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Extracorporeal Membrane Oxygenation for Respiratory Failure: Comparison of Venovenous Versus Venoarterial Bypass

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Abstract

Purpose. This study compared the respiratory status before and during extracorporeal membrane oxygenation (ECMO) in patients receiving venovenous (VV) and venoarterial (VA) ECMO to evaluate the choice of ECMO in patients with respiratory failure.

Method. Between January 2003 and December 2007, 16 patients with respiratory failure required ECMO. Venovenous bypass and VA bypass were used in 9 cases (VV group) and 7 cases (VA group), respectively. The respiratory status before and during ECMO was compared between the two groups.

Results. The percentage of patients requiring renal replacement therapy prior to ECMO use was significantly higher in the VA group than in the VV group. There were no significant differences between the two groups in PaO_2/FIO_2, $AaDO_2$, pulmonary compliance, and the lung injury score prior to ECMO use. These parameters gradually improved in both groups; however, no significant intergroup differences were seen for up to 96 h after ECMO introduction. There was also no significant difference between the two groups in ECMO removal rate (VV group: 56%, VA group: 43%).

Conclusion. These results suggest that VV ECMO is comparable to VA ECMO, and can maintain sufficient respiratory support when VV ECMO is introduced to respiratory failure patients lacking evidence of renal and/or heart failure.

Key words Extracorporeal membrane oxygenation · Respiratory failure · Venovenous · Venoarterial

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Introduction

The use of extracorporeal membrane oxygenation (ECMO) is a final option for patients with acute and severe respiratory failure who do not respond to advanced modes of mechanical ventilation.[1] Extracorporeal membrane oxygenation involves gas exchange through an extracorporeal oxygenator, and provides oxygenation and carbon dioxide removal without interfering with the lungs. The use of ECMO to accomplish gas exchange is based on the premise that "lung rest" facilitates repair of tissue injury, avoiding the baro- or volutrauma of mechanical ventilator management.[2] Extracorporeal membrane oxygenation is a proven modality for the treatment of severe respiratory failure in the neonate.[3,4] In addition, the survival of pediatric patients with acute respiratory failure supported by venovenous (VV) or venoarterial (VA) ECMO is comparable.[5] On the other hand, ECMO has also been used for the treatment of adults with severe respiratory failure since the 1970s, and two randomized trials showed no superiority of ECMO over conventional treatment.[6,7] Recently, there has been encouraging single-center experience of the successful use of ECMO as an effective therapy in adults with severe respiratory failure.[8,9] However, the choice of VV or VA ECMO in adults with severe respiratory failure remains unclear. The purpose of this study was to compare the clinical courses of patients undergoing VV and VA ECMO, and to evaluate the choice of ECMO for severe respiratory failure.

Patients and Methods

Between January 2003 and December 2007, 16 patients with respiratory failure required VV and VA ECMO in the intensive care unit (ICU) of Gunma University Hospital. All 16 patients had severe acute respiratory

distress syndrome (ARDS). The mean age of the patients was 50 ± 26 (range, 4–81) years old, and the male/female ratio was 10:6.

Indications for ECMO

Venovenous or VA ECMO was introduced in patients with acute, reversible, life-threatening respiratory failure unresponsive to conventional therapy. The patients were ventilated under the pressure control ventilation mode. Peak inspiratory pressure (PIP) was maintained at less than 30 cmH_2O. PaO_2 and arterial blood pH were maintained at least at 60–80 mm Hg and above 7.25, respectively. Positive end-expiratory pressure (PEEP) was administered as previously outlined by the ARDS network.[10] The criteria for ECMO entry were (1) PaO_2/FIO_2 (P/F ratio) <100 mm Hg, (2) uncontrollable respiratory acidosis due to severe hypercapnea with conventional ventilator strategies (pH < 7.2), or (3) pulmonary compliance <30 ml/cmH_2O. In general, VV ECMO was preferred for patients with respiratory failure. VA ECMO was utilized for patients with not only respiratory failure but also unstable hemodynamics requiring catecholamine (epinephrine and/or more than 5 μg/kg per minute of dopamine and/or dobutamine) for maintenance of hemodynamics. There was no patient who began VV ECMO but was then converted to VA ECMO for instability or inadequate support.

