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ORIGINAL ARTICLE

Association Between Cannula Size of Extracorporeal Membrane Oxygenation and Prognosis in Patients With Out-of-Hospital Cardiac Arrest

— A Secondary Analysis of the SAVE-J II Study —

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Background: Selecting an appropriate cannula size is crucial for achieving an adequate extracorporeal membrane oxygenation (ECMO) flow rate. However, the association between ECMO cannula size and the prognosis of patients with out-of-hospital cardiac arrest (OHCA) has not been fully elucidated. We examined the associations between ECMO cannula size and neurological outcomes and survival at discharge in patients with OHCA who received ECMO.

Methods and Results: This is a secondary analysis of the Study of Advanced life support for Ventricular fibrillation with Extracorporeal circulation in Japan (SAVE-J II study). The primary and secondary outcomes were favorable neurological outcomes and survival at discharge, respectively. In all, 918 patients were included in the analysis. There were no statistically significant differences between cannula sizes and neurological outcomes. Multivariable analysis showed that increasing body weight (BW)-adjusted sizes of arterial cannulas (odds ratio [OR] 1.04 per 0.01-Fr/kg increase; 95% confidence interval [CI] 1.01–1.07; P=0.011) and venous cannulas (OR 1.04 per 0.01-Fr/kg increase; 95% CI 1.01–1.06; P=0.005) were significantly associated with the survival rate at discharge. Increasing BW-adjusted sizes of arterial cannulas were significantly associated with cannulation site bleeding.

Conclusions: There were no significant associations between favorable neurological outcomes and cannula size, whereas larger-sized arterial and venous cannulas were significantly associated with higher survival rates at discharge in patients with OHCA who received ECMO.

Key Words: Body weight; Cannula size; Extracorporeal cardiopulmonary resuscitation; Extracorporeal membrane oxygenation support; Out-of-hospital cardiac arrest

Improving the prognosis of out-of-hospital cardiac arrest (OHCA) is a significant challenge in developed countries.[1–4] Recently, extracorporeal cardiopulmonary resuscitation (ECPR) has gained widespread acceptance as a rescue treatment for patients with prolonged OHCA, and is expected to contribute to improving neurological prognosis.[5–8] However, OHCA continues to have a poor prognosis.[9]

The guidelines of the Extracorporeal Life Support Organization (ELSO) propose a target flow of approximately 50–70 mL/kg/min for veno-arterial extracorporeal membrane oxygenation (VA-ECMO), although there is insufficient evidence to support this recommendation.[10–13] Patients with prolonged OHCA require sufficient flow to

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Table 1. Patient Characteristics at Baseline (n=918)

Age (years)	60 [49–68]
Male sex	767 (83.6)
Body weight at ICU admission (kg)	69 [60–78.4]
Medical history of heart disease	236 (25.7)
Witnessed cardiac arrest	744 (81.3)
Bystander CPR	552 (60.7)
Initial cardiac rhythm	
Shockable rhythm	646 (70.8)
Pulseless electrical activity	214 (23.5)
Asystole	52 (5.7)
Time from onset of OHCA to ECMO initiation (min)	57 [46–71]
Prehospital ROSC	118 (12.9)
Use of intra-aortic balloon pump	715 (78.0)
Percutaneous cannulation	888 (96.7)
Distal perfusion	248 (27.0)
Outcomes	
Favorable neurological outcomes at discharge	171 (18.6)
In-hospital mortality	584 (63.2)
Total cannulation-related complications	218 (23.8)
Cannulation site bleeding	190 (20.7)
Retroperitoneal hematoma	29 (3.2)
Lower limb ischemia	12 (1.3)

Data are given as the median [interquartile range] or n (%). CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; ROSC, return of spontaneous circulation.

maintain hemodynamics due to post-arrest left ventricular dysfunction.[14] The selection of an appropriately sized cannula is crucial for achieving an adequate ECMO flow rate without compromising on pressure. An inappropriate cannula size in relation to ECMO flow may lead to hemolysis.[15] Thus, a larger cannula may be preferred in patients who received ECPR due to prolonged cardiac arrest. Nevertheless, a small cannula may have the advantage of reducing cannulation-related complications, such as cannulation site bleeding, and lower limb ischemia.[16,17] Thus, there is a knowledge gap as to how to determine the appropriate cannula size in relation to body size for patients who received ECPR due to prolonged OHCA.

