CLINICAL RESEARCH

Cost-effectiveness analysis of early veno-venous hemofiltration for severe acute pancreatitis in China

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Abstract

AIM: To determine the most cost-effective hemofiltration modality for early management of severe acute pancreatitis (SAP) in China.

METHODS: We carried out a search of Pub-Medline and Chinese Biomedical Disk database. Controlled clinical trials on Chinese population were included in the analysis. The four decision branches that were analyzed were: continuous or long-term veno-venous hemofiltration (CVVH/LVVH), short-term veno-venous hemofiltration (SVVH), SVVH plus peritoneal dialysis (PD), and non-hemofiltration control group. The effectiveness of the technique was determined by survival rate, complications prevention and surgery preservation. The total cost of hospitalization was also assessed.

RESULTS: The SVVH only technique was the least costly modality, $5809 (44449 RMB), and was selected as the baseline treatment modality. SVVH only arm achieved the lowest C/E ratio in terms of overall survival, complications prevention and surgery preservation. In incremental cost-effectiveness analysis, the CVVH/LVVH only and the control arms were inferior to other techniques. Sensitivity analysis showed SVVH only and SVVH plus PD arms overlapped in C/survival ratio.

CONCLUSION: The role of early veno-venous

hemofiltration as an alternative therapy for SAP remains controversial. However, we propose that early use of short-term high-volume veno-venous hemofiltration would have a beneficial impact on the management of SAP.

INTRODUCTION

Severe acute pancreatitis (SAP) is a grave illness associated with serious pancreatic and systematic disease. SAP is seen in nearly 20% of all patients with acute pancreatitis[1]. Despite advances in the understanding of the pathophysiology and management of acute pancreatitis over the past several decades, the mortality rate of SAP has not shown a substantial decrease, varying from 8%-15% to more than 30% in some studies[1-4]. The main factors that influence the poor outcome include systematic inflammatory response syndrome (SIRS) in the early stages ($\leqslant$ 14 d) and infection of pancreatic and peri-pancreatic necrotic tissue in the late stages (> 14 d), both of which can precipitate secondary multi-organ deficiency syndrome (MODS)[5]. As some reports indicate, at least 50% of deaths in the early stage of SAP are related to MODS, and when three or more organs fail, the mortality rate increases to 95%[5,6]. Thus, efficient management during the early stages of the illness is important in improving the prognosis.

Since 1991, veno-venous hemofiltration (VVH) has been used in the initial management of SAP[7]. Several studies have indicated that hemofiltration removes from the circulation small and medium sized molecules that stimulate the inflammatory cells. Alternatively, VVH

may directly inhibit the cells that contribute to the systematic response[8]. The use of continuous veno-venous hemofiltration (CVVH) has been assessed in a animal model of SAP and was found to significantly improve the survival time, when used both for therapeutic and prophylactic treatment, especially the latter[9]. However, the efficiency of treatment decreased with continuing use of CVVH, suggesting that the filter membranes were compromised by long-term application[9]. The current consensus in Japan is to start CVVH soon after the onset of SAP, and to use it continuously for 3-14 d, because reduction in the chemical mediators, and improvement in the respiratory function and the incidence of MODS were more obvious if the treatment was started early rather than at a late stage[10]. However, there is no consensus on how long CVVH should be used and when it should be stopped. Therefore, early short-term veno-venous hemofiltration (SVVH) modalities have been examined, including the use of repeated SVVH (RSVVH), intermittent SVVH (ISVVH) and single SVVH (SSVVH). The time interval of hemofiltration plays an important role in the treatment of SAP during its early stage. A comparison of SVVH with prolonged time interval VVH, and long-term veno-venous hemofiltration (LVVH) in the treatment of SAP did not improve the prognosis further but was associated with more side-effects[11]. Therefore, in the decision making process the benefits of CVVH/LVVH and SVVH continue to be controversial. In addition, it should be noted that peritoneal dialysis (PD) is another approach to the treatment of SAP as it removes dialyzable toxins and reduces severe metabolic disturbances[12]. In China, PD has also been used as an additional therapy with early SVVH. Clinical studies in China have reported that the use of early SVVH plus PD results in better prognosis of SAP, since cytokines such as TNF, IL-6 and IL-8 can be removed effectively from the circulation by these techniques[13].