ECMO Methods

The ECMO system contains a hollow-fiber microporous membrane oxygenator, a heat exchanger, a centrifugal pump, arterial and venous cannulae, and standard 3/8-inch tubing. The blood-contact surfaces of these components were heparin-coated. Venovenous ECMO was established with venous drainage (19.5 F or 21 F) from the femoral vein (the tip of the tube was placed in the right atrium) and arterialized blood was returned to the contralateral femoral vein using a 15-F or 16.5-F arterial cannula. Venoarterial ECMO was established with venous drainage (19.5 F or 21 F) from the femoral vein (the tip of the tube was placed in the right atrium), and arterialized blood was returned to the femoral artery using a 15-F or 16.5-F arterial cannula. In recent clinical practice, we have used a Capiox SP Pump Controller Sp-101 and a Capiox circuit (Terumo, Tokyo, Japan). Extracorporeal membrane oxygenation flow was initially maintained in the range 1.0–2.0 l/min per m^2 and activated clotting time was maintained at 150–250 s with the administration of nafamostat mesylate, a potent antiplatelet agent, during the procedure. Antibiotics were not given routinely, but they were administered to treat proven microbial infections.

When lung function improved, ECMO flow rates were gradually decreased. The ECMO circuit was removed if gas exchange was adequate with an ECMO flow rate of less than 1.0 l/min per m^2 and with moderate ventilator settings (FIO_2 < 0.6, PIP < 30 cmH_2O, PEEP < 15 cmH_2O, respiratory rates <40/min) for at least a few hours. After successful weaning from ECMO, patients were ventilated mechanically until pulmonary function met standard extubation criteria. In this study, the clinical courses and respiratory status, i.e., P/F ratio, $AaDO_2$, pulmonary compliance, and Lung Injury Score (LIS) before and during ECMO use was compared in patients receiving VV and VA ECMO.

Statistical Analysis

All results are expressed as the mean ± standard error of the mean (SEM). Statistical comparisons were made using the Mann–Whitney *U*-test and a repeated-measures analysis of variance (ANOVA), followed by Fisher's protected least significant difference test for continuous variables and χ^2 analysis for categorical variables. StatView software version 5.0 (Abacus, Berkeley, CA, USA) was used for the statistical analysis. A *P* value of less than 0.05 was interpreted to be statistically significant.

Results

Venovenous bypass was introduced in 9 patients (VV group) and VA bypass was introduced in 7 patients (VA group). The patient backgrounds in each group are shown in Table 1. As shown in Table 1, there were significant ($P < 0.05$) differences in the numbers of patients with heart failure (requiring catecholamine [epinephrine and/or more than 5 μg/kg/min of dopamine and/or dobutamine] for maintenance of hemodynamics) and with renal failure (serum creatinine level was more than 2.0 mg/dl and/or requiring renal replacement therapy [RRT] such as hemodialysis [HD] and continuous hemodiafiltration [CHDF]) between the two groups. The decision to choose VV or VA ECMO was made by the physicians-in-charge in the ICU at that time.

There was no significant difference in the age between the two groups (Table 2). The mean ECMO support time was longer in the VV group than in the VA group, though this difference was not significant (Table 2). In addition, the mean mechanical ventilator support time, pre-ECMO ventilator time, and the length of ICU stay were shorter in the VV group than in the VA group, though none of these differences reached significance (Table 2). The percentage of patients requiring RRT prior to ECMO use was significantly lower ($P < 0.05$) in the VV group than in the VA group (Table 2). There

Table 1. Background of patients

Causes of respiratory failure	VV group (removal)	VA group (removal)
Pneumonia		
Post-LDLT	1 (0)	3 (1)
Post-thoracic esophagectomy	2 (1)	0
Leukemia (post-BMT)	2 (1)	0
Post-AMI	0	1 (1)
Varicella	0	1 (0)
Other	0	1 (0)
Aspiration pneumonia	2 (1)	0
Multiple lung tumor (benign)	0	1 (1)
Burn of airway	1 (1)	0
Pulmonary fibrosis	1 (1)	0
Total	9 (5)	7 (3)
No. of patients with heart failure ($P = 0.012$)	0	5; 71%
No. of patients with renal failure ($P = 0.013$)	1; 11%	5; 71%

