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Analysis of the Effect of Renal Replacement Therapy: In the Prolonged Extracorporeal Membrane Oxygenation Patients

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Background: This paper aimed to verify the effects of renal replacement therapy on changing the levels of serum creatinine for different veno-arterial and veno-venous configurations in prolonged extracorporeal membrane oxygenation (ECMO) patients. ***Methods:*** The subjects were chosen 71 patients who had undergone more than 1,440 minutes (24 hours) of the therapy from among 117 patients who had undergone ECMO insertion between January 2008 and December 2012. The patients were separated into the veno-arterial configuration group I (51 patients) and the veno-venous configuration group II (20 patients). The difference in the level of serum creatinine ($\triangle$Cr) between before or just after ECMO insertion (Cr_I) and the level when the pump time was between 2,880 and 4,320 minutes (Cr_F) was checked ($\triangle Cr=Cr_F-Cr_I$), and the average $\triangle$Cr for each group was compared using a Student t-test at the confidence interval (CI) of 95%. ***Results:*** The change in the level of serum creatinine was an increase of 0.341 mg/dL (σ=0.9202) for group I and a decrease of 0.120 mg/dL (σ=1.5292) for group II. The change was significantly high for group I (p=0.011, CI=95%). Meanwhile, within group I, when renal replacement therapy was not done, there was a significant increase in the level of serum creatinine (p=0.009, CI=95%). ***Conclusion:*** For ECMO insertion patients whose pump time was more than 1,440 minutes, there was a significant change in the level of serum creatinine when renal replacement therapy was not done, for the veno-arterial configuration of group I.

Key words: 1. Extracorporeal membrane oxygenation
2. Pulsatile flow
3. Renal replacement therapy
4. Renal insufficiency
5. Ultrafiltration

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) or extracorporeal life support refers to techniques that provide assistance in respiratory and/or cardiac functions [1]. Circulation support devices for acute cardiorespiratory failure patients have recently been in rapid development. Among these methods, ECMO is considered to have great success in providing emergency treatment of severe cardiac and respiratory failure patients [2]. However, this method is used as a bridge until recovering of cardiopulmonary function, a more permanent device is used, or the period of waiting for organ transplantation. A conventional ECMO device is an external circulation support device that uses a centrifugal pump and an oxygenator.

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Table 1. Underlying medical condition of the patient who received an extracorporeal membrane oxygenation insertion over 1,440 minutes (n=71)

Variable	Group I (n=51)	Group II (n=20)	Overall (n=71)
Chronic renal failure	7 (13.72)	2 (10.00)	9 (12.68)
Diabetes mellitus	8 (15.69)	9 (45.00)	17 (23.94)
Atrial fibrillation	2 (3.92)	1 (5.00)	3 (4.23)
Hypertension	11 (21.57)	7 (35.00)	18 (25.35)
Congestive heart failure	2 (3.92)	2 (10.00)	4 (5.63)

Values are presented as number (%).

There is a difference in interpretation between research groups on whether the continuous flow of ECMO causes damage in end organs [3-5]. However, renal failure is a common complication among patients who undergo an ECMO insertion. This study aimed to verify whether renal replacement therapy (RRT), which includes ultrafiltration and continuous renal replacement therapy (CRRT), is a useful modality for renal function preservation in prolonged ECMO insertion patients.

METHODS

1) Study population

From among 117 patients who underwent an ECMO insertion procedure between January 2008 and December 2012, 71 patients who had a pump time of more than 1,440 minutes (24 hours) were chosen as subjects. The ages of the patients at the time of the procedure were 49±40 years, and the ratio of men to women was 41:30. They were divided into a patient group who had a veno-arterial (VA) configuration performed (group I, n=51) and a patient group that had a veno-venous (VV) configuration performed (group II, n=20). The mean values of the ECMO pump time was 4,391 minutes (range, 1,493 to 5,455 minutes) for group I and 5,448 minutes for group II (range, 5,835 to 21,715 minutes). Among these 71 patients, 9 patients (12.68%) were diagnosed with chronic renal failure, 17 with diabetes mellitus (23.94%), 3 with atrial fibrillation (4.23%), 18 with hypertension (25.35%), and 4 with congestive heart failure (5.63%) (Table 1). The difference between the level of serum creatinine before or just after ECMO insertion (Cr_I) and the level of serum creatinine (Cr_F) between the pump time of 2,880 minutes and that of 4,320 minutes ($\triangle Cr=Cr_F-Cr_I$) was checked, and the average $\triangle Cr$ for each group was compared using a Student t-test at the significant level of confidence interval. When the pump time was between 1,440 and 2,880 minutes, the latest time was used. The average interval between the two serum creatinine measurement times was 2,284 minutes (σ=1.268).

