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Original Article

A single-center experience of hemofiltration treatment for acute aortic dissection (Stanford type A) complicated with postoperative acute renal failure

Peng Qi[1], Xi-Quan Zhang[2], Xin-Yan Pang[1], Guang-Qing Cao[2], Chang-Cun Fang[2], Shu-Ming Wu[2]

[1]*Department of Cardiac Surgery, Intensive Care Unit, Qilu Hospital of Shandong University, Jinan, Shandong Province, China;* [2]*Department of Cardiac Surgery, Qilu Hospital of Shandong University, Jinan, Shandong Province, China*

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Abstract: Objective: To investigate the effect of continuous venovenous hemofiltration (CVVH) for aortic dissection patients with acute renal failure after surgery in retrospective manner. Methods: A total of thirty-seven aortic dissection patients with postoperative acute renal failure accepted CVVH therapy. The effect of CVVH was evaluated by analyzing clinical condition changes and laboratory examination results. Results: After treatment of CVVH, renal function and clinical symptoms were significantly improved in thirty patients. Eight of the thirty patients got completely renal function recovery within two weeks after CVVH therapy; and twenty-two of the thirty patients got completely renal function recovery within four weeks after CVVH therapy. Nevertheless, seven patients got no benefit from CVVH therapy with poor prognosis. Conclusion: CVVH is an effective treatment to most aortic dissection patients with postoperative acute renal failure. The effect of CVVH was correlated with original renal function, early CVVH therapy, and continuous intensive care.

Keywords: Aortic dissection, acute renal failure, continuous venovenous hemofiltration

Introduction

Along with economic development, the incidence of hypertension elevated gradually year by year in China [1]. Consequently, the incidence of aortic dissection (AD) also elevated year by year in China, especially in developed districts of China. AD occurs when blood pressure dramatically increases and blood flow into media through intimal tear of aorta causing separation of two layers as well as false lumen formation [2]. Subsequently, the true lumen of aorta may be oppressed or even occluded by the false lumen, which result in severe complications including acute renal failure, limb ischemia, brain ischemia, ischemic bowel disease, and even death [3]. The most dangerous complication of AD is dissection rupture which accompanied by hemorrhagic shock [4]. This disease has high inhospital mortality rate ascribe to fast progress course and hard to make accurate diagnosis in time [5]. According to Stanford classification, AD is divided into type A and type B [6]. Stanford type A AD characterized by intimal tear located at ascending aorta and/or aorta arch, while Stanford type B with intimal tear located at descending aorta [7]. Stanford type A AD patients need surgery treatment while Stanford type B can be cured by endovascular stent placement [8]. Besides, Stanford type A accounts for approximate 2/3 of all AD patients [9].

In the present study, we focused on postoperative treatment for Stanford type A aortic dissection (AD) patients.

Acute renal failure and multi-organ dysfunction syndrome (MODS) are main causes of death in postoperative AD patients [10]. Postoperative AD patients complicated with acute renal failure usually characterized by diuretics invalid. It is very difficult to treat these patients with common medications [11].

Continuous renal replacement therapy (CRRT) is widely applied in intensive care unit and often considered as preferable treatment in acute renal failure patients [12]. Continuous venovenous hemofiltration (CVVH) belongs to CRRT and often be used to eliminate moderate and small molecule substance with less influence on hemodynamics [13].

However, studies on CVVH treatment for postoperative AD patients complicated with acute renal failure remain insufficient [14]. Thus, we investigated the effect of continuous venovenous hemofiltration (CVVH) for AD patients with acute renal failure after surgery [15]. In the present study, we found that CVVH was an effective treatment to most AD patients with postoperative renal failure. The effect of CVVH was correlated with original renal function, early CVVH therapy, and continuous intensive care.

Materials and methods

Patients

We analyzed clinical data of 37 AD patients who complicated with acute renal failure after surgery retrospectively. All the 37 AD patients were diagnosed and treated at Qilu Hospital of Shandong University from May 2010 to October 2014. All the 37 patients accepted CVVH therapy in predilution mode. There was no patient with increased bleeding risk (defined as platelet count below 40×10^9/L, and activated partial thromboplastin time (APTT) longer than 60 seconds). There were 27 male patients and 10 female patients in our study group. The patients were aging from 39 to 72 years old, with average age 57.8 ± 14.1 years old. All the patients had history of hypertension but without standard treatments. The cardiac function of all 37 patients was nearly normal. All the 37 patients had severe chest pain but without shock, rupture or cardiac tamponade. These patients were diagnosed and classified using enhanced CT scan examination.

