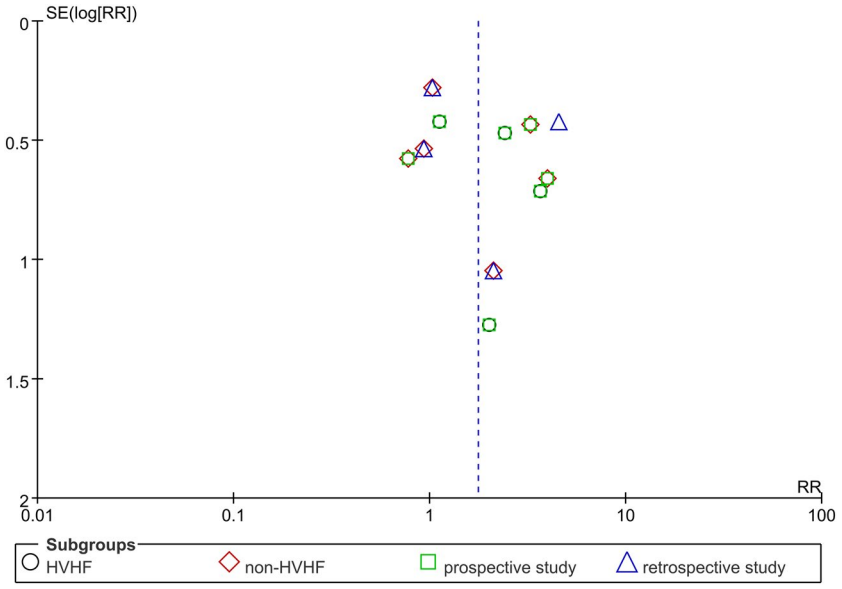

FIGURE 3 Funnel plot of incidence of complications [Color figure can be viewed at wileyonlinelibrary.com]

Our analysis also showed that HVHF had a beneficial effect on the incidence of complications in SAP patients. Four hypotheses may explain the therapeutic mechanisms of HVHF for SAP: the peak concentration hypothesis proposed by Ronco et al,[35] the threshold immunomodulation hypothesis (also known as the Honoré concept),[36] the mediator delivery hypothesis (also known as the Alexander concept),[37] and the regulation of HLA-DR expression in monocytes hypothesis proposed by Peng et al[38,39] The major complications reported in these studies were pancreatic abscess and infection of pancreatic pseudocyst, which were consistent with Peng's hypothesis that HVHF can upregulate HLA-DR and promote its function in monocytes, thereby preventing the occurrence of severe compensatory anti-inflammatory response syndrome, immune-paralysis, or secondary infection. However, the explanation is not convincing enough. In the IVOIRE trial,[40] HVHF showed no benefit on survival rate in sepsis shock patients, which suggests further study is needed to understand HVHF's effect on reducing the short-term mortality in SAP patients.

The heterogeneity of length of stay and cost of hospitalization was high. Meta-regression analysis was performed to determine the source of heterogeneity. Because early fluid resuscitation is an important treatment strategy that reduces the incidence of MODS and mortality. It was proposed by international Surviving sepsis campaign (SSC) in 2004 and then recommend in China.[41] The main difference across studies was the types of BP. And study sample is an