2) Technique

The procedure used was femoro-femoral cannulation in 58 patients and femoro-jugular (or subclavian) cannulation in 13 patients. Each cannula was inserted using Seldinger's technique. Three patients from group I (5.88%) underwent femoro-jugular cannulation, and 10 patients from group II (50.00%) underwent the same procedure. The operation was conducted by 4 surgeons; the equipment used was Terumo Capiox EBS (SP-101; Terumo Inc., Tokyo, Japan), the membrane and circuit used was the Terumo EBS Capiox oxygenator kit, and the Cannula used was Medtronic Inc. (Minneapolis, MN, USA) or Edwards Lifescience Co. (Irvine, CA, USA).

3) Follow-up

Among the abovementioned 71 subject patients, 25 patients (35.21%) had success in achieving ECMO weaning. Eighteen patients in group I (35.29%) and 7 patients in group II (35.00%) had success in achieving weaning.

4) Statistical analysis

The research subjects were separated on the basis of their ECMO configuration (group I and group II), and the average change in the level of serum creatinine was compared using a Student t-test. Also the average change in the level of serum creatinine based on performing RRT without ECMO configuration (group A and group B) was compared using the Student t-test as well. In addition, the change in the level of serum creatinine was compared for each group separated on

Table 2. Basal characteristics based on the extracorporeal membrane oxygenation configuration

Characteristic	Group I (veno-arterial configuration) (n=51)	Group II (veno-venous configuration) (n=20)
Male:female	26:25	15:5
Mean age (yr)	66.04	62.65
Mean pump time (min)	4,391	5,448
Weaning case	18 (35.29)	7 (35.00)
Death	33 (64.71)	13 (65.00)

Values are presented as number or number (%).

Table 3. A comparison in the change in the serum creatinine based on the ECMO configuration

Variable	Group I (veno-arterial configuration)		Group II (veno-venous configuration)	
	Variate (mg/dL)	p-value (95% CI)	Variate (mg/dL)	p-value (95% CI)
Comparison by ECMO configuration	0.3412±0.9202	0.011 (0.082 to 0.600)	-0.120±1.5292	0.729 (-0.836 to 0.596)

Values are presented as mean±standard deviation.
ECMO, extracorporeal membrane oxygenation; CI, confidence interval.

Table 4. Basal characteristics based on whether RRT was used

Characteristic	Group A (perform RRT) (n=36)	Group B (did not perform RRT) (n=35)
Male:female	26:10	15:20
Mean age (yr)	63.81	62.40
Mean pump time (min)	4,579	4,801
Weaning case	11 (30.56)	14 (40.00)
Death	25 (69.44)	21 (60.00)

Values are presented as number or number (%).
RRT, renal replacement therapy.

the basis of the ECMO configuration according to whether RRT (group IA, group IB and group IIA, group IIB) was conducted by using a Student t-test. The significance level was set at CI=95% (p-value≤0.05). A statistical analysis of all data was performed by using PASW SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

1) Comparison of the change in serum creatinine based on the extracorporeal membrane oxygenation configuration

The average age for group I and group II was 66.04 years and 62.65 years, respectively, and the pump time was 4,391 minutes and 5,448 minutes for each group, respectively (Table 2). The change in the level of serum creatinine (△Cr) was increased by 0.3412 mg/dL (σ=0.9202) in group I and decreased by 0.1200 mg/dL (σ=1.5292) in group II. In the end, it was found that serum creatinine increased significantly for group I (VV configuration) (95% CI, 0.082 to 0.600; p=0.011) (Table 3).

2) Comparison of the change in serum creatinine based on whether renal replacement therapy was used

Irrespective of the ECMO configuration, the change in the level of serum creatinine was compared by separating the patient group that received RRT (group A, n=36) and the group that did not (group B, n=35). The average age of group A and group B was 63.81 years and 62.40 years, respectively, and the average pump time for each group was 4,579 minutes and 4,801 minutes, respectively (Table 4). The change in the level of serum creatinine was 0.1028 mg/dL (σ=1.4423) in

Table 5. A comparison the change in serum creatinine based on whether RRT

Variable	Group A (perform RRT)		Group B (did not perform RRT)	
	Variate (mg/dL)	p-value (95% CI)	Variate (mg/dL)	p-value (95% CI)
Comparison by perform RRT	0.1028±1.4423	0.672 (-0.385 to 0.591)	0.3229±0.6907	0.009 (0.086 to 0.560)

Values are presented as mean±standard deviation.
RRT, renal replacement therapy; CI, confidence interval.

Table 6. Basal characteristics based on whether renal replacement therapy was conducted for each ECMO configuration

Variable	Group I (veno-arterial configuration)		Group II (veno-venous configuration)	
	Group IA (VA & RRT) (n=22)	Group IB (VA only) (n=29)	Group IIA (VV & RRT) (n=14)	Group IIB (VV only) (n=6)
Male:female	10:12	16:13	10:4	5:1
Mean age (yr)	66.45	60.90	60.93	66.67
Mean pump time (min)	4,020	4,672	5,457	5,425
Weaning case	5 (22.73)	13 (44.83)	5 (35.71)	2 (33.33)
Death	17 (77.27)	16 (55.17)	9 (64.28)	4 (66.67)

Values are presented as number or number (%).
ECMO, extracorporeal membrane oxygenation; VA, veno-arterial configuration ECMO; RRT, renal replacement therapy; VV, veno-venous configuration ECMO.

