

# Outcomes in Trauma Patients Undergoing Venovenous Extracorporeal Membrane Oxygenation for Adult Respiratory Distress Syndrome

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## Research Article

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# Abstract

**Background:** Use of venovenous extracorporeal membrane oxygenation (VV ECMO) remains controversial in trauma patients with adult respiratory distress syndrome (ARDS). Here, we aimed to investigate its therapeutic benefits and the factors affecting patient outcomes.

**Methods:** From 2017–2019, 21/1938 trauma patients (median age: 47 years; 20 men) at a level I trauma center received VV ECMO for post-traumatic ARDS. Demographic, injury-specific, ECMO, and outcome data were prospectively collected and retrospectively reviewed to analyze the factors affecting hospital mortality and ECMO results.

**Results:** Nineteen patients (90.5%) were successfully weaned off ECMO; 16 patients (76.2%) survived to discharge. In the univariate analysis, there was a significant difference in survival between the groups with a Trauma and Injury Severity Score (TRISS)  $\geq 0.5$  and TRISS  $< 0.5$  ( $p=0.05$ ). The area under the receiver operating characteristic curve (AUC) of both TRISS and Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) scores in death was 0.78. In those who failed ECMO weaning, the AUCs of TRISS and RESP scores were 0.90 and 0.80, respectively.

**Conclusions:** In patients with ARDS caused by severe trauma and supported by VV ECMO, survival is associated with TRISS; TRISS and RESP scores may be predictive of mortality and failure of ECMO weaning.

## Introduction

Acute respiratory distress syndrome (ARDS) is a common cause of death in trauma patients, with an incidence of 4.3–8.5 % and an associated mortality of 20–40%.<sup>1</sup> If conventional treatment fails, venovenous extracorporeal membrane oxygenation (VV ECMO) may be an optimal strategy to assure sufficient gas exchange and tissue perfusion while reducing positive pressure ventilation and allowing the lungs to heal.

Since the first ECMO performed on a trauma patient by Hill *et al.*<sup>2</sup>, several case reports and a series of small single-center cases have been published; they have reported that mortality rates improve by using ECMO as a bridge until trauma patients recover from the underlying lung damage.<sup>3–12</sup> Although VV ECMO is an established salvage therapy for adults with refractory ARDS, the use of ECMO remains controversial in adult trauma patients due to bleeding risks during/after cannulation in case of consumption coagulation, contraindications to recommended anticoagulation during ECMO, reduced venous return due to abdominal packing during injury control surgery, and the risk of secondary intracranial bleeding after traumatic brain injury.<sup>13</sup>

The objective of this study was to evaluate the outcomes in adult trauma patients requiring VV ECMO for respiratory failure and identify factors that may be helpful in predicting the prognosis.

# Methods

All clinical data in this analysis were prospectively collected and retrospectively reviewed. To conduct the study we recruited patients who were admitted to our level I trauma center for severe trauma who underwent VV ECMO owing to severe hypoxemic respiratory failure. Between March 2017 and February 2019, a total of 1938 adult patients with serious trauma, aged >18 years and with an injury severity score (ISS) >15, were admitted to our center. ECMO was performed in 28/1938 (1.4 %) patients. Five patients who underwent extracorporeal cardiopulmonary resuscitation (ECPR) due to rupture of heart and major vessels caused by severe chest trauma with veno-arterial ECMO were excluded.<sup>14</sup> Two patients who underwent VV ECMO for the treatment of major airway injury were excluded as ARDS was not caused by trauma.<sup>15</sup> A total of 21 patients underwent VV ECMO at our center due to severe hypoxemic respiratory failure after severe trauma (Figure 1). The study was conducted according to the principles of the Declaration of Helsinki and ethical approval was obtained from the Institutional Review Board of our hospital (1909-028-083). The informed consent was obtained from all subjects or their legal guardians.

## Indication for ECMO

ECMO was performed based on the indications specified by the Extracorporeal Life Support Organization (ELSO).<sup>16</sup> All adult patients who were treated with ECMO, with conventional mechanical ventilation failing to control hypoxemia or correcting hypercapnia and respiratory acidosis, were included in the study. We actively performed VV ECMO when the arterial oxygen partial pressure to fractional inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) ratio reached <80 on the mechanical ventilator, and the  $\text{FiO}_2$  was >0.9, despite optimal care for  $\leq 6$  hours.<sup>16</sup>

## Contraindication for ECMO

We performed enhanced trauma computed tomography in advance to identify traumatic brain/spine injury, aortic dissection, and internal organ injuries. ECMO was not performed in trauma patients with central nervous system (CNS) hemorrhage, nonrecoverable comorbidity such as major CNS damage, or terminal malignancy.<sup>16</sup> However, ECMO was performed in patients with post-traumatic brain hemorrhage, with a small amount of bleeding or with controllable risk of bleeding.