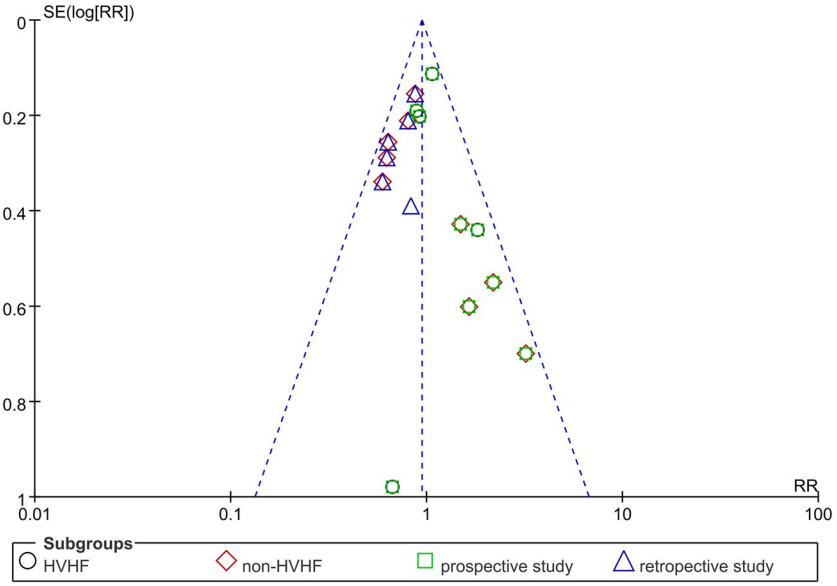

FIGURE 4 Funnel plot of MODS [Color figure can be viewed at wileyonlinelibrary.com]

important factor contributed to test power, so we analyzed the BP methods, study duration, county, and sample using the meta-regression approach. None of them was the source of heterogeneity.

There are some limitations in the present study. Firstly, not all studies were randomized clinical trials, especially high-quality ones, which might affect the pooled results of the study. Secondly, BP methods, patient population, initial time of treatment, and anticoagulation methods were lacking or varied across studies, which may lead to heterogeneity in the analysis. Some studies did not report these characteristics. Finally, some articles did not report the results following the CONSORT or STROBE, which might also cause bias.

5 | CONCLUSION

This study demonstrated that HVHF might reduce the short-term mortality (<4 weeks) of SAP patients by decreasing the incidence of infection. By contrast, other BP types did not show a survival benefit for SAP. On the other hand, HVHF did not affect the duration of hospital stay, cost of hospitalization, or incidence of MODS. To meet the lowest power of the study ($\alpha = 0.05$, $\beta = 0.8$), the sample size in each group should be higher than 380. Therefore, a large-scale, randomized, blinded, multi-center study is needed to evaluate the efficacy and safety of blood purification in SAP.

ACKNOWLEDGMENTS

Li Jiangfa who works at school of public health of Guangxi Medical University contributed to check statistical analysis and meta-regression analysis. Also this study is generally supported by the intensive care unit departmental chair of Huang Zhai.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Contributed to study planning, design, data analysis, data interpretation, and manuscript writing: Hongwei

Contributed to data collecting, checking and interpretation: Qin

Contributed to study planning, design, and manuscript review: Menghua

ETHICAL APPROVAL

The present study was a meta-analysis that analyzed existing studies; therefore did not need to handle individual patient data and ethical approval.

ORCID

Hongwei Huang https://orcid.org/0000-0001-8697-1913

REFERENCES

1. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–11.
2. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology. 2011;141:1254–63.
3. Chen X, Sun M, Mao X, Liu X, Sun W. Effectiveness of continuous veno-venous hemofiltration in the treatment of severe acute pancreatitis. Exp Ther Med. 2019;17:2720–4.
4. Gao N, Yan C, Zhang G. Changes of serum procalcitonin (PCT), C-reactive protein (CRP), interleukin-17 (IL-17), interleukin-6 (IL-6), high mobility group protein-B1 (HMGB1) and D-Dimer in patients with severe acute pancreatitis treated with continuous