Study protocol and data collection

12 patients accepted ascending aorta vessel replacement therapy and 13 patients accepted aortic arch replacement treatment. 7 patients accepted Bentall procedure plus with aortic arch replacement and 5 patients accepted Bentall procedure only.

We carried out initial medical management as followed, controlling blood pressure, focusing on heart rate, and relieving pain. Besides, we also monitored the patients' hemodynamic change and mental change continuously. The patients were stabilized soon with blood pressure down to about 100-120/75-90 mmHg using beta receptor blockers or vasodilators. We also used morphine or pethidine to relieve patients' pain and anxiety. The blood pressure, arterial oxygen saturation, blood gas analysis record, blood electrolyte, renal function (include creatinine, blood urea nitrogen), intake and output volume of AD patients before and after operation were monitored and detailed recorded.

The CVVH device was manufactured by Plasauto (Japan) which labeled IQ21. The bicarbonate-buffered hemofiltration replacement solution was supplied by the Blood Purification Center of Qilu Hospital of Shandong University. All the patients were injected with furosemide at dose of 0.1-0.5 mg/kg/h but with urine volume less than 0.5 ml/kg/h as a result. Therefore, the diuretic treatment was invalid for these patients in our research. In other words, the patients in our study were suitable for CVVH treatment. We constructed vascular passage successfully using Seldinger method and dwelled double lumen catheter subsequently. The therapy mode was set as CVVH, acted as anticoagulation and buffer in predilution mode. Patients anticoagulated with low molecular heparin (manufactured by Qilu Pharmaceuticals, Shandong, China) at initial dose of 2500 IU prior to the beginning of CVVH. The continuous injection of low molecular heparin was given at dose of 500 IU per hour and adjusted targeting a systemic APTT of fifty seconds. In patients with low molecular heparin treatment, the APTT was determined every 6 to 8 hours. The blood flow was maintained at level of 150-200 ml/min using blood pump and replacement fluid input flow was maintained at 1900-2800 ml/h. The hyperfiltration volume and treatment time were determined by patients' volume load and concrete condition. The average hyperfiltration volume was about 150-250 ml/h. The severe hemorrhagic tendency in patients was endpoint of heparin treatment.

Standard of diagnosis of AD and acute aortic dissection

1. Clinical diagnosis 1.1 severe chest and back pain history; 1.2. Blood pressure difference

Table 1. Renal function improved in renal failure patients after CVVH therapy

	Before CVVH	After CVVH			
		6 h	12 h	24 h	48 h
BUN (mmol/L)	23.9 ± 4.12	16.98 ± 3.13*	12.59 ± 2.29*	10.60 ± 1.89*	9.86 ± 1.78*
Cr (μmol/L)	398.2 ± 56.3	234.19 ± 47.82*	199.36 ± 35.6*	165.32 ± 52.31*	157.32 ± 36.9*

*Before CVVH VS After CVVH, $P < 0.05$.

Table 2. Oxidative stress damage relieved in renal failure patients after CVVH therapy

	Before CVVH	After CVVH			
		6 h	12 h	24 h	48 h
APACHE III	79.6 ± 16.1	74.9 ± 16.1	68.3 ± 11.1*	62.8 ± 11.2*	59.9 ± 11.2*
MODS score	9.2 ± 3.3	9.6 ± 3.82	9.3 ± 1.6	8.2 ± 4.31*	8.1 ± 3.9*
MDA (μmol/L)	9.8 ± 5.3	9.8 ± 4.31	9.3 ± 3.2	8.1 ± 2.2	7.8 ± 3.3*
SOD (nU/mL)	142.2 ± 41.3	134.19 ± 42.82	134.36 ± 41.6	113.32 ± 40.31*	112.2 ± 40.9*
GSH-Px (U/L)	143.2 ± 21.1	130.9 ± 31.91*	122.3 ± 31.1*	132.9 ± 31.2*	132.8 ± 41.2*

*Before CVVH VS After CVVH, $P < 0.05$.