VV, venovenous; VA, venoarterial; LDLT, living donor liver transplantation; BMT, bone marrow transplantation; AMI, acute myocardial infarction

Table 2. Comparisons between VV and VA groups

	VV group ($n = 9$)	VA group ($n = 7$)	
Age (y/o)	52 ± 8 (8–79)	47 ± 11 (4–81)	NS
ECMO support time (h)	222 ± 70 (47–749)	156 ± 82 (14–628)	NS
Total mechanical ventilation time (h)	692 ± 211 (97–1832)	962 ± 316 (147–2452)	NS
pre-ECMO mechanical ventilation time (h)	233 ± 110 (1–876)	406 ± 151 (70–1197)	NS
The rate of RRT (CHDF/HD) therapy prior to ECMO	11% (1/9)	71% (5/7)	$P = 0.013$
ICU length of stay (days)	32 ± 8 (6–74)	52 ± 15 (7–103)	NS
ECMO removal rate	56% (5/9)	43% (3/7)	NS
Hospital discharge rate	33% (3/9)	14% (1/7)	NS

Values are mean ± SEM (range)
ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; CHDF, continuous hemodiafiltration; HD, hemodialysis; ICU, intensive care unit; NS, not significant

was no significant difference between the two groups in the ECMO removal rate or discharge rate from hospital (Table 2). In the VV group, 5 patients (56%) were removed from ECMO, 3 patients were discharged from hospital, and 2 patients died following multiple organ failure due to sepsis. On the other hand, in the VA group 3 patients (43%) were removed from ECMO, 1 patient (14%) was discharged from hospital, and 2 patients died following multiple organ failure due to sepsis.

Figure 1 shows the changes of P/F ratio and SpO_2 for up to 96 h after the introduction of ECMO in both groups. There were no significant differences between the two groups in these parameters prior to ECMO use, although those parameters were better in the VV group than in the VA group. While both improved after the introduction of ECMO, there were still no significant differences between the two groups in either parameter for up to 96 h. The $AaDO_2$ values in the VV group tended to be lower than in the VA group, though the differences were nonsignificant except at 12 h after the introduction of ECMO (Fig. 2). Pulmonary compliance and LIS prior to ECMO use were almost the same between the two groups (Fig. 3). The APACHE II (Acute Physiology and Chronic Health Evaluation II) score prior to ECMO use was better in the VV group than in the VA group, without a significant difference (Fig. 4). As shown in Figs. 2, 3, and 4, the increase in arterial blood pH, and improved pulmonary compliance, LIS, and APACHE II score were seen at 96 h after the introduction of ECMO use in both groups; however, there were no significant intergroup differences in these parameters. The ECMO flow rate was maintained at less than 2 l/min per m^2 for up to 96 h after the introduction of ECMO, and thus respiration was maintained with relatively low flow of ECMO (Fig. 4).

Discussion

Extracorporeal membrane oxygenation has an established place in the treatment of acute cardiopulmonary

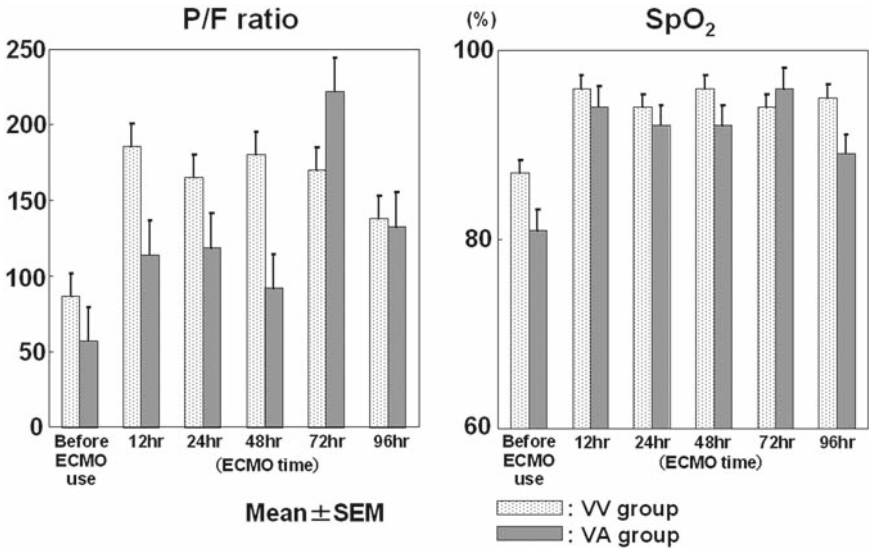

Fig. 1. Changes of P/F ratio and SpO_2. Data shown are mean ± standard error of the mean (SEM). *ECMO*, extracorporeal membrane oxygenation