renal replacement therapy (CRRT) and its clinical significance. Med Sci Monit. 2018;24:5881–6.
5. Gruda MC, Ruggeberg K-G, O'Sullivan P, Guliashvili T, Scheirer AR, Golobish TD, et al. Broad adsorption of sepsis-related PAMP and DAMP molecules, mycotoxins, and cytokines from whole blood using CytoSorb® sorbent porous polymer beads. PLoS ONE. 2018;13:e0191676.
6. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019;14:27.
7. Hirota M, Takada T, Kitamura N, Ito T, Hirata K, Yoshida M, et al. Fundamental and intensive care of acute pancreatitis. J Hepatobiliary Pancreat Sci. 2010;17:45–52.
8. Yokoe M, Takada T, Mayumi T, Yoshida M, Isaji S, Wada K, et al. Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015. J Hepatobiliary Pancreat Sci. 2015;22:405–32.
9. Wang S, Xu L, Feng X, Li S, Feng Q, Liu C, et al. Is continuous venovenous hemofiltration effective against severe acute pancreatitis? Artif Organs. 2013;37:615–22.
10. Lin Y, He S, Gong J, Liu Z, Ding X, Gong J, et al. Continuous veno-venous hemofiltration for severe acute pancreatitis. Cochrane Database Syst Rev. 2019;10:Cd012959.
11. Guo Y, Cao F, Li C, Yang H, Xia S, Li F. Continuous hemofiltration reduces mortality in severe acute pancreatitis: a meta-analysis. Emerg Med Int. 2020;2020:6474308.
12. Guo H, Suo DW, Zhu HP, Sun XM, Chen J. Early blood purification therapy of severe acute pancreatitis complicated by acute lung injury. Eur Rev Med Pharmacol Sci. 2016;20:873–8.
13. Zhu YiLin, Yuan J, Zhang P, Hu X, He Q, Han F, et al. Adjunctive continuous high-volume hemofiltration in patients with acute severe pancreatitis: a prospective nonrandomized study. Pancreas. 2011;40:109–13.
14. Gong D, Zhang P, Ji D, Chen Z, Li W, Li J, et al. Improvement of immune dysfunction in patients with severe acute pancreatitis by high-volume hemofiltration: a preliminary report. Int J Artif Organs. 2010;33:22–9.
15. Sun S, He L, Bai M, Liu H, Li Y, Li LI, et al. High-volume hemofiltration plus hemoperfusion for hyperlipidemic severe acute pancreatitis: a controlled pilot study. Ann Saudi Med. 2015;35:352–8.
16. Abulimiti A, Husaiyin A, Sailai Y. Evaluation of HVHF for the treatment of severe acute pancreatitis accompanying MODS. Medicine. 2018;97:e9417.
17. Guo J, Huang W, Yang X-N, Jin T, Altaf K, Javed MA, et al. Short-term continuous high-volume hemofiltration on clinical outcomes of severe acute pancreatitis. Pancreas. 2014;43:250–4.
18. Yang ZH, Yang J, Wang YJ. Protective effect of continuous veno-venous hemofiltration on tissue and organ damage in patients with severe acute pancreatitis. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue. 2004;16:232–4.
19. Wang G, Liu H, Xu L, Wen P, Wen J, Zhou S-F, et al. Effect of laparoscopic peritoneal lavage and drainage and continuous venovenous diahemofiltration on severe acute pancreatitis. J Laparoendosc Adv Surg Tech A. 2017;27:1145–50.
20. Yang C, Guanghua F, Wei Z, Zhong J, Penghui J, Xin F, et al. Combination of hemofiltration and peritoneal dialysis in the treatment of severe acute pancreatitis. Pancreas. 2010;39:16–9.
21. Xia L, Qian KJ, Zeng ZG, Liu P, Liu F, Jiang R, et al. A clinical study of early continuous high-volume-hemofiltration in the treatment of severe acute pancreatitis. Zhonghua Nei Ke Za Zhi. 2012;51:871–4.
22. Pupelis G, Plaudis H, Zeiza K, Drozdova N, Mukans M, Kazaka I. Early continuous veno-venous haemofiltration in the management of severe acute pancreatitis complicated with intra-abdominal hypertension: retrospective review of 10 years' experience. Ann Intensive Care. 2012;2 Suppl 1:S21.
23. Abe R, Oda S, Shinozaki K, Hirasawa H. Continuous hemodiafiltration using a polymethyl methacrylate membrane hemofilter for severe acute pancreatitis. Contrib Nephrol. 2010;166:54–63.