Table 3. Electrolyte disturbance of renal failure patients were improved after CVVH therapy

	Before CVVH	After CVVH			
		6 h	12 h	24 h	48 h
Glu (mmol/L)	7.2 ± 1.1	6.9 ± 0.91	7.0 ± 1.1	6.8 ± 1.2	6.9 ± 1.2
Na (mmol/L)	139.2 ± 11.3	134.19 ± 12.82	139.36 ± 11.6	138.32 ± 10.31	139.32 ± 10.9
K (mmol/L)	5.5 ± 0.3	4.3 ± 0.31*	3.9 ± 0.2*	3.7 ± 0.2*	3.8 ± 0.3*
Cl (mmol/L)	102.2 ± 11.3	104.19 ± 12.82	101.36 ± 11.6	103.32 ± 10.31	99.32 ± 10.9
HCO_3 (mmol/L)	23.2 ± 1.1	21.9 ± 1.91	22.3 ± 1.1	22.9 ± 1.2	22.8 ± 1.2

*Before CVVH VS After CVVH, $P < 0.05$.

among limbs, murmur of aortic valve, paradoxical pulse, symptoms of heart failure [16].

2. Plain X-Ray diagnosis, we can found mediastinal shadow enlargement in aortic dissection patients, however, this sign is nonspecific [16].

3. CT diagnosis, CT examination is of great value and necessary for diagnosis of aortic dissection. We can classify aortic dissection into communicating dissection and non-communicating dissection according to CT scan findings. In communicating dissection patients, the false lumen cannot be visualized in early-phase contrast ascribed to slow blood flow; Therefore, it is necessary to obtain late contrast-enhanced CT images. In non-communicating dissection patients, CT images are featured by the presence of a false lumen, the false lumen presented as a crescent or annular shadow. The false lumen shadow might show higher density than the true lumen on plain CT images [16].

4. Ultrasonography is useful for diagnosis of aortic dissection especially in patients with renal failure or allergy to contrast drug. Ultrasonography are usually used to evaluate branch dissection and complications of dissection. The cardiac tamponade, aortic valve regurgitation, cardiac function of AD patients can be evaluated by Ultrasonography [16].

5. MR/MRA diagnosis, We can evaluate any section of vascular wall and lumen without the use of contrast agents through Magnetic resonance imaging (MRI) examination. The most common procedure for aorta is contrast-enhanced MRA (Magnetic resonance angiography). The MRA views of AD characterized by flexed part and turbulent part of blood flow in the lumen. Compared with MR method, MRA is advantageous in that a shorter imaging time is required [16].

Statistical analysis

Demographic data and medical conditions of the patients were analyzed to compare the differences between the patients before and after

Table 4. CVVH caused no significant hemodynamic change in renal failure patients

	Before CVVH	After CVVH			
		6 h	12 h	24 h	48 h
HR/min	133 ± 16.1	104.9 ± 16.1*	95.3 ± 10.1*	92.8 ± 11.2*	95.9 ± 9.2*
MAP mmHg	10.2 ± 0.3	10.6 ± 0.82	9.9 ± 0.6	10.2 ± 0.31	9.8 ± 0.5
CVP (mmHg)	12.8 ± 3.3	12.8 ± 3.31	12.3 ± 2.2	13.1 ± 3.2	11.8 ± 2.3
PAWP (mmHg)	16.89 ± 2.82	16.3 ± 2.6	17.2 ± 3.31	16.9 ± 2.9	17.2 ± 2.3

*Before CVVH VS After CVVH, P < 0.05.

Table 5. Oxygenation index of renal failure patients were improved after CVVH therapy

	Before CVVH	After CVVH			
		6 h	12 h	24 h	48 h
PaO_2/FiO_2	233.9 ± 49.2	300.8 ± 63.3*	362.9 ± 62.9*	350.6 ± 51.9*	363.8 ± 41.8*
PaO_2/FiO_2	4.3 ± 0.3	3.9 ± 0.8	4.1 ± 0.8	4.2 ± 0.3	4.3 ± 0.2

*Before CVVH VS After CVVH, P < 0.05.

CVVH. We used mean ± SD to describe numerical variables and count (percentage) for categorical variables according to descriptive statistics. *P* values from one-way ANOVA or two-group student *t* tests for numerical variables were reported.

Statistical tests were performed using two-sided tests at the 0.05 level of significance. All analyses were performed using SPSS software version 16.0. Actually, the statistical significance of differences between after and before CVVH in **Tables 1-5** were analyzed using two-group student *t* tests method. Besides, the statistical significance of differences between after and before CVVH in **Table 2** was analyzed using one-way ANOVA method.