In China, which is a developing country with a huge population and relatively low income, the use of early CVVH/LVVH carries a great economic burden because of its high cost. For this reason, early SVVH may be more acceptable. However, which one of these therapeutic modalities provides reasonable effectiveness at a lower cost needs to be further explored. The present cost-effectiveness analysis is based on a review of the literature, with a view to determine as to which approach is the most cost-effective treatment of SAP in China.

MATERIALS AND METHODS

The model

The cost-effectiveness analysis was based on a decision tree designed to simulate a simplified clinical course of SAP treated with or without early VVH (Figure 1). In the general structure of the tree, there were four intervention decision arms: conventional therapy without hemofiltration (control arm), conventional therapy combined with early CVVH or LVVH (CVVH/LVVH only), SVVH only, and SVVH plus PD. All the hemofiltration modalities were started in the early stage of SAP, generally 3-5 d after onset of the disease.
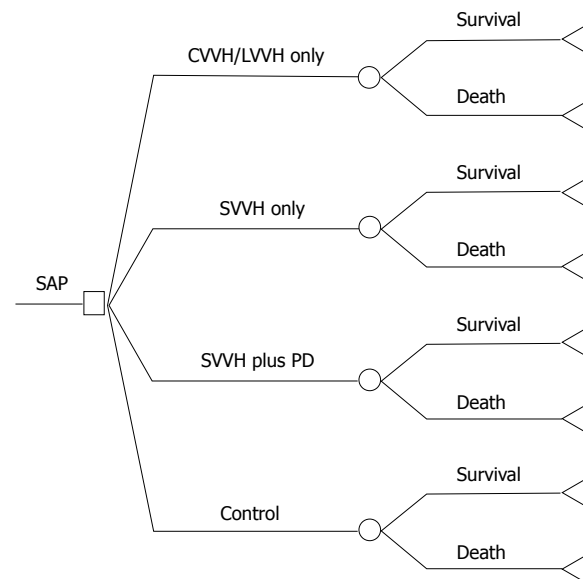

Figure 1 Decision tree of early hemofiltration for SAP.

Effectiveness data

The primary effectiveness variable was overall survival rate. The secondary effectiveness variables were the overall complication prevention rate and overall surgery preservation rate since complications and surgery were the factors most likely to increase the cost of hospitalization. The complications analyzed included severe local and systematic infections, and MODS. Surgery was mainly performed for necrosectomy. Thus, the primary clinical outcome measure was survival (alive = 1, death = 0), while the secondary outcome measures were complications (none = 1, occurrence = 0) and surgery (no = 1, yes = 0). The specified probabilities were retrieved from our previous systematic review (Table 1)[14].

Cost data

The direct health care cost, i.e. total cost of hospitalization (currency, RMB), was calculated as mean ± SD obtained from each of the studies, and the weighted costs were combined by the formula $\Sigma(\chi_i n_i)/\Sigma(n_i)$, of which χ = total cost of hospitalization, n = number of assigned patients in any of the intervention arms, and i = number of included studies. All the costs were converted to the price index as of 2005, taking into account the annual increase in the Chinese prices, i.e. 1.0% in 1999-2000, 2000-2001, 2001-2002 and 2002-2003, 1.2% in 2003-2004, and 3.9% in 2004-2005[15]. One RMB was converted to 0.130688 U.S. dollars.

Literature search and selection

We searched Pub-Medline and Chinese Biomedical Disk (CBMdisc) database from 1990 to 2006. The search strategy was combining the subheading and text words hemofiltration and pancreatitis. The studies based on Chinese population were selected regardless of the language. All patients were diagnosed to have SAP based on the Atlanta classification, APACHE Ⅱ score > 8, Ranson score > 3, or Balthazar CT grading of D or E. All clinical studies which assessed cost comparing

Table 1 Outcomes based on a previous systematic review[14]