In this study, we examined the association between ECMO cannula size and patient size, as well as the effects of ECMO cannula size on neurological status at hospital discharge and survival rate in patients treated with ECPR for OHCA, using data from a Japanese multicenter registry of patients with OHCA who underwent ECPR.

Methods

The SAVE-J II Study

This observational study was a secondary analysis of data from the Study of Advanced Life support for Ventricular Fibrillation with Extracorporeal Circulation in Japan (SAVE-J II study),[18] which was prospectively registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (Registration no. UMIN000036490). The study adhered to the Declaration of Helsinki, and, because of the retrospective nature of this study, the requirement for informed consent from patients was waived. The SAVE-J II study is a multicenter study of patients with OHCA resuscitated with ECPR, involving 36 participating institutions in Japan.[18] The study includes data for consecutive patients, aged ≥18 years, who were admitted to the emergency department with OHCA between January 1, 2013 and December 31, 2018 and received ECPR. The following patient data were collected from the SAVE-J II study database: age, sex, medical history, etiology of cardiac arrest, prehospital information, time course, body weight (BW) at the time of admission to the intensive care unit (ICU), height, ECMO flow rate at ICU admission, ECMO rotation speed at ICU admission, ECMO cannula size, complications, and outcomes. Return of spontaneous circulation (ROSC) was defined as spontaneous palpable pulsations for at least 60 consecutive seconds. Cannulation site bleeding was defined as the need for surgical intervention, interventional radiology, or transfusion. Lower limb ischemia was defined as the need for fasciotomies, leg amputation, or other interventions.

Study Design and Setting

This study included patients who received VA-ECMO before ICU admission. Patients were excluded from the study if they: received VA-ECMO after ICU admission; were withdrawn from the study after cannulation because of ROSC; had already achieved ROSC at ECMO initiation; experienced OHCA of unknown or non-cardiac etiology (acute aortic dissection, aortic aneurysm, hypothermia, primary cerebral disorders, infection, drug intoxication, trauma, suffocation, drowning, and other external causes); and had missing data regarding ECMO cannula size.

Outcomes

The primary outcome was a favorable neurological outcome based on the Cerebral Performance Category (CPC) scale[19] at hospital discharge. A favorable neurological outcome was defined as a CPC score of 1 (good cerebral performance) or 2 (moderate cerebral disability), whereas a poor outcome was defined as a CPC score of 3 (severe cerebral disability), 4 (coma or vegetative state), or 5 (death). Secondary outcomes were survival rate at hospital discharge and a composite of cannulation-related complications (cannulation site bleeding, retroperitoneal hematoma, and lower limb ischemia).

Statistical Analysis

We examined relationships among ECMO cannula size, outcomes, length of ECMO support, ICU stay, and hospital stay. First, we assessed the association between arterial and venous cannula size and BW. Second, we adjusted the cannula size by BW and evaluated the association between BW-adjusted cannula size and outcomes. Finally, we classified patients treated with ECPR into 3 groups based on the interquartile range (IQR) of arterial cannula and venous cannula size corrected for BW, namely small (Q1; ≤0.20 and ≤0.26 Fr/BW for arterial and venous cannulas, respectively), middle-sized (Q2 and Q3; cannulas 0.20–0.27 and 0.26–0.35 Fr/BW, respectively), and large (Q4; cannulas ≥0.27 and ≥ 0.35 Fr/BW, respectively). We then assessed the primary and secondary outcomes among these 3 groups.

Continuous variables are presented as the median with IQR and were compared using the Wilcoxon rank-sum test. Categorical variables are presented as percentages and were compared using Pearson's Chi-squared test. Logistic regression analysis was performed for favorable neurological outcomes and survival to hospital discharge with