Results

Outcome of patients

All the 37 patients were diagnosed by enhanced CT examination (**Figure 1**). The mean CVVH treatment time for renal failure patients was about 80.3 hours and CVVH treatment was carried out three times a week. In our study, a total of 37 patients with postoperative acute renal failure accepted CVVH therapy, and ultimately 30 patients achieved recovery of renal function. There were 7 patients got no sign of relief after CVVH therapy and died in the end. Among the 30 patients who responded valid to CVVH therapy, 8 patients of them got urine volume returned to normal within 5 to 10 days and renal function return to normal within two weeks. Besides, 22 patients of them got urine volume returned to normal within 14 to 20 days and renal function returned to normal within 4 weeks.

Renal function improved in renal failure patients after CVVH therapy

Aside from urine volume, serum creatinine and urea nitrogen are important evaluation indicators for renal function. In our study, we found that the patients' serum creatinine and urea nitrogen level were gradually declined after CVVH therapy which suggested that patients' renal function were improved by CVVH therapy (**Table 1**).

Oxidative stress damage relieved in renal failure patients after CVVH therapy

We used APACHE III score [17], MODS score, methane dicarboxylic aldehyde (MDA) level, superoxide dismutase (SOD) level and glutathione (GSH) level to evaluate oxidative stress damage of renal failure patients. Our results showed that oxidative stress damage indicators (above) were gradually reduced after CVVH therapy in postoperative acute renal failure patients which indicated an alleviation of oxidative stress damage by CVVH therapy (**Table 2**).

Electrolyte disturbance of renal failure patients were improved after CVVH therapy

Electrolyte disturbance is a main cause of poor prognosis in renal failure patients. Our results

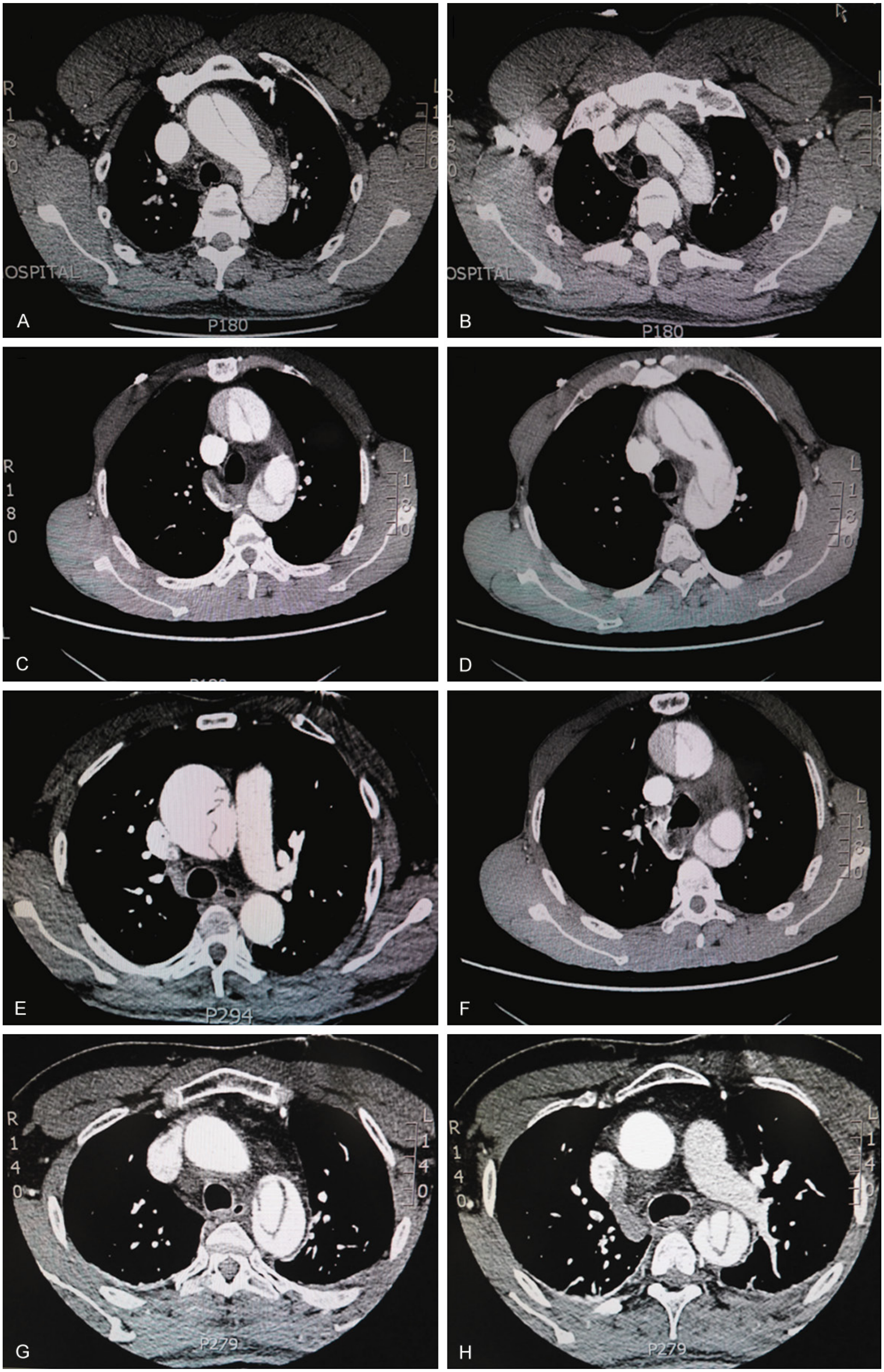
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Figure 1. A-F were representative images of Stanford type A AD; G, H were representative images of Stanford B AD.