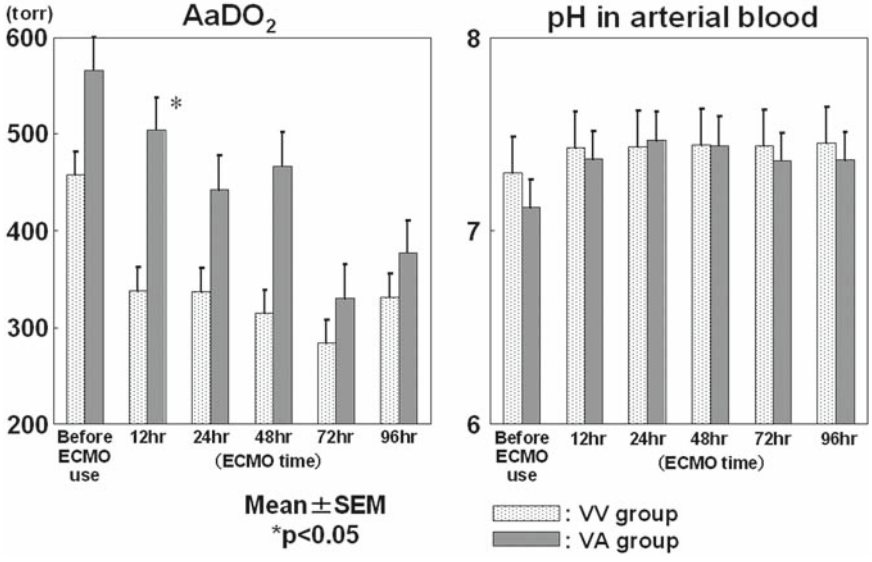

Fig. 2. Changes of $AaDO_2$ and arterial blood pH. Data shown are mean ± SEM. *ECMO*, extracorporeal membrane oxygenation. $^*P < 0.05$

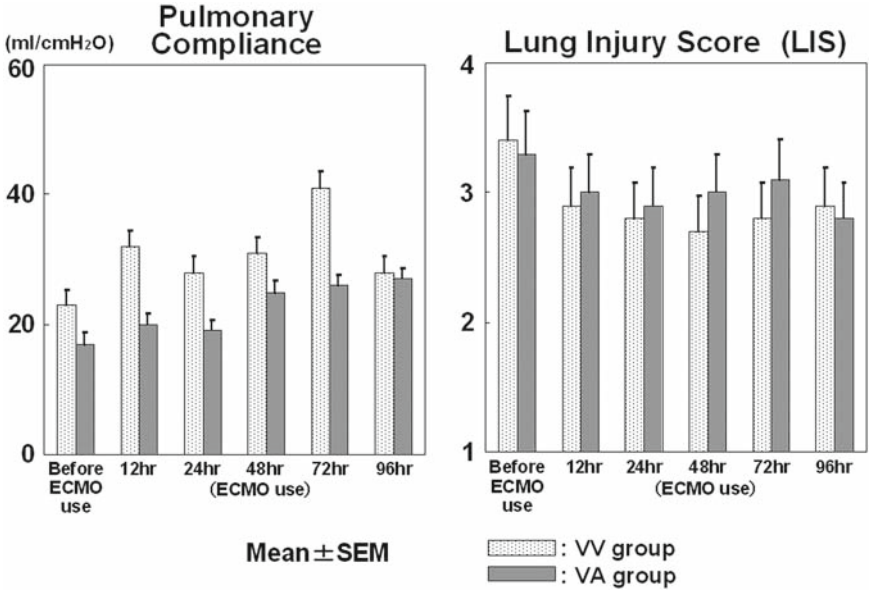

Fig. 3. Changes of pulmonary compliance and Lung Injury Score (LIS). Data shown are mean ± SEM. *ECMO*, extracorporeal membrane oxygenation