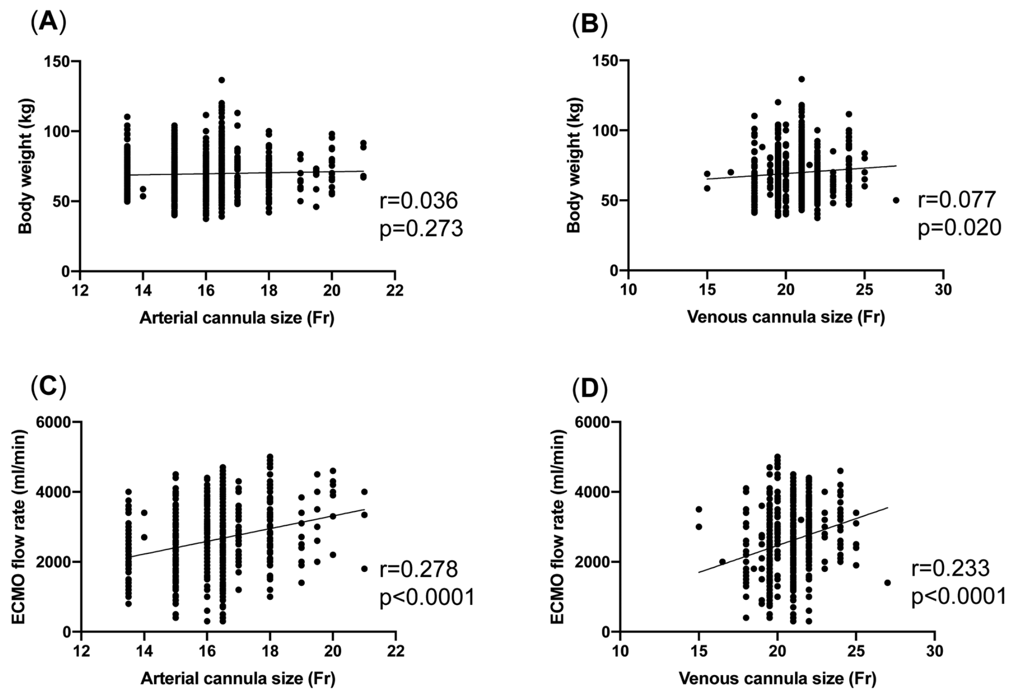

Figure 1. (**A**,**B**) Correlations between arterial (**A**) and venous (**B**) cannula size and body weight. (**C**,**D**) Correlations between extracorporeal membrane oxygenation (ECMO) flow rate at the time of admission to the intensive care unit and arterial (**C**) and venous (**D**) cannula size.

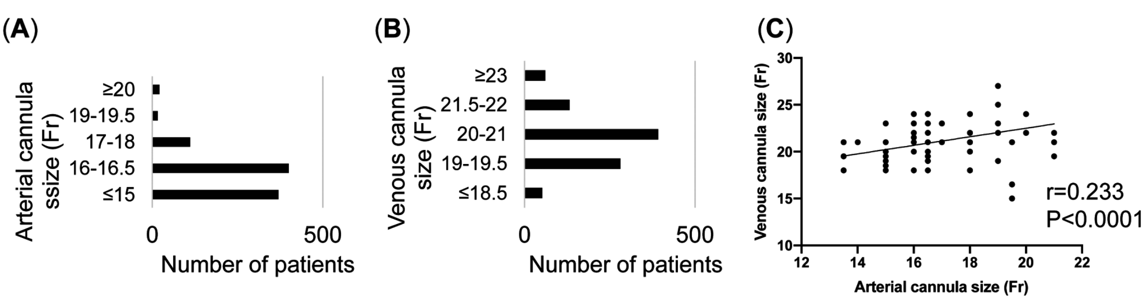

Figure 2. Distribution of arterial and venous cannula sizes. (**A**) Distribution of arterial cannula sizes. (**B**) Distribution of venous cannula sizes. (**C**) Correlation between venous and arterial cannula sizes.

multivariable adjustment for age,[20] sex,[21] witnessed cardiac arrest,[22] bystander-initiated cardiopulmonary resuscitation (CPR),[22] initial cardiac rhythm (shockable rhythm or non-shockable),[1] prehospital ROSC,[23] and time from onset of OHCA to ECMO initiation.[24,25] Statistical significance was set at two-tailed P<0.05. Statistical analyses were performed using STATA Version 17 (StataCorp LP, College Station, TX, USA). We did not impute the missing data.