Outcomes	CVVH /LVVH only		SVVH only		SVVH plus PD		Control	
Overall mortality rate (%, ratio)	0.149	40/47	0.058	129/137	0.147	29/34	0.179	322/392
Survival rate (%)	0.851		0.942		0.853		0.821	
Overall complications rate (%, ratio)	0.267	4/15	0.208	15/72	0.157	8/51	0.412	120/291
Complications prevention rate (%)	0.733		0.792		0.843		0.588	
Surgery rate (%, ratio)	0.075	3/40	0.016	1/62	0.082	5/61	0.294	58/197
Surgery preservation rate (%)	0.925		0.984		0.918		0.706	

CVVH: Continuous veno-venous hemofiltration; LVVH: Long-term veno-venous hemofiltration; SVVH: Short-term veno-venous hemofiltration; PD: Peritoneal dialysis.

Table 2 Total hospitalization costs obtained from published Chinese articles (10 000 RMB)

Study	Refence	CVVH/LVVH only			SVVH only			SVVH plus PD			Control		
		Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Mao EQ 1999	[23]	-	-	-	5.32	1.6	10	-	-	-	8.91	2.5	10
Mao EQ 2003	[19]	13.7	10.5	16	5.66	5.64	20	-	-	-	-	-	-
Feng GH 2004	[21]	-	-	-	-	-	-	6.1	1.9	25	9.4	3.1	15
Yang FF 2005	[24]	-	-	-	-	-	-	5.8	2.2	36	10.2	4.3	64
Zhang T 2005	[25]	-	-	-	3.29	1.279	38	-	-	-	6.884	4.868	71

CVVH: Continuous veno-venous hemofiltration; LVVH: Long-term veno-venous hemofiltration; SVVH: Short-term veno-venous hemofiltration; PD: Peritoneal dialysis.

Table 3 Weighted total hospitalization costs

Modalities	Cost (C)[1]			Incremental cost (ΔC)[2]
	WM	Max	Min	WMD
CVVH/LVVH only	$18 826 (144 051 RMB)	$33 254 (254 455 RMB)	$4397 (33 647 RMB)	$13 017 (99 602 RMB)
SVVH only	$5809 (44 449 RMB)	$9359 (71 613 RMB)	$2259 (17 286 RMB)	
SVVH plus PD	$7868 (60 205 RMB)	$10 622 (81 279 RMB)	$5114 (39 130 RMB)	$2059 (15 756 RMB)
Control	$11 317 (86 597 RMB)	$17 006 (130 128 RMB)	$5628 (43 066 RMB)	$5508 (42 148 RMB)

[1]All the costs were converted to 2005 price before combination. [2]SVVH only, the least costly arm, was selected as common baseline for other arms to reference to. WM: Weighted mean; WMD: Weighted mean difference; CVVH: Continuous veno-venous hemofiltration; LVVH: Long-term veno-venous hemofiltration; SVVH: Short-term veno-venous hemofiltration; PD: Peritoneal dialysis.

hemofiltration with either a control group or another treatment modality were eligible for inclusion in the analysis.

Statistical analysis

TreeAge Pro Healthcare 2006 software was used in modeling and analyses. Both the cost-effectiveness analyses and the incremental cost-effectiveness analyses were examined, with C/E ratio and incremental C/E ($\Delta C/\Delta E$) ratio calculated separately. The treatment arm with the lowest cost was selected as the common baseline for comparison with other treatment arms. If there was uncertainty with regard to decision making, sensitivity analysis was carried out by alternating the variables to maximal and minimal limits (two-way), including the total cost of hospitalization and overall survival rate.

RESULTS

Our previous systematic review analyzed 10 randomized controlled trials and 6 clinical controlled trials comprising of a total of 891 Chinese patients[14]. The meta-analysis

showed that the overall mortality rate was significantly reduced in the hemofiltration group [RR = 0.49, 95% CI (0.32, 0.74), P = 0.0008][14]. The specified probabilities of the clinical outcomes of each treatment arm were retrieved based on the sub-group analysis of the systematic review. The overall survival rates improved in the CVVH/LVVH only, SVVH only and SVVH plus PD arms by diverse extent (Table 1). Five controlled studies from 4 Chinese medical institutions which provided the data on cost were included in the present analysis[11,13,16-18], and the detailed data were extracted and combined (Tables 2 and 3). Interestingly, both SVVH only and SVVH plus PD reduced the total cost of hospitalization compared with the control arm, while the CVVH/LVVH only approach was the most costly. By contrast, the SVVH only approach was the least costly arm, and was therefore selected as the baseline for the purpose of comparing the cost-effectiveness and incremental cost-effectiveness with the other treatment arms.