24. Zhang X, Sun S, Li S, Feng X, Wang S, Liu C, et al. Early classic hemofiltration exhibits no benefits in severe acute pancreatitis with early organ failure: a retrospective case-matched study. Artif Organs. 2014;38:335–41.
25. Chen JH, Yeh JH, Lai HW, Liao CS. Therapeutic plasma exchange in patients with hyperlipidemic pancreatitis. World J Gastroenterol. 2004;10:2272–4.
26. Sun B, Zhang C, Lin T, Liu S, Wang Z, Zhang J, et al. Effect of continuous renal replacement therapy during percutaneous drainage in severe acute pancreatitis patients: a retrospective cohort study. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2019;31:714–8.
27. Aleksandrova I, Ilynsky M, Rei S, Berdnikov G, Marchenkova L, Kiselev V. Early application of CVVH In the complex treatment of patients with early severe acute pancreatitis. Crit Care. 2012;16:362.
28. Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lo S, et al. Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med. 2009;361:1627–38.
29. Moher D, Jadad AR, Tugwell P. Assessing the quality of randomized controlled trials. current issues and future directions. Int J Technol Assess Health Care. 1996;12:195–208.
30. Wells GA, Shea B, O'connell D, Peterson J, Welch V, Losos M, et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses 2008.
31. Nieminen A, Maksimow M, Mentula P, Kyhälä L, Kylänpää L, Puolakkainen P, et al. Circulating cytokines in predicting development of severe acute pancreatitis. Crit Care. 2014;18:R104.
32. Inagaki T, Hoshino M, Hayakawa T, Ohara H, Yamada T, Yamada H, et al. Interleukin-6 is a useful marker for early prediction of the severity of acute pancreatitis. Pancreas. 1997;14:1–8.
33. Curley PJ, McMahon MJ, Lancaster F, Banks RE, Barclay GR, Shefta J, et al. Reduction in circulating levels of CD4-positive lymphocytes in acute pancreatitis: relationship to endotoxin, interleukin 6 and disease severity. Br J Surg. 1993;80:1312–5.
34. Jiang K, Chen XZ, Xia Q, Tang WF, Wang L. Cost-effectiveness analysis of early veno-venous hemofiltration for severe acute pancreatitis in China. World J Gastroenterol. 2008;14:1872–7.
35. Ronco C, Tetta C, Mariano F, Wratten ML, Bonello M, Bordoni V, et al. Interpreting the mechanisms of continuous renal replacement therapy in sepsis: the peak concentration hypothesis. Artif Organs. 2003;27:792–801.
36. Honoré PM, Matson JR. Extracorporeal removal for sepsis: acting at the tissue level—the beginning of a new era for this treatment modality in septic shock. Crit Care Med. 2004;32:896–7.
37. Di Carlo JV, Alexander SR. Hemofiltration for cytokine-driven illnesses: the mediator delivery hypothesis. Int J Artif Organs. 2005;28:777–86.
38. Peng Z, Pai P, Hong-Bao L, Rong L, Han-Min W, Chen H. The impacts of continuous veno-venous hemofiltration on plasma cytokines and monocyte human leukocyte antigen-DR expression in septic patients. Cytokine. 2010;50:186–91.

39. Peng Z, Singbartl K, Simon P, Rimmelé T, Bishop J, Clermont G, et al. Blood purification in sepsis: a new paradigm. Contrib Nephrol. 2010;165:322–8.
40. Joannes-Boyau O, Honoré PM, Perez P, Bagshaw SM, Grand H, Canivet J-L, et al. High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial. Intensive Care Med. 2013;39:1535–46.
41. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med. 2004;32:858–73.

How to cite this article: Hongwei H, Qin Z, Menghua C. High-volume hemofiltration reduces short-term mortality with no influence on the incidence of MODS, hospital stay, and hospitalization cost in patients with severe-acute pancreatitis: A meta-analysis. Artif. Organs. 2021;45:1456–1465. https://doi.org/10.1111/aor.14016