## ECMO management

The patients were placed on an extracorporeal circuit with venous access achieved via the right internal jugular vein and one or both common femoral veins, using the percutaneous Seldinger technique guided by ultrasound. The patients received intensive care treatment after ECMO was established. We used the Permanent Life Support system (GETINGE, Gothenburg, Sweden). The anticoagulation was based on the ELSO Guidelines for Adult Respiratory Failure 2017.<sup>16</sup> Activated clotting time (ACT) was checked in all patients before commencing ECPR. The dose of heparin was adjusted to a target ACT of between 150 and 200 seconds considering the bleeding risk in these patients.<sup>14</sup> In patients with a substantial risk of bleeding, no anticoagulation was administered until the risk of bleeding decreased. In those patients, we

kept the ECMO at high flow to prevent clot formation.<sup>13</sup> The platelet count was kept at >80,000.<sup>16</sup> Otherwise, treatment of severe bleeding in trauma patients requiring ECMO support did not differ from the treatment of hemorrhagic shock and coagulopathy in trauma patients without ECMO.

## **Ventilation management for ECMO**

During the application of ECMO, the existing mechanical ventilation was continued to prevent the occurrence of collapse. In accordance with the concept of pulmonary protective ventilation, the peak pressure was kept to a minimum with a low respiratory rate (6–8 breaths per minute) and a small tidal volume.<sup>17</sup> To avoid fluid retention, loop diuretics were used and a relatively negative fluid balance was maintained.<sup>13</sup> When urine output decreased and acute renal injury was suspected, continuous renal replacement therapy was actively considered in consultation with a nephrologist. Patients with acute kidney injury according to the risk injury failure loss end-stage kidney disease criteria<sup>18, 19</sup> received early continuous kidney replacement therapy/continuous VV blood filtration (CVVH) in the circuit. The CVVH machine (Plasmafex system; Baxter, Deerfield, IL, USA) was connected to the ECMO circuit for hemodialysis in case of renal failure. Tracheostomy was performed within 14 days if extubation was not possible or planned by this time.

## **ECMO weaning**

Weaning from ECMO was considered once significant pulmonary improvements were observed. The pump flow was tapered to 2.0 L/min, following which, the ECMO sweep gas flow was decreased gradually to zero. Decannulation was performed after 12 hours if the patient remained stable. The weaning process was stopped in case of hemodynamic instability or increased oxygen demand under lung protective ventilation.

## **Statistical analysis**

The R package (Version 3.5.0, R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses, and  $p < 0.05$  was considered statistically significant. Continuous data with a normal distribution are reported as mean and standard deviation. Categorical variables are expressed as numbers and percentages. The Cox proportional hazards model was used in the survival analysis to explore the factors affecting death and ECMO weaning failure. To evaluate the prediction ability of the injury scoring system for death and ECMO weaning failure, we used the Harrell's concordance index for the Cox model, seeking the point that maximizes the log-rank test statistic (or minimizes the p-value of the log-rank test) to determine the optimal cut-off value. The receiver operating characteristic (ROC) curve (Figure 2) shows the optimal cut-off value observed in the survival analysis.

# **Results**

Table 1 summarizes the baseline characteristics. Most patients were men (18, 85.7%), and the mean patient age was  $45.0 \pm 17.8$  years. Traffic accident (16, 76.2%) was the most common cause of injury. ISS ( $28.9 \pm 11.0$ ) indicates that most patients were severely injured. The patients underwent various procedures before the initiation of ECMO. Damage-control laparotomy was performed in seven (33.3%) patients, one of whom underwent peritoneal packing. Transcatheter arterial embolization was performed in seven (33.3%) patients: five cases of the internal iliac artery, three cases of the liver and spleen, and two cases of the intercostal artery. A thoracotomy was performed in the emergency department in two patients owing to a massive hemothorax; one of them had a ruptured left subclavian artery. Bleeding control and repair surgery were performed on ECMO support. Four patients received neurosurgery, including two cases of craniectomy and surgical fixation of the cervical spine each. Tracheostomy (n = 15, 71.4%) was performed within 2 weeks of initiation of mechanical ventilation.

Table 1  
Baseline characteristics and surgical interventions of the study population

Variables	N = 21
Age (years)	45.0 ± 17.8
Sex	
Male	18 (85.7%)
Mechanism of Trauma	
Traffic accident	16 (76.2%)
Fall	2 (9.5%)
Crushing	2 (9.5%)
Stab wound	1 (4.8%)
GCS score	11.0 ± 3.7
RTS	6.2 ± 1.6
ISS	28.9 ± 11.0
TRISS	0.7 ± 0.3
RESP score	1.81 ± 3.71
Interventions prior to ECMO	
Damage control laparotomy	7 (33.3%)
Thoracic surgery	3 (9.1%)
Neurosurgery	4 (12.1%)
Facial surgery	1 (3%)
Orthopedic surgery	4 (12.1%)
Transcatheter arterial embolization	7 (33.3%)
Values are presented as mean ± SD or n (%).	
GCS = Glasgow Coma Scale; RTS = Revised Trauma Score; ISS = Injury Severity score; TRISS = Trauma and Injury Severity score; RESP score = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score; ECMO = extracorporeal membrane oxygenation	

ECMO was performed after a mean of 3.5 ± 3.5 days following trauma. The mean oxygenation index (PaO<sub>2</sub>/FiO<sub>2</sub> ratio) before performing ECMO was 55.4 ± 13.1. The mean duration of mechanical ventilation before ECMO was 2.7 ± 3.5 days. After 4 hours on ECMO, gas exchange improved to a mean oxygenation

ratio of  $193.6 \pm 56.4$ . The mean duration on ECMO was  $9.4 \pm 5.3$  days. There were no complications directly related to the ECMO procedure.