Cost-effectiveness analysis

In the cost-effectiveness analysis, the lowest ratios C/

survival rate, C/complication prevention rate and C/surgery preservation rate were $6167 (47186 RMB), $7334 (56122 RMB) and $5903 (45172 RMB) respectively in SVVH only arm. These findings indicate that a patient treated with SVVH would pay an additional $62 (472 RMB), $73 (561 RMB) and $59 (452 RMB) respectively to gain 1% higher probability of each benefit. To summarize, the cost-effectiveness analysis can be ranked in the order of superior to inferior as SVVH only, SVVH plus PD, control and CVVH/LVVH only (Table 4).

In incremental cost-effectiveness analysis, the CVVH/LVVH only, SVVH plus PD and control arms were inferior to SVVH only arm in outcomes of overall survival and overall surgery preservation, while the CVVH/LVVH only and control arms were inferior to SVVH only and SVVH plus PD arms in the aspect of overall complication prevention (Table 4, Figure 2). The incremental C/complication prevention ratio of SVVH plus PD arm was $40385 (308941 RMB), which suggest that a patient treated with SVVH plus PD will pay an additional $404 (3089 RMB) compared to SVVH only to obtain a 1% higher probability of preventing complications.

Sensitivity analysis

SVVH plus PD was the closest to SVVH only in both cost and effectiveness. Therefore, we performed sensitivity analysis to compare SVVH only and SVVH plus PD arms by changing the survival rate and cost in their ranges (Figure 3). The variable range of survival rates of SVVH only and SVVH plus PD arms were 0.900-1.000 and 0.853-1.000 respectively, which were retrieved from our previous meta-analysis[14]. The range of cost is listed in Table 3. It is clear that there is overlapping in the variable areas of the two modalities. The minimal and maximal C/survival rate ratios were $2259 (17286 RMB) - $10399 (79570 RMB) and $5114 (39130 RMB) - $12453 (95286 RMB) in SVVH only and SVVH plus PD arms respectively. If in area A, SVVH only was superior to SVVH plus PD modality, the ratio of C/survival rate was less than $5114 (39130 RMB). By contrast, if in area B, SVVH plus PD was inferior to SVVH only, the ratio of C/survival rate was more than $10399 (79570 RMB).

DISCUSSION

Persistent SIRS, which is an early sign of SAP, is associated with MODS and even death[19]. About 50% of deaths in patients with SAP occur in the early stage of the disease; these patients experience a severe initial attack and develop an exaggerated SIRS with the development of MODS and death[20]. Therefore, several treatment modalities which target the inflammatory response in patients with SAP have been under consideration[21].

The onset and subsequent rapid deterioration seen in SAP is likely due to the over-production of pro-inflammatory cytokines, which are considered critical to the pathogenesis of the disease[14]. Thus, cytokines derived from macrophages are believed to play an integral role in the evolution of acute pancreatitis[22]. It has been suggested that the local pancreatic lesion activates macrophages to release pro-inflammatory cytokines[14,23]. This results in an

Table 4 Results of cost-effectiveness analyses ($/%)

Subsets	CVVH/LVVH only	SVVH only	SVVH plus PD	Control
C/Survival	$22122	$6167	$9224	$13785
C/Complication prevention	$25683	$7334	$9333	$19247
C/Surgery preservation	$20352	$5903	$8571	$16030
ΔC/ΔSurvival	Dominated	-	Dominated	Dominated
ΔC/ΔComplication prévention	Dominated	-	$40375	Dominated
ΔC/ΔSurgery preservation	Dominated	-	Dominated	Dominated

CVVH: Continuous veno-venous hemofiltration; LVVH: Long-term veno-venous hemofiltration; SVVH: Short-term veno-venous hemofiltration. SVVH only, the least costly arm, was selected as common baseline for other arms to reference to; PD: Peritoneal dialysis.