Results

Patient Characteristics

Of the 2,157 patients registered in the SAVE-J II study database, 918 met the inclusion criteria for this study (**Supplementary Figure**). The median age was 60 years (IQR 49–68 years), and 767 (83.6%) patients were male. In all, 744 (81.3%) arrests were witnessed by a bystander and 552 (60.7%) patients received bystander-initiated CPR. Of the 918 patients, 646 (70.4%) had a shockable initial cardiac rhythm, and the median time from onset to ECMO initiation was 57 min (IQR 46–71 min; **Table 1**). In-hospital mortality occurred in 584 (63.6%) patients, and 171 (18.6%) patients had favorable neurological outcomes at hospital discharge. Cannulation site bleeding and retroperitoneal hematomas were observed in 190 (20.7%) and 29 (3.2%) patients, respectively. Twelve (1.3%) patients were treated

Table 2. Association of Cannula Size to BW Ratio for Primary and Secondary Outcomes After Multivariable Adjustment

Variables	Adjusted OR	95% CI	P value
Favorable neurological outcomes			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.01	0.98–1.05	0.477
Venous cannula size to BW ratio (0.01 Fr/kg)	1.01	0.98–0.99	0.42
Survival rate at hospital discharge			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.04	1.01–1.07	0.02
Venous cannula size to BW ratio (0.01 Fr/kg)	1.03	1.01–1.06	0.012
Composite of cannulation-related complications			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.03	1.00–1.07	0.079
Venous cannula size to BW ratio (0.01 Fr/kg)	1.01	0.99–1.04	0.322
Cannulation site bleeding			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.04	1.00–1.07	0.042
Venous cannula size to BW ratio (0.01 Fr/kg)	1.01	0.99–1.04	0.315
Retroperitoneal hematoma			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.03	0.96–1.12	0.392
Venous cannula size to BW ratio (0.01 Fr/kg)	1.06	0.99–1.12	0.092
Lower limb ischemia			
Arterial cannula size to BW ratio (0.01 Fr/kg)	1.04	0.92–1.18	0.499
Venous cannula size to BW ratio (0.01 Fr/kg)	1.03	0.93–1.14	0.563

The factors adjusted for in the multivariable analysis were age, sex, witnessed cardiac arrest, bystander cardiopulmonary resuscitation, initial cardiac rhythm, prehospital return of spontaneous circulation, and time from onset of OHCA to extracorporeal membrane oxygenation initiation. BW, body weight; CI, confidence interval; OR, odds ratio.

Table 3. Adjusted ORs for Primary and Secondary Outcomes Stratified According to Arterial and Venous Cannula Size Corrected for Body Weight After Multivariable Adjustment

Outcomes	No. patients (%)	Adjusted OR	95% CI	P value
Favorable neurological outcomes at discharge				
Arterial cannulas				
Small	37 (18)	1 (Ref.)		
Middle-sized	91 (19)	1.10	0.70–1.74	0.671
Large	43 (19)	1.16	0.67–2.02	0.597
Venous cannulas				
Small	39 (19)	1 (Ref.)		
Middle-sized	88 (18)	0.95	0.60–1.48	0.813
Large	44 (20)	1.25	0.72–2.17	0.43
Survival rate at discharge				
Arterial cannulas				
Small	67 (32)	1 (Ref.)		
Middle-sized	181 (37)	1.37	0.94–2.0	0.101
Large	86 (39)	1.59	1.00–2.53	0.051
Venous cannulas				
Small	69 (34)	1 (Ref.)		
Middle-sized	174 (35)	1.13	0.77–1.64	0.536
Large	91 (42)	1.63	1.02–2.61	0.043
Composite of cannulation-related complication				
Arterial cannulas				
Small	43 (21)	1 (Ref.)		
Middle-sized	112 (23)	1.21	0.79–1.86	0.375
Large	63 (28)	2.00	1.21–3.31	0.007
Venous cannulas				
Small	47 (23)	1 (Ref.)		
Middle-sized	119 (24)	1.00	0.66–1.51	0.989
Large	52 (24)	1.15	0.68–1.91	0.605

The factors adjusted for in the multivariable analysis were age, sex, witnessed cardiac arrest, bystander cardiopulmonary resuscitation, initial cardiac rhythm, prehospital return of spontaneous circulation, and time from onset of OHCA to extracorporeal membrane oxygenation initiation. CI, confidence interval; OR, odds ratio; Ref., reference.