Ten (47.6%) patients initially underwent heparin-free ECMO. However, there were no device-related complications or complications due to thromboembolism. All of these patients were at a high risk of bleeding complications, such as recent damage control surgery, conservatively treated internal organ bleeding, or multiple trauma within 24 hours. Heparin-related complications such as bleeding were not observed in 11 patients (52.4%) who received heparin intravenously. Most of the patients left the intensive care unit with ECMO installed and moved at least twice for repeated imaging follow-up or adjuvant radiologic intervention or surgeries. All ECMO transfers were safely performed under supervision by at least three members of the ECMO team.

The mean values of the ISS, Revised Trauma Score, and Trauma and Injury Severity Score (TRISS) were  $28.9 \pm 11.0$ ,  $6.2 \pm 1.6$ , and  $0.7 \pm 0.3$ , respectively. Nineteen (90.5%) patients were severely injured (ISS > 15). Five (23.8%) patients were diagnosed with intracranial hemorrhages (epidural hematoma, one; subdural hematoma, two; subarachnoid hemorrhage, four) and two (9.5%) patients had cerebral contusion before ECMO. Surgical intervention was required in two of five patients with intracranial hemorrhages, and all five survived. However, one patient had severe neurologic sequelae. All patients had thoracic injuries with an Abbreviated Injury Scale score  $\geq 3$ , except for one patient with cervical injuries. The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score was  $\geq 0$  in 15 (71.4%) patients (mean,  $1.8 \pm 3.7$ ).

Table 2 lists the results of survival analysis using Cox proportional hazards regression model between the group that succeeded in ECMO weaning and the group that failed. There was no significant relationship among the variables examined regarding ECMO weaning. Table 3 lists the results of survival analysis using the Cox proportional hazards regression model between the survivors and non-survivors. There was no significant relationship among the variables examined regarding survival.

Table 2  
Factors associated with ECMO weaning

	<b>Weaning Success (N = 19, 90.5%)</b>	<b>Weaning Failure (N = 2, 9.5%)</b>	<b>HR [95% CI]</b>	<b>p-value</b>
Age (years)	44.5 ± 16.8	49.5 ± 34.7	1.013 [0.929, 1.104]	0.78
GCS score	10.9 ± 3.9	12.0 ± 0.0	1.066 [0.686, 1.658]	0.78
RTS	6.3 ± 1.6	5.8 ± 0.52	0.788 [0.267, 2.325]	0.67
ISS	28.3 ± 10.9	34.5 ± 14.9	0.982 [0.847, 1.139]	0.81
TRISS	0.7 ± 0.25	0.3 ± 0.08	0.001 [0.000, 1.394]	0.24
RESP score	2.2 ± 3.6	-1.5 ± 3.5	0.721 [0.462, 1.125]	0.15
Pre-ECMO MV (h)	67.7 ± 86.8	40.9 ± 8.3	0.996 [0.973, 1.019]	0.71
Trauma to ECMO (h)	88.0 ± 86.1	41.0 ± 8.5	0.991 [0.966, 1.018]	0.52
Prior to ECMO P/F ratio	56.0 ± 12.9	49.0 ± 18.5	0.952 [0.846, 1.071]	0.41
4h post-ECMO P/F ratio	193.7 ± 55.1	193.0 ± 94.8	1.003 [0.984, 1.022]	0.78
The Cox proportional hazards model (univariate analysis) was used for the survival analysis.				
Values are presented as mean ± SD.				
ECMO = extracorporeal membrane oxygenation; HR = hazard ratio; CI = confidence interval; GCS = Glasgow Coma Scale; RTS = Revised Trauma score; ISS = Injury Severity score; TRISS = Trauma and Injury Severity score; RESP score = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score; MV = mechanical ventilation; Trauma to ECMO = time to initiate ECMO from injury; P/F ratio = oxygenation index (PaO <sub>2</sub> /FiO <sub>2</sub> ratio); h = hour				