imbalance between pro- and anti-inflammatory cytokines, resulting in the development of SIRS. Some mediators, such as TNF-alpha, phospholipase, and kinin, are increased greatly in animal models of SAP[9], and some studies have shown that there is a significant correlation between the serum levels of IL-1-beta, IL-6, IL-8, IL-10 and IL-11 and the severity of acute pancreatitis[24-27]. Animal studies have shown that early blockade of the cytokine cascade at the level of the IL-1 receptor significantly decreases the severity of pancreatitis and intrinsic pancreatic damage, as well as the mortality from SAP[28,29]. Several antagonists of the inflammatory mediators have been used successfully in the laboratory setting and are currently being examined in prospective randomized trials[30]. The effectiveness of any antagonist depends not only on its ability to block the effects of the inflammatory mediators but also on its administration early enough in the course of the disease, before pancreatic necrosis and organ dysfunction sets in[30]. Thus, the inhibition of the cytokine cascade should potentially alleviate the pancreatic and systematic inflammation and improve the outcome of SAP.

The present cost analysis was carried out to determine the most economical and effective hemofiltration modality in China. CVVH has been considered as a potentially effective approach in the management SAP for nearly a decade. However, in China, both CVVH and LVVH are too costly for the common public. Thus, the less costly approach, SVVH was analyzed. Several clinical studies of SVVH administrated to patients with SAP in the early stage of the disease have been carried out in various institutions in China. However, these studies had limited scale of participation, were methodologically of poor quality (only a few studies were randomized) and very few discussed the cost outcomes. Therefore, our results may be biased by these confounding factors.

Our previous meta-analysis, based on controlled trials carried out in China indicated that early SVVH was effective and safe for SAP, but the efficacy of CVVH/LVVH could not be proven[14]. Our initial findings inspired us to explore further the role of other treatment modalities in decision making. The results of the present analysis showed that SVVH is the most suitable approach
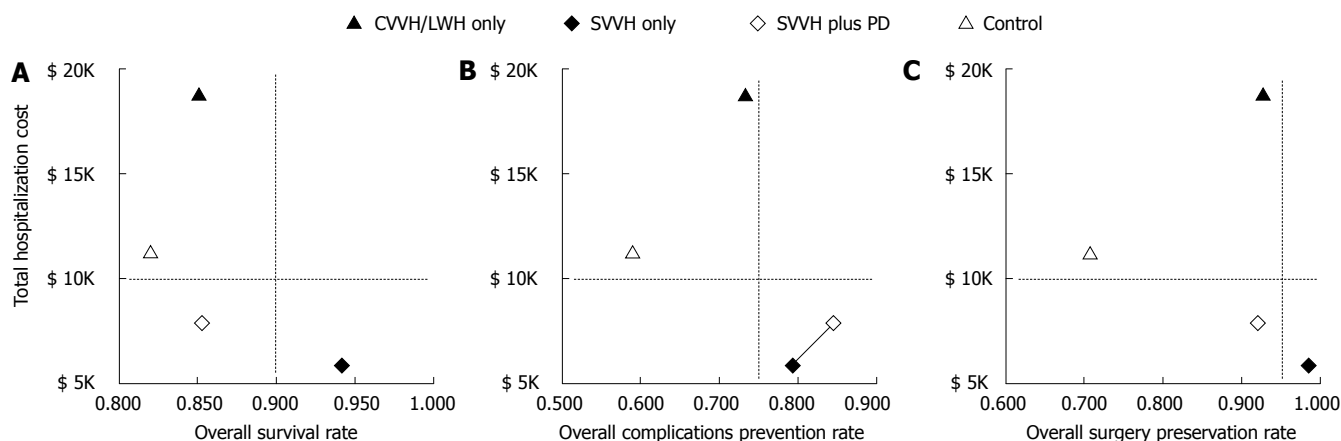
Figure 2 Cost-effectiveness analysis plots. **A**: Cost-survival ratio; **B**: Cost-complications prevention ratio; **C**: Cost-surgery preservation ratio.