Table 4. Adjusted ORs for Complications Stratified According to Arterial and Venous Cannula Size Corrected for Body Weight After Multivariable Adjustment

Complications	No. events (%)	Adjusted OR	95% CI	P value
Cannulation site bleeding				
Arterial cannulas				
Small	36 (17)	1 (Ref.)		
Middle-sized	96 (20)	1.26	0.80–1.98	0.313
Large	58 (26)	2.19	1.30–3.71	0.003
Venous cannulas				
Small	42 (20)	1 (Ref.)		
Middle-sized	100 (20)	0.93	0.60–1.43	0.736
Large	48 (22)	1.12	0.66–1.91	0.67
Retroperitoneal hematoma				
Arterial cannulas				
Small	6 (2.9)	1 (Ref.)		
Middle-sized	16 (3.3)	1.14	0.39–3.36	0.806
Large	7 (3.1)	1.68	0.49–5.75	0.412
Venous cannulas				
Small	5 (2.4)	1 (Ref.)		
Middle-sized	17 (3.5)	1.63	0.52–5.14	0.406
Large	7 (3.2)	2.21	0.58–8.35	0.244
Lower limb ischemia				
Arterial cannulas				
Small	2 (1.0)	1 (Ref.)		
Middle-sized	5 (1.0)	1.16	0.22–6.22	0.863
Large	5 (2.3)	2.48	0.42–14.7	0.317
Venous cannulas				
Small	1 (0.5)	1 (Ref.)		
Middle-sized	8 (1.6)	3.08	0.37–25.9	0.300
Large	3 (1.4)	3.61	0.35–37.8	0.283

The factors adjusted for in the multivariable analysis were age, sex, witnessed cardiac arrest, bystander cardiopulmonary resuscitation, initial cardiac rhythm, prehospital return of spontaneous circulation, and time from onset of OHCA to extracorporeal membrane oxygenation initiation. CI, confidence interval; OR, odds ratio; Ref., reference.

for lower limb ischemia. Patient characteristics according to arterial and venous cannula size categories are presented in **Supplementary Tables 1** and **2**.

Cannula Size, BW, and Flow Rate

Arterial and venous cannula sizes were not significantly correlated with BW (**Figure 1A**,**B**), although statistically significant correlations were found between cannula size and ECMO flow rate (**Figure 1C**,**D**). **Figure 2A**,**B** shows the distribution of arterial and venous cannula sizes. Arterial cannula size was significantly correlated with venous cannula size (r=0.464, P<0.001; **Figure 2C**).

Effects of Cannula Size on Primary and Secondary Outcomes

When cannula size was adjusted by BW, the median arterial and venous cannula size to BW ratios were 0.23 Fr/kg (IQR 0.20–0.27 Fr/kg) and 0.30 Fr/kg (IQR 0.26–0.35 Fr/kg), respectively. Odds ratios (OR) for outcomes with increasing cannula size (per 0.01-Fr/kg increase) after multivariable adjustment for age, sex, witnessed cardiac arrest, bystander CPR, initial cardiac rhythm, prehospital ROSC, and time from onset to ECMO initiation are presented in **Table 2**. Multivariable analysis showed no significant association between arterial cannula size and favorable neurological outcome (adjusted [a] OR 1.01; 95% confidence interval [CI] 0.98–1.05; P=0.477). Similarly, the venous cannula size to BW ratio was not associated with favorable neurological outcomes (aOR 1.01 per 0.01-Fr/kg increase; 95% CI: 0.98–0.99; P=0.42). After multivariable adjustment, the aOR for the arterial cannula size to BW ratio for survival rate at discharge was 1.04 (95% CI 1.01–1.07 per 0.01-Fr/kg increase; P=0.02), and there was a significant association between a larger venous cannula size to BW ratio and the survival rate at discharge (aOR 1.03 per 0.01-Fr/kg increase; 95% CI: 1.01–1.06; P=0.012). There was no statistically significant association between either artery or vein cannula size to BW ratio and the composite of cannulation-related complications, but a larger arterial cannula size to BW ratio was significantly associated with cannulation site bleeding after multivariable adjustment (aOR 1.04 per 0.01-Fr/kg increase; 95% CI: 1.00–1.07; P=0.042).