Table 3  
Factors associated with survival

	<b>Survivors (N = 16, 76.2%)</b>	<b>Non-survivors (N = 5, 23.8%)</b>	<b>HR [95% CI]</b>	<b>p-value</b>
Age (years)	42.9 ± 17.9	51.6 ± 17.6	1.023 [0.960, 1.089]	0.48
GCS score	10.7 ± 3.9	12.0 ± 3.1	1.082 [0.844, 1.387]	0.53
RTS	6.2 ± 1.7	6.2 ± 1.3	0.953 [0.564, 1.610]	0.86
ISS	26.6 ± 9.1	36.4 ± 14.1	1.060 [0.993, 1.132]	0.08
TRISS	0.8 ± 0.3	0.5 ± 0.2	0.081 [0.004, 1.723]	0.11
RESP score	2.6 ± 3.6	-0.6 ± 3.2	0.838 [0.667, 1.054]	0.13
Pre-ECMO MV(h)	66.9 ± 88.8	59.5 ± 68.4	0.999 [0.988, 1.010]	0.88
Trauma to ECMO (h)	89.2 ± 85.3	65.4 ± 81.2	0.997 [0.985, 1.009]	0.57
Prior to ECMO P/F ratio	56.6 ± 13.9	51.5 ± 10.1	0.966 [0.902, 1.033]	0.31
4h post-ECMO P/F ratio	196.2 ± 57.1	185.3 ± 59.7	0.996 [0.979, 1.013]	0.64
The Cox proportional hazards model (univariate analysis) was used for survival analysis.				
Values are presented as mean ± SD.				
ECMO = extracorporeal membrane oxygenation; HR = hazard ratio; CI = confidence interval; GCS = Glasgow Coma Scale; RTS = Revised Trauma score; ISS = Injury Severity score; TRISS = Trauma and Injury Severity score; RESP score = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score; MV = mechanical ventilation; Trauma to ECMO = time to initiate ECMO from injury; P/F ratio = oxygenation index (PaO <sub>2</sub> /FiO <sub>2</sub> ratio); h = hour				

We compared survival and ECMO weaning between two groups: those with TRISS  $\geq 0.5$  and those with TRISS  $< 0.5$ .<sup>20</sup> There was a significant difference in survival between the two groups (hazard ratio [HR]: 6.051,  $p = 0.05$ , 95% confidence interval [CI]:1.004–36.456). Six out of 21 (28.6%) had TRISS  $< 0.5$ , and 15 (71.4%) had TRISS  $\geq 0.5$ . Of the six patients with TRISS  $< 0.5$ , three (50%) died and three (50%) survived. Of the 15 patients with TRISS  $\geq 0.5$ , two (13.3%) died and 13 (86.7%) survived. We also compared the groups with ISS  $\leq 15$  and ISS  $> 15$ , and the groups with an RESP score  $\geq 0$  and RESP score  $< 0$ ; there were no statistically significant differences in survival or ECMO weaning among these groups.

Figure 2 shows the ROC curve of each scoring system. The cut-off point that maximizes the sensitivity and specificity was selected using the Youden index. The area under the ROC curve (AUC) of both the TRISS and RESP scores in death was 0.78. The optimal cut-off values of TRISS and RESP scores were 0.72 and 3.0, respectively, and sensitivity and specificity are shown in Table 4. In the case of failure of ECMO weaning, the AUCs of the TRISS and RESP scores were 0.90 and 0.80, respectively. The optimal

cut-off values for the TRISS and RESP scores were 0.47 and 1.0, respectively, and the sensitivity and specificity are shown in Table 5.

Table 4  
Predictive ability of the GCS score, ISS, TRISS, and RESP score in non-survivors

	<b>Sensitivity</b> <b>[95% CI]</b>	<b>Specificity</b> <b>[95% CI]</b>	<b>AUC</b> <b>[95% CI]</b>
GCS score	0.80 [0.40–1.00]	0.63 [0.38–0.88]	0.57 [0.29–0.85]
ISS	0.40 [0.00–0.80]	1.00 [1.00–1.00]	0.66 [0.34–0.99]
<b>TRISS</b>	0.80 [0.40–1.00]	0.69 [0.44–0.88]	<b>0.78</b> [0.54–1.00]
<b>RESP score</b>	1.00 [1.00–1.00]	0.56 [0.31–0.81]	<b>0.78</b> [0.57–0.99]
<p>The cut-off point that maximizes the sensitivity and specificity was selected using the Youden index. CI = confidence interval; AUC = area under the curve; GCS = Glasgow Coma Scale; ISS = Injury Severity Score; TRISS = Trauma and Injury Severity score; RESP score = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score</p>			

Table 5  
 Predictive ability of the GCS score, ISS, TRISS, and RESP score in failure to wean off ECMO

	<b>Sensitivity</b> <b>[95% CI]</b>	<b>Specificity</b> <b>[95% CI]</b>	<b>AUC</b> <b>[95% CI]</b>
GCS score	1.00 [1.00–1.00]	0.58 [0.368–0.789]	0.58 [0.35–0.81]
ISS	0.50 [0.00–1.00]	0.95 [0.84–1.00]	0.55 [0.00–1.00]
<b>TRISS</b>	1.00 [1.00–1.00]	0.84 [0.68–1.00]	<b>0.90</b> [0.74–1.00]
<b>RESP score</b>	1.00 [1.00–1.00]	0.63 [0.42–0.84]	<b>0.80</b> [0.53–1.00]
The cut-off point that maximizes the sensitivity and specificity was selected using the Youden index. CI = confidence interval; AUC = area under the curve; GCS = Glasgow Coma Scale; ISS = Injury Severity Score; TRISS = Trauma and Injury Severity score; RESP score = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score			