in the treatment of SAP in China. The use of SVVH only would result in the best clinical outcome with reduction in the overall mortality, and prevention of complications and surgery. Furthermore, SVVH only modality is the least costly compared to other treatment options, including CVVH/LVVH only, SVVH plus PD and non-hemofiltration modalities. The CVVH/LVVH only and non-hemofiltration modalities were surpassed by SVVH only. The SVVH plus PD modality was fairly close to SVVH only in efficacy and cost, but SVVH was superior. However, the sensitivity analysis showed overlapping of the cost-effectiveness ratio between SVVH only and SVVH plus PD modalities. These findings suggest that SVVH is not entirely superior to SVVH plus PD, and SVVH plus PD should be considered as a suitable alternative option in China, and requires further investigation about its cost-effectiveness.

The timing of hemofiltration is considered as a critical factor in the outcome of patients with SIRS or sepsis. The subset of patients with these complications may benefit from the use of early short-term pulse hemofiltration[31]. The use of LVVH did not improve the prognosis but was associated with more side-effects than SVVH[11]. Another factor which may influence the outcome of patients with SIRS or sepsis is the ultrafiltration rate. It has been noted that the beneficial effects are greater with "very high" ultrafiltration rates ($\geq$ 100 mL/kg per hour)[31].

The benefit of VVH remains to be defined as an alternative therapy for SAP with SIRS or sepsis. A definite conclusion cannot be drawn because the studies have been small, are of poor quality and are heterogeneous in nature. Thus, there is no evidence in humans to recommend the use of VVH as an adjuvant therapy in patients with SAP. There continues to be uncertainty about the absolute indication, timing interval, dosing volume and the type of membrane required. Therefore, more randomized clinical trials are required before definite recommendations can be made about the clinical management of SAP. However, based on the present cost-effectiveness analysis in China, we suggest that the use of early short-term high-volume VVH is likely to play an important role in the management severe acute pancreatitis accompanied with SIRS, sepsis or organ failure.
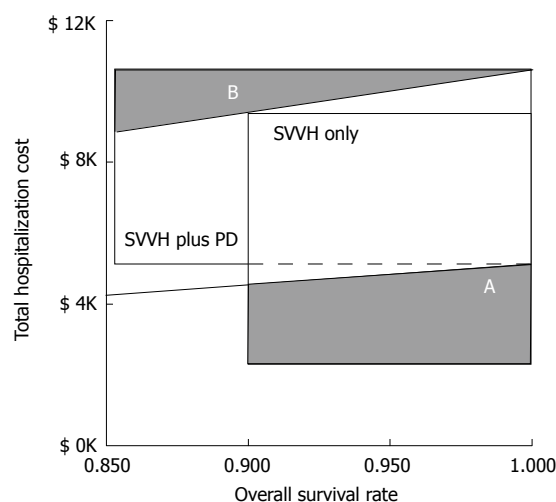

Figure 3 Two way sensitivity analysis of C/E ratio between SVVH only and SVVH plus PD modalities.

COMMENTS

Background

Nearly 50% of deaths in severe acute pancreatitis (SAP) occur during the early stage of the disease. These patients experience a severe initial attack and develop an exaggerated systemic inflammatory response syndrome (SIRS), with the development of multiple organ dysfunction syndrome (MODS) and death. Therefore, the role for therapy targeting the inflammatory response in SAP has been under much consideration recently.

Research frontiers

The onset and the poor outcome of SAP is likely due to the over-production of pro-inflammatory cytokines, which is considered as the critical factor in this condition. Inhibition of the cytokine cascade should potentially alleviate the pancreatic and systematic inflammatory response, and improve the outcome of SAP. Thus, veno-venous hemofiltration which can effectively eliminate the cytokines, has been used in the early management of SAP. Several different modalities of hemofiltration are available, but their effectiveness is controversial. In particular, expensive treatments should be used with much discretion in China, a developing country.

Innovations and breakthroughs

Based on our previous meta-analysis, early veno-venous hemofiltration may significantly reduce the overall mortality compared to no treatment. Analysis of different modalities showed that continuous or long-term veno-venous hemofiltration (CVVH/LVVH) and short-term veno-venous hemofiltration plus peritoneal dialysis (SVVH + PD) do not reduce the mortality significantly, whereas short-term only modality (SVVH only) was superior to other treatments in this

respect. A cost-effectiveness analysis based on the Chinese literature showed that SVVH only was the most cost-effective modality in reducing mortality, and in preventing complications and surgery. It can be implied that the timing of veno-venous hemofiltration should be regarded as a critical factor in the outcome of patients with SIRS or sepsis.