demonstrated that patients' electrolyte disturbance such as hyperkalemia was effectively corrected after CVVH therapy (**Table 3**).

CVVH caused no significant hemodynamic change in renal failure patients

The patients' hemodynamic change can be reflected by mean arterial pressure (MAP), central venous pressure (CVP), pulmonary artery wedge pressure (PAWP). Our results illustrated that patients' hemodynamic indicators were basically unchanged during and after CVVH therapy. Therefore, CVVH had no obvious effect on hemodynamics (**Table 4**).

Oxygenation index of renal failure patients were improved after CVVH therapy

Hypoxemia and carbon dioxide retention are main causes of death in renal failure patients. Hypoxemia can be reflected by ratio of arterial partial pressure of oxygen (PaO_2) and fraction of inspired oxygen (FiO_2). Besides, carbon dioxide retention can be indicated by arterial partial pressure of carbon dioxide ($PaCO_2$). We found that patients' hypoxemia and carbon dioxide retention were significantly improved after CVVH therapy (**Table 5**).

Discussion

AD is a disease of aorta media layer which characterized with separation of aorta layers [18]. The blood flow into media layer through intimal tear and form false lumen [19]. The dissection may spread antegrade or retrograde or bidirection and cause dissection of aorta branch vessels and severe hemodynamic change [20]. The clinical manifestation is sudden severe thoracic pain, which can be misdiagnosed as acute coronary syndrome [21]. The severe complications of AD are disturbance of consciousness, internal hemorrhage, renal failure, small intestine ischemia or necrosis, limb ischemia or even death [22]. Through anatomized the patients' chief complaints, we found that AD patients often described their pain as 'sharp, or tear, or rip' and their thoracic pain was more severe than myocardial infarction patients [23]. Due to fast progression and difficulty of accurate diagnosis, the AD patients had high mortality [24]. The incidence of AD is about five/million/year according to data from International Society for Acute Aortic Dissection [25]. The most important method for accurate diagnosis of AD is enhanced CT scan. Among AD patients, the most prevalent risk factors are hypertension, age, diabetes mellitus, atherosclerosis, male gender, aortic aneurysm, smoking, and prior heart operations [26].

AD is typically classified according to dissection location [27]. The DeBakey's classification system based on the tear site and spread of dissection was gradually superseded by Stanford classification system [28]. According to Stanford classification system, AD was classified into type A and type B [29]. The Stanford type A AD includes all directions involving the ascending aorta, regardless of dissection origin [30]. Besides, the type B AD only involved descending aorta [31]. In AD patients, type A accounts for about 2/3, while type B accounts for about 1/3. Stanford type B AD patients usually accept stent implantation treatment and type A AD patients have no choice but to accept thoracotomy treatment [32].