Nineteen patients (90.5%) succeeded in ECMO weaning, and 16 (76.2%) survived to discharge. All survivors were transferred to a rehabilitation hospital for further treatment after the acute treatment was complete. The average length of hospital stay for the survivors was 86.3 ± 50.0 days. A total of five patients died, and three died after ECMO weaning. They died from multi-organ failure, including hepatic dysfunction with overwhelming sepsis. These patients died within an average of 8.3 days after ECMO withdrawal, and two of them already had hepatitis C liver cirrhosis. The two patients who failed ECMO weaning also died from multi-organ failure due to septic shock.

## Discussion

Compared to traditional ARDS treatment, ECMO treatment for traumatic ARDS raises concerns due to multi-organ involvement, higher bleeding risk, and the frequent need for prior surgical intervention or cardiopulmonary resuscitation.<sup>3,21-23</sup> Nevertheless, ECMO has the advantage of being able to support gas exchange without further lung damage due to invasive positive pressure ventilation (barotrauma) in adult patients with fulminant respiratory failure, and may improve patient survival.<sup>24</sup> Current ECMO therapy provides rescue therapy for severe trauma patients with chest injury who suffer from refractory acute respiratory failure when the existing treatment options for ARDS are exhausted.<sup>9,25</sup> Previous studies have reported that an extracorporeal life support (ELS) device has been safely used in adult trauma patients with multiple injuries and severe pulmonary insufficiency, and that it improved survival after early administration.<sup>3</sup>

In this study, we observed that the success rate of ECMO weaning was 90.5% and hospital survival was 76.2% in patients with severe trauma who underwent VV ECMO after suffering ARDS. According to a retrospective review of adult ( $\geq 16$  years) trauma patients receiving ECMO support in the ELSO registry (1989–2016),<sup>26</sup> the success rate of VV ECMO weaning was 74% and hospital survival was 63%. Our overall hospital survival rate was 76.2%, which was superior to the hospital survival rate (63%) in trauma patients with VV ECMO in the ELSO registry.

There was a statistically significant difference in terms of survival between the group with TRISS  $\geq 0.5$  and the group with TRISS  $< 0.5$  (HR: 6.051,  $p = 0.05$ , 95% CI: 1.004–36.456). Although various scoring systems exist, TRISS is the standard method of estimating survival and assessing trauma centers,<sup>27</sup> despite widely documented limitations.<sup>28,29</sup> The use of the TRISS formula has been proposed to consider definitively preventable deaths in trauma patients. In one study, the hospital survival rate was similar to TRISS (mean  $0.7 \pm 0.3$ ), and the expected survival rate according to the RESP score (mean  $1.8 \pm 3.7$ , Risk Class III) was 57%, which was lower than the hospital survival rate in our study.<sup>30</sup> Among the various scoring systems used in trauma, TRISS also showed good prediction performance in a study analyzing Korean patients.<sup>31</sup> In our study, TRISS reflected the trauma-related survival probability better than RESP.

Analysis of the ROC curve revealed that the TRISS and RESP scores were useful factors in predicting the prognosis of death and failure to wean from ECMO in patients with severe trauma undergoing VV ECMO due to ARDS. In particular, TRISS and RESP scores were observed to be useful as factors predicting failure of ECMO weaning, and showed high accuracy (AUC  $> 0.90$  and  $0.80$ ). Although VV ECMO was performed for the treatment of ARDS, we observed that TRISS, which determines the probability of survival in trauma, and the RESP score are important factors in predicting death and failure when weaning from ECMO.

ECMO is a treatment that can potentially cause serious complications.<sup>32</sup> In the past, especially in trauma patients, bleeding has been a major complication of ELS devices associated with systemic anticoagulant therapy.<sup>33</sup> Hemorrhagic complications have been reduced due to advances in the ECMO system and improved anticoagulant management of circuits (heparin coated).<sup>25,34</sup> The compact ECMO system with improved oxygen supply, circuit, and centrifugal pump has significantly reduced bleeding complications; therefore, it may be implemented in patients with a high bleeding risk.<sup>32</sup> Arlt *et al.*<sup>9</sup> reported that initial heparin-free ECMO support can improve therapy and outcomes even in disastrous trauma patients with coexisting bleeding shock. In this study, heparin-free ECMO was initially administered in 10 (47.6%) patients with high bleeding risk, and there were no device-related complications or complications of thromboembolism.

Another concern is whether traumatic brain injury (TBI) should be a contraindication even if heparin-free ECMO is used in patients with severe traumatic lung injury. In the CESAR study,<sup>35</sup> TBI with hemorrhage was considered a contraindication to ECMO management. In this study, 5 out of 21 patients had pre-ECMO intracranial hemorrhages. All five patients survived, though severe neurologic sequelae occurred in

one patient. It was difficult for our research to produce meaningful results on this subject. Additionally, the literature has limited cases and experiences with ECMO in patients with TBI.<sup>9, 36, 37</sup> Therefore, further research is needed.