Applications

Early veno-venous hemofiltration is considered as an effective alternative therapy for SAP, although it is expensive for the general population in China. Based on the current evidence, hemofiltration can control to a certain extent SIRS and even MODS, if used during the early stage of the disease, with SVVH only the most cost-effective modality in China. We believe that early short-term high-volume veno-venous hemofiltration will play an important role in the management of SAP with SIRS, sepsis or organ failure.

Terminology

Severe acute pancreatitis (SAP) is a serious disease with intense pancreatic and systematic inflammation, seen in about 20% of patients with acute pancreatitis. Veno-venous hemofiltration removes waste products including cytokines by passing the blood through extracorporeal filters in the veno-venous access, which is categorized as continuous, long-term and short-term modalities based on the duration of hemofiltration.

Peer review

It is a well written article dealing with the cost-effective of veno-venous hemofiltration in the early treatment of SAP.

REFERENCES

1   **Heinrich S**, Schafer M, Rousson V, Clavien PA. Evidence-based treatment of acute pancreatitis: a look at established paradigms. *Ann Surg* 2006; **243**: 154-168

2   **Spitzer AL**, Barcia AM, Schell MT, Barber A, Norman J, Grendell J, Harris HW. Applying Ockham's razor to pancreatitis prognostication: a four-variable predictive model. *Ann Surg* 2006; **243**: 380-388

3   **Whitcomb DC**. Clinical practice. Acute pancreatitis. *N Engl J Med* 2006; **354**: 2142-2150

4   **Malangoni MA**, Martin AS. Outcome of severe acute pancreatitis. *Am J Surg* 2005; **189**: 273-277

5   **Carnovale A**, Rabitti PG, Manes G, Esposito P, Pacelli L, Uomo G. Mortality in acute pancreatitis: is it an early or a late event? *JOP* 2005; **6**: 438-444

6   **Knaus WA**, Draper EA, Wagner DP, Zimmerman JE. Prognosis in acute organ-system failure. *Ann Surg* 1985; **202**: 685-693

7   **Blinzler L**, Hausser J, Bodeker H, Zaune U, Martin E, Gebhardt C. Conservative treatment of severe necrotizing pancreatitis using early continuous venovenous hemofiltration. *Contrib Nephrol* 1991; **93**: 234-236

8   **DiScipio AW**, Burchard KW. Continuous arteriovenous hemofiltration attenuates polymorphonuclear leukocyte phagocytosis in porcine intra-abdominal sepsis. *Am J Surg* 1997; **173**: 174-180

9   **Yekebas EF**, Treede H, Knoefel WT, Bloechle C, Fink E, Izbicki JR. Influence of zero-balanced hemofiltration on the course of severe experimental pancreatitis in pigs. *Ann Surg* 1999; **229**: 514-522

10 **Otsuki M**, Hirota M, Arata S, Koizumi M, Kawa S, Kamisawa T, Takeda K, Mayumi T, Kitagawa M, Ito T, Inui K, Shimosegawa T, Tanaka S, Kataoka K, Saisho H, Okazaki K, Kuroda Y, Sawabu N, Takeyama Y. Consensus of primary care in acute pancreatitis in Japan. *World J Gastroenterol* 2006; **12**: 3314-3323

11 **Mao EQ**, Tang YQ, Zhang SD. Effects of time interval for hemofiltration on the prognosis of severe acute pancreatitis. *World J Gastroenterol* 2003; **9**: 373-376

12 **Labato MA**. Peritoneal dialysis in emergency and critical care medicine. *Clin Tech Small Anim Pract* 2000; **15**: 126-135

13 **Feng GH**, Cai Y, Jia PH, Yang QJ, Jia Z, Zhang J, Zhang XP. Combination of hemofiltration and peritoneal dialysis in the treatment of severe acute pancreatitis. *Zhonghua Waike Zazhi* 2004; **42**: 272-275