Small- vs. Middle-Sized vs. Large Cannulas

Patients were divided into 3 groups based on the BW-adjusted cannula size. For arterial cannulas, there were 207 patients in the small arterial cannula group (≤0.20 Fr/BW; reference), 488 in the group with middle-sized arterial cannulas (0.20–0.27 Fr/BW), and 223 in the group with large arterial cannulas (≥0.27 Fr/BW). For venous cannulas, there were 206 patients in the small venous cannula group

Table 5. ECMO Support at the Time of ICU Admission and Length of Hospital Stay Stratified by Arterial and Venous Cannula Sizes Corrected for Body Weight

Variables	Small cannula group (Ref.; n=207)	Middle-sized cannula (n=488)	Large cannula (n=223)	P value	
				Middle-sized vs. Ref.	Large vs. Ref.
ECMO at ICU admission					
Arterial cannula					
ECMO flow rate (L/min)	2.5 [2.0–3.0]	2.5 [1.9–3.2]	2.5 [2.0–3.1]	0.421	0.712
ECMO rotation speed (r.p.m.)	2,250 [2,000–2,660]	2,355 [2,000–2,744]	2,243 [2,000–2,922]	0.269	0.571
ECMO flow to rotation speed ratio (mL/min/r.p.m.)	1.06 [0.90–1.30]	1.04 [0.86–1.27]	1.00 [0.83–1.30]	0.514	0.495
Venous cannula					
ECMO flow rate (L/min)	2.5 [2.0–3.1]	2.5 [1.9–3.2]	2.5 [2.0–3.0]	0.820	0.636
ECMO rotation speed (r.p.m.)	2,223 [2,000–2,600]	2,368 [2,008–2,749]	2,242 [1,994–3,000]	0.083	0.429
ECMO flow to rotation speed ratio (mL/min/r.p.m.)	1.09 [0.91–1.33]	1.05 [0.84–1.28]	1.00 [0.86–1.24]	0.063	0.028
Duration of support and ICU/hospital stays					
Arterial cannula					
Length of ECMO support (days)	3 [2–4]	4 [3–5]	4 [3–6]	0.018	<0.001
Length of ICU stay (days)	6 [2–11]	6 [2–12]	8 [3–15]	0.470	0.006
Length of hospital stay (days)	6 [2–23]	7 [2–29]	12 [3–35]	0.320	0.006
Venous cannula					
Length of ECMO support (days)	3 [2–5]	3 [2–5]	4 [3–5]	0.380	0.051
Length of ICU stay (days)	6 [2–12]	6 [2–12]	8 [3–14]	0.535	0.063
Length of hospital stay (days)	6 [2–25]	7 [2–28]	13 [3–33]	0.590	0.005

Unless indicated otherwise, data are given as the median [interquartile range]. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; Ref., reference group.

(≤0.26 Fr/BW; reference), 493 in the group with middle-sized venous cannulas (0.26–0.35 Fr/BW), and 219 in the group with large venous cannulas (≥0.35 Fr/BW).

Table 3 presents multivariable models of primary and secondary outcomes stratified by arterial and venous cannula size corrected for BW. For the primary outcome, compared with the small arterial cannula group, the groups with middle-sized (aOR 1.10; 95% CI: 0.70–1.74; P=0.671) and large (aOR 1.16; 95% CI 0.67–2.02, P=0.597) middle-sized and large cannula groups were not associated with MORE favorable outcomes than the small cannula group. Regarding venous cannulas, there were no significant differences in neurological outcomes at hospital discharge between the small venous cannula group and the middle-sized (aOR 0.95; 95% CI 0.60–1.48; P=0.813) and large (aOR 1.25; 95% CI 0.72–2.17; P=0.43) venous cannula groups.