This study has some limitations. The main limitations are that this was a single-center study, with a small sample size, and with a retrospective non-random design with no control group. We were unable to provide data on long-term survival. Additionally, it was difficult to collect all relevant data in this study due to the multifactorial nature of the patients with severe trauma with ARDS who received ECMO support.

## Conclusions

In patients with ARDS caused by severe trauma who are supported by VV ECMO, survival is associated with TRISS, and TRISS and RESP scores may be considered as predictive factors for death and the failure of ECMO weaning. If the protocol is applied to appropriate patients with traumatic ARDS, we can expect better outcomes with VV ECMO than if it was not administered. To appropriately perform VV ECMO, a tool that can predict outcomes is needed, and we present TRISS as one such tool. However, a prospective study with a larger number of patients is necessary.

## Declarations

**Acknowledgements:** None.

**Author Contributions:** SHK, UH, SS, MSK, IJW, and YJT analyzed and interpreted the patient data. SHK, UH, and SS were major contributors to writing the manuscript. SHK and UH contributed equally to this study. All authors read and approved the final manuscript.

## Additional Information

**Ethics approval:** The study was conducted according to the principles of the Declaration of Helsinki and ethical approval was obtained from the Institutional Review Board of our hospital (1909-028-083).

**Consent for publication:** Not applicable.

**Competing interests:** The authors declare no competing interests.

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## References

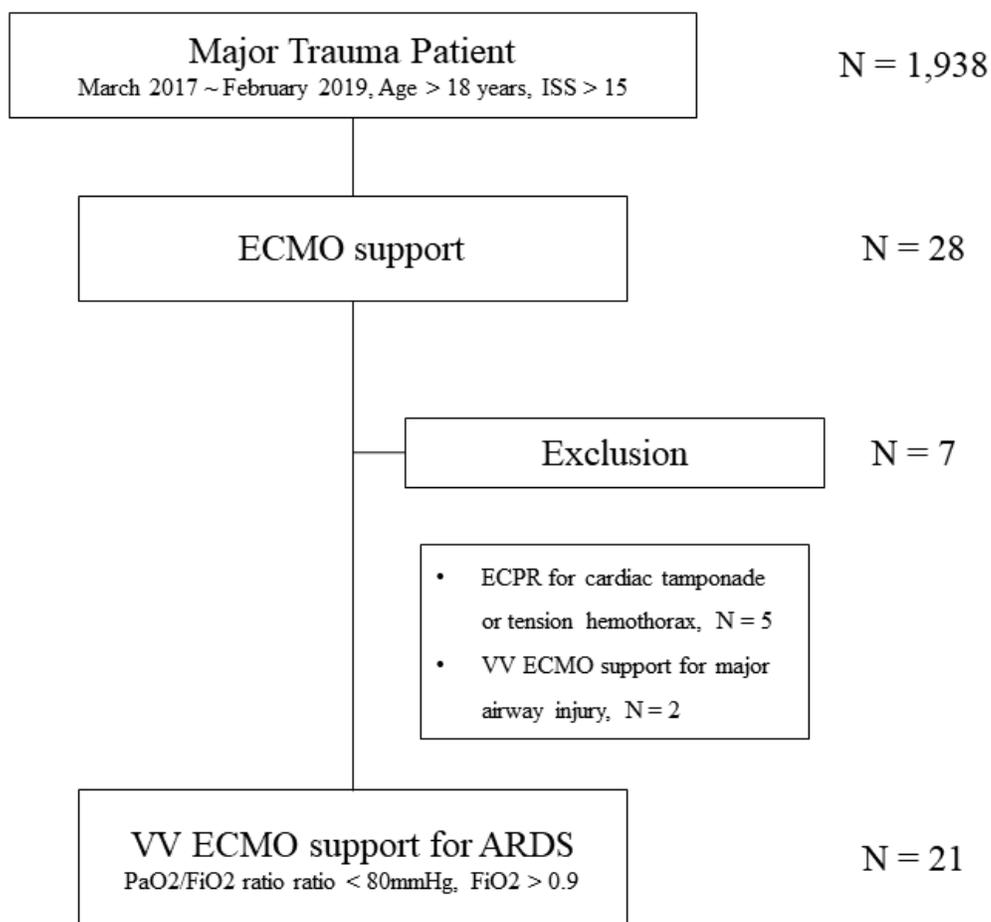
1. Navarrete-Navarro, P. Adult respiratory distress syndrome among blunt and penetrating trauma patients: demographics, mortality, and resource utilization over 8 years. *J. Crit. Care*, **16**, 47–53 (2001).