14 **Jiang K**, Chen XZ, Xia Q, Tang WF, Wang L. Early veno-venous hemofiltration for severe acute pancreatitis: a systematic review. *Zhongguo Xunzheng Yixue Zazhi* 2007; **7**: 121-134

15 **Liu SH**, Chen QS. Predictive goal of regulation of the residents' consumer price index in China. *Jingjishi* 2005; **10**: 50,52

16 **Mao EQ**, Tang YQ, Han TQ, Zhai HP, Yuan ZR, Yin HR, Zhang SD. Effects of short veno-venous hemofiltration on severe acute pancreatitis. *Zhonghua Waike Zazhi* 1999; **37**: 141-143

17 **Yang FF**, You YW, Lin X, Wang H, Lu GR, He MJ. Clinical observation of short-time hemofiltration and peritoneal dialysis on severe acute pancreatitis. *Youjiang Yixue* 2005; **33**: 233-234

18 **Zhang T**, Zhou L, Chen XQ, Zhang YH, Zhang ZL. Effectiveness evaluation of hemofiltration for severe acute pancreatitis. *Zhonghua Shiyong Zhongxiyi Zazhi* 2005; **18**: 1132-1133

19 **Mofidi R**, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. *Br J Surg* 2006; **93**: 738-744

20 **Bhatia M**, Wong FL, Cao Y, Lau HY, Huang J, Puneet P, Chevali L. Pathophysiology of acute pancreatitis. *Pancreatology* 2005; **5**: 132-144

21 **Nathens AB**, Curtis JR, Beale RJ, Cook DJ, Moreno RP, Romand JA, Skerrett SJ, Stapleton RD, Ware LB, Waldmann CS. Management of the critically ill patient with severe acute pancreatitis. *Crit Care Med* 2004; **32**: 2524-2536

22 **Kusske AM**, Rongione AJ, Ashley SW, McFadden DW, Reber HA. Interleukin-10 prevents death in lethal necrotizing pancreatitis in mice. *Surgery* 1996; **120**: 284-288; discussion 289

23 **Kusske AM**, Rongione AJ, Reber HA. Cytokines and acute pancreatitis. *Gastroenterology* 1996; **110**: 639-642

24 **Heath DI**, Cruickshank A, Gudgeon M, Jehanli A, Shenkin A, Imrie CW. Role of interleukin-6 in mediating the acute phase protein response and potential as an early means of severity assessment in acute pancreatitis. *Gut* 1993; **34**: 41-45

25 **Chen CC**, Wang SS, Lee FY, Chang FY, Lee SD. Proinflammatory cytokines in early assessment of the prognosis of acute pancreatitis. *Am J Gastroenterol* 1999; **94**: 213-218

26 **Chen CC**, Wang SS, Lu RH, Chang FY, Lee SD. Serum interleukin 10 and interleukin 11 in patients with acute pancreatitis. *Gut* 1999; **45**: 895-899

27 **Mentula P**, Kylanpaa ML, Kemppainen E, Jansson SE, Sarna S, Puolakkainen P, Haapiainen R, Repo H. Early prediction of organ failure by combined markers in patients with acute pancreatitis. *Br J Surg* 2005; **92**: 68-75

28 **Norman J**, Franz M, Messina J, Riker A, Fabri PJ, Rosemurgy AS, Gower WR Jr. Interleukin-1 receptor antagonist decreases severity of experimental acute pancreatitis. *Surgery* 1995; **117**: 648-655

29 **Norman JG**, Franz MG, Fink GS, Messina J, Fabri PJ, Gower WR, Carey LC. Decreased mortality of severe acute pancreatitis after proximal cytokine blockade. *Ann Surg* 1995; **221**: 625-631; discussion 631-634

30 **Denham W**, Norman J. The potential role of therapeutic cytokine manipulation in acute pancreatitis. *Surg Clin North Am* 1999; **79**: 767-781

31 **Bouman CS**, Oudemans-van Straaten HM, Schultz MJ, Vroom MB. Hemofiltration in sepsis and systemic inflammatory response syndrome: the role of dosing and timing. *J Crit Care* 2007; **22**: 1-12