The Stanford type A patients are apt to develop acute renal failure after surgery [33]. The main causes of postoperative acute renal failure were summarized as followed. First, some AD patients had poor basic renal function due to diabetic nephropathy or other chronic nephropathy [34]. Second, the renal blood flow and perfusion were insufficient during extracorporeal circulation [35]. Besides, the red blood cells can be destroyed during extracorporeal circulation and plenty of free hemoglobin may cause obstruction of renal tubules and decrease of glomerular filtration rate [36]. Moreover, the blood can be diluted during extracorporeal circulation and cause decline of oxygen carrying capacity and aggravated kidney damage [37]. In addition, patients who accepted cardiac surgery often complicated with postoperative low cardiac output syndrome which cause low renal perfusion and promote renal failure [38]. We often use plenty of booster drugs which may cause contraction of renal artery and renal ischemia during perioperative period [39]. Once the postoperative acute renal failure occurs, the patients' urine volume will decline quickly which leads to fast progression of heart failure or even death [40]. More and more experts advocate early CVVH therapy for postoperative acute renal failure patients [41].

The CT images are representative pictures of Stanford type A aortic dissection patients (**Figure 1**). Through CT scanning examination, we can make accurate diagnosis of aortic dissection and its types which contribute to appropriate and timely clinical treatment of this disease. In our study, we found that renal function of aortic dissection patients were remarkably improved after CVVH therapy (**Table 1**). This result indicated that CVVH was an effective treatment for aortic dissection patients who suffered from renal failure. APACHE III score system and MODS score system are usually used to evaluate clinical condition of critical patients. The APACHE III score less than or equal to twenty score means serious condition. Besides, APACHE III score less than fifty score and more than twenty score means severe condition. Moreover, APACHE III more than or equal to fifty score means critical condition [17]. The MODS score range from nine to twelve means mortality less than twenty-five percent. MODS score range from thirteen to sixteen means mortality less than fifty percent. MODS score range from seventeen to twenty means mortality less than seventy-five percent and more than fifty percent [42]. Moreover, the MODS score more than twenty means mortality up to one hundred percent. In our study, we observed that APACHE III and MODS score decreased significantly after CVVH treatment (**Table 2**). Besides, the MDA, SOD and GSH level which reflect oxidative stress injury were significantly decrease in aortic dissection patients after CVVH therapy. These results indicated that patients' condition improved and oxidative stress injury alleviated after CVVH therapy. From the results above, we can found that patients' serum kalium level were significantly declined after CVVH (**Table 3**). The high serum kalium level is one of the most dangerous factors caused by renal failure. The drop of serum kalium level caused by CVVH therapy will lead to improvement of prognosis in aortic dissection patients. The common blood purification therapy used for renal failure includes hemofiltration [42] and hemodialysis [43]. Compared with hemodialysis, hemofiltration has better curative effect on renal failure and pneumonedema [44]. The hemodynamic changes during hemofiltration treatment are more gently than hemodialysis [45-47]. The patients who accepted hemofiltration treatment have little incidence of low blood pressure [48]. The input of intravenous fluid and intake of protein are not to be strictly confined during CVVH therapy [49]. Our result also showed that CVVH had no significant influence on hemodynamics of aortic dissection patients (**Table 4**). The stability of hemodynamics is very important for postoperative aortic dissection patients. Due to no significant influence on hemodynamics, the application of CVVH for postoperative aortic dissection patients are of no limit. In our current study, we showed that patients' oxygenation condition was improved remarkably after CVVH treatment (**Table 5**). The improvement of oxygenation condition indicated better prognosis of postoperative aortic dissection patients. Recently, patients with postoperative acute renal failure are recommended to accept CVVH therapy [50].

By analysis of seven patients who were invalid against CVVH in our study, we found that these patients were complicated with severe postoperative multi-organ dysfunction syndrome (MODS) and with very poor prognosis. Therefore, we concluded that it's very important to avoid nephrotoxic drugs, maintain renal perfusion, short operation time and extracorporeal circulation time, perform intensive postoperative care, carry out CVVH early for improving patients' prognosis. In summary, CVVH is effective for most AD patients with postoperative acute renal failure. Besides, the curative effect of CVVH is related to basic renal function, beginning time of CVVH and continuous intensive care.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Shu-Ming Wu, Department of Cardiac Surgery, Qilu Hospital of Shandong University, Jinan, Shandong Province, China. Tel: +86-0531-82166510; Fax: +86-0531-82166512; E-mail: 280715708@qq.com

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