2. Hill, J. D. *et al.* Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. *N. Engl. J. Med*, **286**, 629–634 (1972).
3. Michaels, A. J. *et al.* Extracorporeal life support in pulmonary failure after trauma.. *J. Trauma*, **46**, 638–645 (1999).
4. Cordell-Smith, J. A., Roberts, N., Peek, G. J. & Firmin, R. K. Traumatic lung injury treated by extracorporeal membrane oxygenation (. *ECMO*). *Injury*, **37**, 29–32 (2006).
5. Biderman, P. *et al.* Extracorporeal life support in patients with multiple injuries and severe respiratory failure: a single-center experience. *J. Trauma Acute Care Surg*, **75**, 907–912 (2013).
6. Ried, M. *et al.* Extracorporeal lung support in trauma patients with severe chest injury and acute lung failure: a 10-year institutional experience. *Crit Care*, **17**, R110 (2013).
7. Wu, S. C. *et al.* Use of extracorporeal membrane oxygenation in severe traumatic lung injury with respiratory failure. *Am. J. Emerg. Med*, **33**, 658–682 (2015).
8. Guirand, D. M. *et al.* Venovenous extracorporeal life support improves survival in adult trauma patients with acute hypoxemic respiratory failure: a multicenter retrospective cohort study. *J. Trauma Acute Care Surg*, **76**, 1275–1281 (2014).
9. Arlt, M. *et al.* Extracorporeal membrane oxygenation in severe trauma patients with bleeding shock. *Resuscitation*, **81**, 804–809 (2010).
10. Yuan, K. C., Fang, J. F. & Chen, M. F. Treatment of endobronchial hemorrhage after blunt chest trauma with extracorporeal membrane oxygenation (ECMO). *J. Trauma*, **65**, 1151–1154 (2008).
11. Chughtai, T. *et al.* Successful use of extracorporeal life support in two cases of posttraumatic adult respiratory distress syndrome. *J. Trauma*, **50**, 1137–1139 (2001).
12. Huang, L. *et al.* Performance of multiple risk assessment tools to predict mortality for adult respiratory distress syndrome with extracorporeal membrane oxygenation therapy: an external validation study based on chinese single-center data. *Chin. Med. J. (Engl)*, **129**, 1688–1695 (2016).
13. Biderman, P. *et al.* Extracorporeal life support in patients with multiple injuries and severe respiratory failure: a single-center experience? *J. Trauma Acute Care Surg*, **75**, 907–912 (2014).
14. Huh, U. *et al.* Is extracorporeal cardiopulmonary resuscitation practical in severe chest trauma? A systematic review in single center of developing country. *J. Trauma Acute Care Surg*, **83**, 903–907 (2017).
15. Noh, D., Lee, C. K., Hwang, J. J. & Cho, H. M. Concomitant avulsion injury of the subclavian vessels and the main bronchus caused by blunt trauma. *Korean J. Thorac. Cardiovasc. Surg*, **51**, 153–155 (2018).
16. Extracorporeal Life Support Organization (ELSO). Guidelines for adult respiratory failure <https://www.elseo.org/Resources/Guidelines.aspx> (2017).
17. Petrucci, N. & Iacovelli, W. Lung protective ventilation strategy for the acute respiratory distress syndrome. *Cochrane Database Syst. Rev*, **3**, CD003844 (2007).

18. Bellomo, R. *et al.* Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit. Care*, **8**, R204–212(2004).
19. Bouman, C., Kellum, J. A. & Lamiere, N. Definition for acute renal failure. Acute Dialysis Quality Initiative—2nd International Consensus Conference. <http://www.adqi.net> (2003).
20. Moon, J. H., Seo, B. R., Jang, J. W., Lee, J. K. & Moon, H. S. Evaluation of probability of survival using Trauma and Injury Severity Score Method in severe neurotrauma patients. *J. Korean Neurosurg. Soc*, **54**, 42–46 (2013).
21. Perchinsky, M. J., Long, W. B., Hill, J. G., Parsons, J. A. & Bennett, J. B. Extracorporeal cardiopulmonary life support with heparin-bonded circuitry in the resuscitation of massively injured trauma patients. *Am. J. Surg*, **169**, 488–491 (1995).
22. Cordell-Smith, J. A., Roberts, N., Peek, G. J. & Firmin, R. K. Traumatic lung injury treated by extracorporeal membrane oxygenation (ECMO). *Injury*, **37**, 29–32 (2006).
23. Lewandowski, K. Extracorporeal membrane oxygenation for severe acute respiratory failure. *Crit. Care*, **4**, 156–168 (2000).
24. Peek, G. J. *et al.* Randomised controlled trial and parallel economic evaluation of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR). *Health Technol. Assess*, **14**, 1–46 (2010).
25. Huang, Y. K. *et al.* Extracorporeal life support in post-traumatic respiratory distress patients. *Resuscitation*, **80**, 535–539 (2009).
26. Swol, J. *et al.* Indications and outcomes of extracorporeal life support in trauma patients. *J. Trauma Acute Care Surg*, **84**, 831–837 (2018).
27. Gabbe, B. J., Cameron, P. A. & Wolfe, R. TRISS: does it get better than this. *Acad. Emerg. Med*, **11**, 181–186 (2004).
28. Hannan, E. L. *et al.* Validation of TRISS and ASCOT using a non-MTOS trauma registry. *J. Trauma*, **38**, 83–88 (1995).
29. Kirkham, J. J. A comparison of hospital performance with non-ignorable missing covariates: an application to trauma care data. *Stat. Med*, **27**, 5725–5744 (2008).
30. Schmidt, M. *et al.* Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. *Am. J. Respir. Crit. Care Med*, **189**, 1374–1382 (2014).
31. Jung, K. *et al.* The best prediction model for trauma outcomes of the current Korean population: a comparative study of three injury severity scoring systems. *Korean J. Crit. Care Med*, **31**, 221–228 (2016).
32. Müller, T. *et al.* A new miniaturized system for extracorporeal membrane oxygenation in adult respiratory failure. *Crit. Care*, **13**, R205 (2009).