With respect to secondary outcomes, there were no statistically significant differences in the survival rate at discharge between the small arterial cannula group and the middle-sized (aOR 1.37; 95% CI 0.94–2.00; P=0.101) and large (aOR 1.59; 95% CI 1.00–2.53, P=0.051) arterial cannula groups. Similarly, multivariable analysis showed no significant difference in survival rate at discharge between the small and middle-sized venous cannula groups (aOR 1.13; 95% CI 0.77–1.64; P=0.536). However, after multivariable adjustment, the survival rate at discharge was significantly higher in the large venous cannula group (aOR 1.63; 95% CI 1.02–2.61; P=0.043) than in the group with small venous cannulas. The composite of cannulation-related complications was not significantly associated with arterial or venous cannula size. For arterial cannulas, the incidence of cannulation site bleeding was significantly greater in the group with large arterial cannulas than in the small arterial cannula group (26.0% [58/223] vs. 17.4% [36/207], respectively; P=0.031; **Table 4**.

As indicated in **Table 5**, the group with middle-sized arterial cannulas had a significantly longer length of ECMO support than the group with small arterial cannulas (4 [IQR 3–5] vs. 3 [IQR 2–4] days, respectively; P=0.018). The group with large arterial cannulas had a significantly longer length of ECMO support (4 [IQR 3–6] vs. 3 [IQR 2–4] days, respectively; P<0.001), and longer ICU (8 [IQR 3–15] vs. 6 [IQR 2–11] days, respectively; P=0.006) and hospital (12 [IQR 3–35] vs. 6 [IQR 2–23] days, respectively; P=0.006) stays than the group with small arterial cannulas. The length of hospital stay was significantly longer in the group with large venous cannulas than in the group with small venous cannulas (13 [IQR 3–33] vs. 6 [IQR 2–25] days, respectively; P=0.005).

Discussion

Our analysis, which was based on SAVE-J II study data, found no significant associations between neurological outcomes and either BW-adjusted arterial or venous cannula sizes, although survival rates were significantly higher with larger than small BW-adjusted venous cannulas. In addition, in multivariable analysis, larger BW-adjusted arterial and venous cannulas were significantly associated with higher survival rate at discharge (**Figure 3**).

The cannula size for ECPR is expected to affect the various factors in ECMO management. Several studies have reported that the appropriate cannula size depends on a patient's anatomic features, BW, or body surface area because the actual size of the vessels is affected by sex, age,

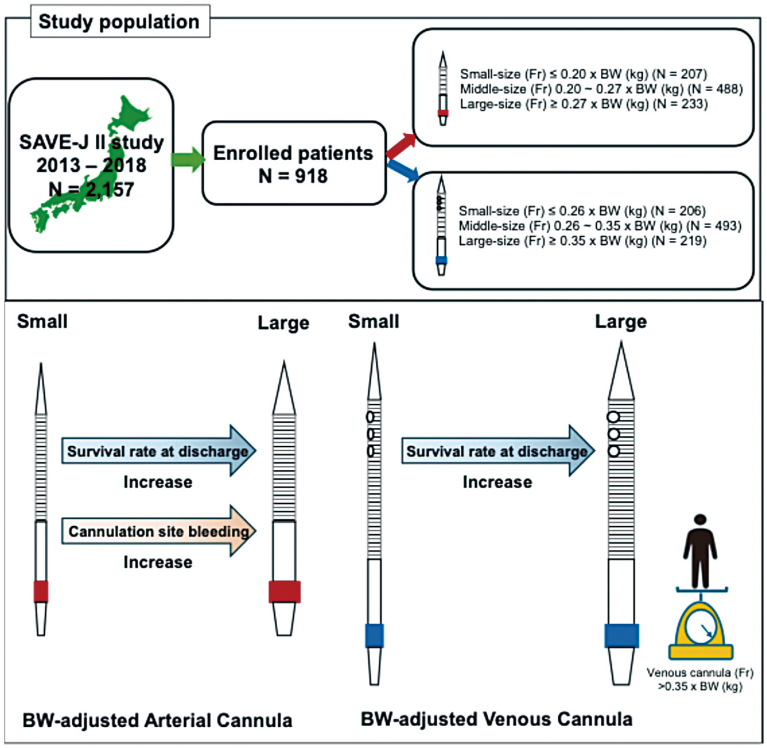

Figure 3. Central Illustration. Cannula sizes were adjusted for body weight (BW). Extracorporeal membrane oxygenation (ECMO) support was significantly longer in patients with larger BW-adjusted arterial cannulas. Compared with small BW-adjusted arterial cannulas, large BW-adjusted arterial cannulas were associated with a longer duration of ECMO support, longer intensive care unit (ICU) and hospital stays, and a higher incidence of cannulation site bleeding. Conversely, large BW-adjusted venous cannulas were associated with a higher survival rate and incidence of cannula site bleeding than small venous cannulas. In multivariable analysis, larger BW-adjusted arterial and venous cannulas were significantly associated with a higher survival rate at discharge. In addition, larger BW-adjusted arterial cannulas were significantly associated with a higher incidence of cannulation site bleeding.