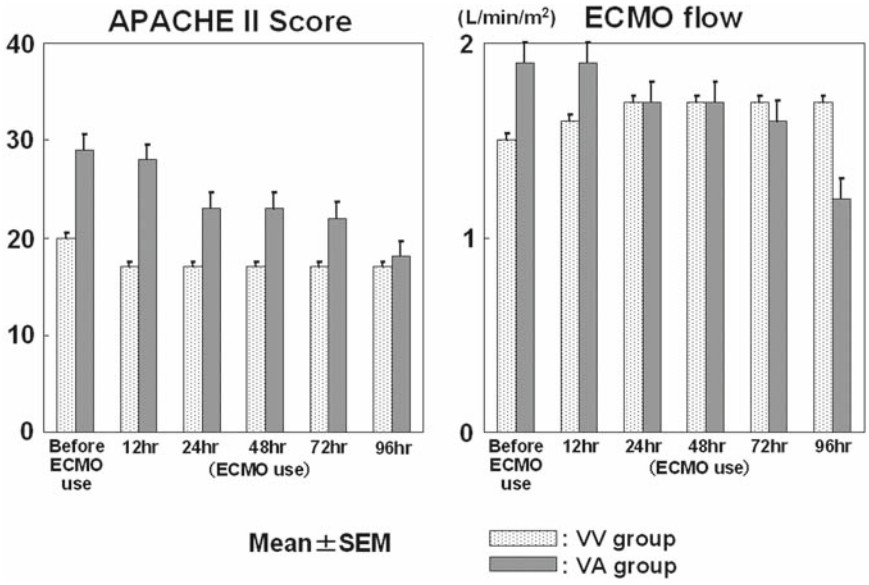

Fig. 4. Changes of the APACHE II score and extracorporeal membrane oxygenation (*ECMO*) flow. Data shown are mean ± SEM

failure in children, based on over 25 years of accumulated clinical experience.[11] The most extensive database of patients who received ECMO support is documented in the Extracorporeal Life Support Organization (ELSO) Registry at the University of Michigan in Ann Arbor. The ELSO database now contains outcome data on over 20 000 patients, with survival rates varying from more than 80% in neonates to 40%–50% in older children.[11] A randomized study in the United Kingdom showed the superiority of ECMO over conventional ventilation in treating neonates with severe respiratory failure.[4] There have also been reports comparing the efficacy of VV and VA bypass in children with severe respiratory failure. Zahraa et al. reported that overall survival of pediatric patients with acute respiratory failure supported by VA or VV ECMO was comparable.[5] Kugelman et al. concluded that VV ECMO was as reliable as VA ECMO in newborns with congenital diaphragmatic hernia in severe respiratory failure; however, these authors suggested that VV ECMO might be preferable to VA ECMO because of its potential advantages.[12] Cannulation during the introduction of ECMO is different in pediatric patients in comparison to adults. Insertion of the cannula into the carotid artery is required in newborns and infants to establish VA ECMO, a procedure that influences cerebral blood flow. Fukuda et al. demonstrated that VV ECMO had advantages in stabilizing brain hemodynamics compared with VA ECMO.[13] Roberts et al. also recommended VV ECMO for neonatal respiratory failure in all cases, except where double lumen cannulation is impossible, or when septic shock is refractory to inotropic support.[14]

Extracorporeal membrane oxygenation has been also used for the treatment of adults with severe respiratory failure since the 1970s, and two randomized trials showed no superiority of ECMO over conventional treatment.[6,7] However, there has been encouraging single-center experience of the successful use of ECMO as an effective therapy in adults with severe respiratory failure.[8] Furthermore, it has been shown that ECMO for severe ARDS in adults is a successful therapeutic option in those patients who do not respond to conventional mechanical ventilator strategies.[9,15,16]

Table 3. Characteristic differences between VV and VA ECMO

	VV bypass	VA bypass
Blood drainage	RA	RA
Blood returning	SVC, IVC	FA, SCA, CA
Oxygenation	±	++
Removal of CO_2	++	++
Circulatory support	Impossible	Possible
Risk of air emboli	+	+++
Risk of bleeding	+	++