Table 7. A Comparison in the change in the serum creatinine based on whether RRT was conducted for each ECMO configuration

Variable	Group I (veno-arterial configuration)		Group II (veno-venous configuration)	
	Variate (mg/dL)	p-value (95% CI)	Variate (mg/dL)	p-value (95% CI)
Group A (perform RRT)	0.3136±1.1720	0.223 (-0.206 to 0.833)	-0.2290±1.7856	0.0640 (-1.260 to 0.802)
Group B (ECMO only)	0.3621±0.6951	0.009 (0.098 to 0.626)	0.1333±0.6976	0.659 (-0.599 to 0.865)

Values are presented as mean±standard deviation.
ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy.

group A and 0.3229 mg/dL (σ=0.6907) in group B. In the end, it was found that serum creatinine increased significantly for group B (without RRT, irrespective of the ECMO configuration) (95% CI, 0.086 to 0.560; p=0.009) (Table 5).

3) Comparison of the change in serum creatinine based on whether renal replacement therapy was performed for each extracorporeal membrane oxygenation configuration

Group I and group II were divided on the basis of the ECMO configuration, and each group was further divided into two groups (group IA and group IIA) that had RRT such as ultrafiltration and CRRT performed and groups that did not (group IB and group IIB). The change in the serum creatinine of the four groups was then compared. Upon analysis, when RRT was not conducted in group I, there was a statistically significant increase in the average change in the level of serum creatinine, which was 0.3621 mg/dL (95% CI, 0.098 to 0.626; p=0.009) (Tables 6, 7).

DISCUSSION

ECMO is a very important initial treatment modality for cardiorespiratory patients. However, ECMO can induce not only terminal organ damage due to non-pulsatile perfusion but also many complications such as bleeding by coagulop-

athy, peripheral ischemia, air embolism, and thromboembolism [1]. The present research was performed by focusing on whether the renal function is preserved when exposed to non-pulsatile perfusion. According to Rossi et al. [3], if adequate perfusion pressure is maintained, the function of organs is surprisingly well preserved [4]. However, according to Askenazi et al. [6], approximately 70% to 85% of all ECMO patients become candidates for RRT. In this study as well, it was found that irrespective of the ECMO configuration, when RRT was not done, the level of serum creatinine increased significantly, and for the VA configuration in particular, when RRT was not done, the increase in serum creatinine was significantly higher than with RRT.

RRT in ECMO patients is conducted by inserting a hemofilter or CRRT between the ECMO circuits. Damage to kidneys is delayed since RRT maintains the fluid balance and controls the metabolites.

In the case of VA configuration, the cardiac output consists of the mixture of native cardiac flow and ECMO pump flow, and the blood pressure and flow generally increase in major organs including the kidneys [6]. In contrast, in the case of VV configuration, the effect on the blood pressure and blood flow of major organs is relatively low. Moreover, vasoconstrictors, inotropes, or the like are often used in the case of VA configuration, which suddenly changes the hemodynamics of the kidney, resulting in the exposure of the kidney to ischemia-reperfusion injury [5].

In the present research, the epidemiology of the patients is inaccurate since the medical history of the patients is not reliable due to the fact that a significant number of the patients were admitted through emergency medical services and cardiopulmonary resuscitation was performed in many cases. Thus, it is difficult to state that the numerical values of the initial serum creatinine were baseline values. Furthermore, although the overall patient death rate was 64.79%, the VA configuration with RRT group (group IA) had the highest death rate, at 77.27%. Although an inference can be made that the death rate is high for the VA configuration with the RRT patient group (group IA) attributable to the fact that the underlying diseases of the patients who were sent to emergency room (ER) were not properly understood and the fact that an overwhelming majority of the VA configuration patient group was sent to ER due to cardiac arrest, it ultimately remains a limitation of this study. Moreover, standardization did not occur, (the laboratory value, follow-up time, equipment, flow rate, etc.), they exist as limitation in this study.

For ECMO patients, renal failure is a common complication. RRT is an optional modality selected for the purpose of preventing permanent damage to the kidney. Thus, it can be said that the initial application of RRT plays a very important role in the short-term and long-term prognosis of patients. In particular, it was confirmed that when RRT is not done for VA configuration ECMO patients, the level of creatinine in the blood increased significantly, and when RRT is done, the level was maintained. In conclusion, for VA configuration ECMO patients, it was confirmed that RRT is a useful method for renal function preservation.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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