and body size.[26,27] Previous studies and ELSO guidelines report target values as flow rate per BW.[28,29] Therefore, it makes sense to correct the cannula size for BW, and a simple index is useful in emergency situations for patients with OHCA. Previous studies focused on patients with cardiogenic shock, and no previous studies focused on ECMO cannula size in patients with OHCA who received ECPR. In the present study, focusing on patients with ECPR, multivariable analysis showed no significant differences in the survival rate at discharge between the groups with small and middle-sized venous cannulas, but the group with large venous cannulas had significantly higher odds of survival at discharge than the group with small venous cannulas. We speculate that a larger cannula size may lead to a higher ECMO flow rate (**Figure 1**) and may be placed in a vein more safely than in an artery. It is difficult to generalize that the large venous cannulas are able to gain a higher ECMO flow rate than the small cannulas safely from the result of the present study. To confirm the relationship between the venous cannula size and the ECMO flow rate, further studies are needed.

In a retrospective observational study of a single-center registry by Kim et al., which included 165 patients with cardiogenic shock who underwent ECMO, the duration of ECMO support was shorter in the group with small (14- to 15-Fr) arterial cannulas than in the group with large (16- to 21-Fr) arterial cannulas (median 2.6 [IQR 0.7–5.2] vs. 4.0 [IQR 1.3–7.8] days, respectively; P<0.01).[17] Our results regarding the duration of ECMO support are consistent with those results. In addition, we found that large BW-adjusted arterial cannulas were associated with longer ICU and hospital stays. Similar results were obtained for venous cannulas. Prolonged ECMO support may affect frailty and delay social rehabilitation. There is a possibility that large cannulas are used for severely ill patients who are expected to require long-term ECMO.

Regarding complications, we found no significant differences between BW-adjusted cannula size and the composite of complications related to cannulation, whereas cannulation site bleeding was significantly increased in the group with large arterial cannulas than in the group with small arterial cannulas. Some studies have reported an increase in complications in the group with large arterial cannulas compared with the group with small cannulas.[16,30] Our results are in agreement with these previous reports. In the present study, the occurrence of limb ischemia was merely 1.3%, in contrast with rates of 9.7% and 4.0% reported in previous studies.[16,17] Consequently, it is plausible that our study had an insufficient number of patients to detect a statistically significant difference. Whereas previous studies examined only arterial cannulas,[16,17,31] we examined both arterial and venous cannulas because a larger cannula is generally used in veins rather than in arteries. There were no significant differences in complications according to venous cannula size. Appelt et al. reported that small cannulas are associated with hemolysis.[32] We could not assess hemolysis in this study; however, it should be recognized that small cannulas also have potential disadvantages. Based on these findings, the beneficial range for the venous cannula size (in Fr) is ≥0.35×BW (in kg), although further studies are needed to confirm our findings.

Our study has several limitations. First, this was a retrospective analysis based on data obtained from a multicenter registry. Thus, there is a possibility of selection bias related to the quality of treatment between the participating institutions. However, consecutive participants were enrolled, and we adjusted for potential selection bias. Second, 41% of patients (642/1,560) were excluded due to missing BW data at the time of ICU admission. Third, information on the actual vessel diameter and detailed information on the cannula, such as the manufacturer, model, and M-number,[33] were not obtained.

Conclusions

Our analysis of a multicenter ECPR registry in Japan found that there was no significant association between favorable neurological outcomes and cannula size; however, increasing cannula size was significantly associated with a higher survival rate at discharge for both arterial and venous catheters. In particular, ≥ venous cannula size ≥0.35×BW (Fr/kg) is significantly associated with a higher survival rate at discharge in patients with OHCA who received ECPR. Although our study should be regarded as exploratory, our results can help inform the design of future trials.

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Supplementary Files

Please find supplementary file(s);
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