RA, right atrium; IVC, inferior vena cava; SVC, superior vena cava; FA, femoral artery; SCA, subclavian artery; CA, carotid artery

The characteristic differences between VV and VA ECMO are shown in Table 3.[5,17,18] While the efficiency of carbon dioxide removal was high under both bypass conditions, the extent of blood oxygenation was greater in VA than in VV bypass. This is because oxygenated blood is directly returned to the artery during VA bypass. The risk of air emboli increases in VA bypass. Circulatory support is not possible during VV bypass; however, insertion of the catheter into the artery is not necessary and the risk of bleeding is therefore less than during VA bypass. Therefore, there is less risk with VV

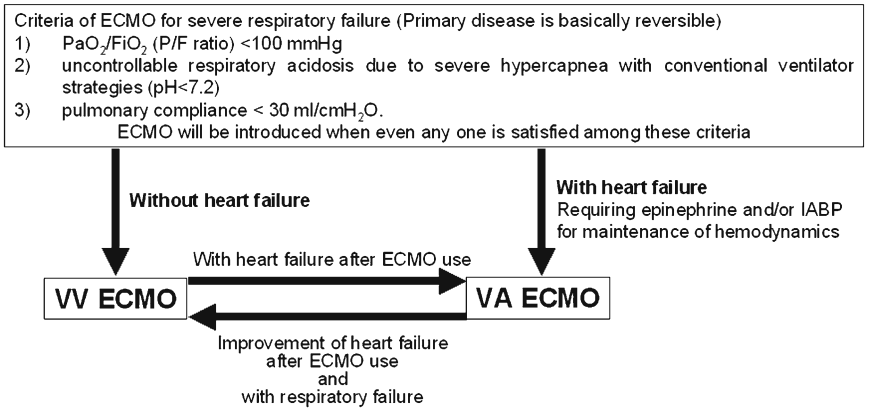

Fig. 5. General criteria for ECMO introduction in our hospital. *IABP*, intra-aortic balloon pumping

ECMO, which is also safer than VA ECMO. Both VV and VA ECMO are used for patients with severe respiratory failure;[8,19] however, there has been no precise indication regarding a choice between VV and VA ECMO for respiratory failure.

In this study, the clinical courses and respiratory status before and after ECMO introduction were compared in patients receiving VV and VA ECMO. As a result, the APACHE II score and P/F ratio prior to ECMO use was better in VV than in VA ECMO without significant differences. The rate of RRT use prior to ECMO was significantly higher in VA than in VV ECMO. The requirement of RRT means that patients have renal dysfunction; therefore, this result showed that the rate of patients with renal dysfunction was significantly higher in patients with VA ECMO than with VV ECMO. The introduction of ECMO tended to occur earlier in VV ECMO than in VA ECMO. There were no significant differences between the two groups in SpO_2, $AaDO_2$, arterial blood pH, pulmonary compliance, and LIS prior to ECMO introduction. In addition, the improvements in these parameters were maintained for up to 96 h after introduction of ECMO in both groups (intergroup differences were nonsignificant). To summarize the results, patients with VA ECMO were in more severe condition prior to ECMO use than patients with VV ECMO in this study, because the rate of patients with renal dysfunction was significantly higher and the APACHE II score and P/F ratio were worse in patients with VA ECMO. Although there were differences in the patients' background, the improvements of respiratory status were comparable between the two groups. Venovenous ECMO is as reliable as VA ECMO when patients are in severe respiratory failure which is reversible and which cannot be controlled using conventional mechanical ventilation, and where there is no evidence of organ failure apart from the lung. On the other hand, VA ECMO should be recommended if patients have not only respiratory failure that cannot be controlled with conventional mechanical ventilation but also other organ dysfunction such as the heart and/or kidney.

General criteria have been established in this hospital for the introduction of ECMO for severe respiratory failure (Fig. 5). Venovenous ECMO is used as a treatment of first choice for patients with severe respiratory failure in the absence of additional evidence of severe organ failure. Further studies are required to fully clarify the indications for ECMO (VV or VA) bypass for patients with respiratory failure, because this study has a limitation based on the small number of patients.

In conclusion, these results suggest that respiratory support by VV ECMO is possible in patients lacking evidence of renal failure and/or heart failure. Early application of VV ECMO may improve outcomes in patients with respiratory failure.

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