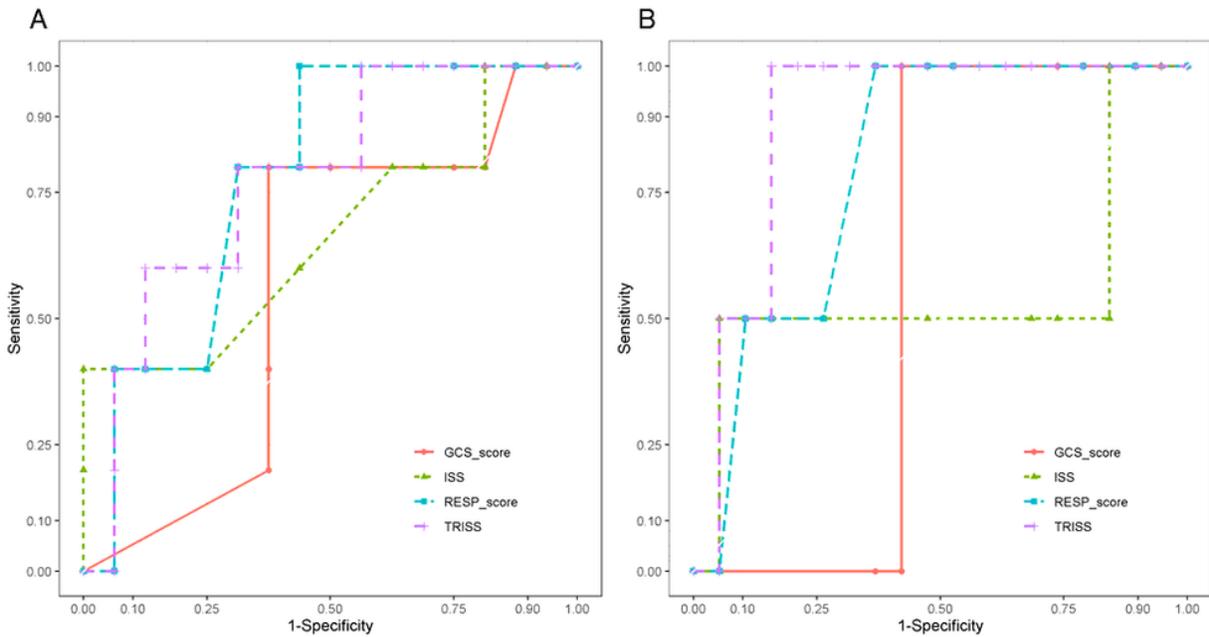
33. Voelckel, W. *et al.* Temporary extracorporeal membrane oxygenation in the treatment of acute traumatic lung injury. *Can. J. Anaesth*, **45**, 1097–1102 (1998).
34. Madershahian, N. *et al.* Application of ECMO in multitrauma patients with ARDS as rescue therapy. *J. Card. Surg*, **22**, 180–184 (2007).
35. Peek, G. J. *et al.* Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*, **374**, 1351–1363 (2009).
36. Biderman, P. *et al.* Extracorporeal life support in patients with multiple injuries and severe respiratory failure: a single center experience? *J. Trauma Acute Care Surg*, **75**, 907–912 (2013).
37. Muellenbach, R. M. *et al.* Prolonged heparin-free extracorporeal membrane oxygenation in multiple injured acute respiratory distress syndrome patients with traumatic brain injury. *J. Trauma Acute Care Surg*, **72**, 1444–1447 (2012).

## Figures



## Figure 1

Flow chart of the included patients ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; VV, veno-venous; ARDS, acute respiratory distress syndrome



## Figure 2

Receiver operating characteristic (ROC) curve of each scoring system A. ROC curve of the GCS score, ISS, TRISS, and RESP score in death. B. ROC curve of the GCS score, ISS, TRISS, and RESP score in failure of ECMO weaning. GCS, Glasgow Coma Scale; ISS, Injury Severity Score; TRISS, Trauma and Injury Severity Score; RESP score, Respiratory Extracorporeal Membrane Oxygenation Survival Prediction score.