

Supplementary Appendix.

Table S1. Annual Number and Incidence of Patients Who Received Venoarterial Extracorporeal Membrane Oxygenation

Year	Overall (n=29,231)		Annual patients per 100,000 inhabitants	Japanese population (million)
2010	1,696	(5.8%)	1.32	128.1
2011	2,605	(8.9%)	2.03	127.8
2012	3,273	(11%)	2.57	127.6
2013	3,479	(12%)	2.73	127.4
2014	4,096	(14%)	3.21	127.3
2015	4,322	(15%)	3.40	127.1
2016	4,716	(16%)	3.71	127.0
2017	5,044	(17%)	3.98	126.8
Average	3,654	(13%)	2.87	127.4

Table S2. Primary Diagnosis, Timing of Venoarterial Extracorporeal Membrane Oxygenation, and Proportions of Intervention and Death According to Level of Consciousness

	Consciousness on admission	
	Alert (n=13,624)	Disturbance (n=15,608)
Primary diagnosis		
Cardiogenic shock	11,177 (82%)	13,732 (88%)
Septic shock	685 (5.0%)	794 (5.1%)
Hypothermia	20 (0.2%)	278 (1.8%)
Poisoning	14 (0.1%)	118 (0.8%)
Starting VA-ECMO, mean days (±SD)	9.6 (28)	2.0 (5.6)
Leg-intervention†*	37 (0.3%)	61 (0.4%)
Death‡	8,492 (62%)	11,878 (76%)
VA-ECMO, venoarterial extracorporeal membrane oxygenation; SD, standard deviation		

Table S3. Additional Data for Age Categories†

	Patient age							
	Overall		Young (≤18 years)		Adult (19–59 years)		Elderly (≥60 years)	
	(n=29,231)		(n=948)		(n=9,195)		(n=19,088)	
Observational period	11	(2,35)	34	(11,78)	10	(2,35)	10	(2,33)
Timing of								
Leg-intervention*	6	(2,19)	6	(4,16)	4	(2,22)	6	(2,18)
Death	4	(2,12)	8	(2,24)	3	(1,9)	2	(1,8)
Leg intervention during VA-ECMO	26	(0.09%)	3	(0.32%)	14	(0.15%)	9	(0.05%)
Cardiac surgery	5,618	(19%)	101	(11%)	1,072	(12%)	4,445	(23%)
†Data was given as median day (IQR). *Timing of fasciotomy or amputation after starting VA-ECMO.								
VA-ECMO, venoarterial extracorporeal membrane oxygenation; IQR, interquartile range								

Table S4. Demographic Data of Surviving Patients Only Who Received Venoarterial Extracorporeal Membrane Oxygenation Among Age Category

Demographic data	Patient age				<i>p</i>
	Overall (<i>n</i> =8,861)	Young (≤18 years) (<i>n</i> =427)	Adult (19–59 years) (<i>n</i> =3,158)	Elderly (≥60 years) (<i>n</i> =5,276)	
Sex, <i>n</i> (%)					<0.001
Male	6,122 (69)	214 (50)	2,283 (72)	3,625 (69)	
Female	2,739 (31)	213 (50)	875 (28)	1,651 (31)	
Body mass index (kg/m ²), <i>n</i> (%)					<0.001
Underweight (<18.5)	1,047 (12)	293 (77)	291 (10)	463 (9.4)	
Normal weight (18.5–24.9)	4,813 (54)	73 (19)	1,575 (54)	3,165 (64)	
Overweight (≥25)	2,330 (26)	14 (3.7)	1,031 (36)	1,285 (26)	
Comorbid conditions at admission, <i>n</i> (%)					
Diabetes mellitus	1,905 (22)	4 (0.9)	499 (16)	1,402 (27)	<0.001
Hypertension	2,471 (28)	11 (2.6)	678 (22)	1,782 (34)	<0.001
Chronic lung disease	237 (2.7)	10 (2.3)	64 (2.0)	163 (3.1)	0.013
Cerebrovascular disease	378 (4.3)	4 (0.9)	89 (2.0)	285 (5.4)	<0.001
Cardiac disease	5,939 (67)	221 (52)	2,111 (67)	3,607 (68)	<0.001
Atherosclerotic disease	2,184 (25)	12 (2.8)	598 (19)	1,574 (30)	<0.001
At least one comorbidity	7,176 (81)	235 (55)	2,451 (78)	4,490 (85)	<0.001
Episode of arrest at admission, <i>n</i> (%)	1,051 (12)	35 (8.2)	493 (16)	523 (9.9)	<0.001
Charlson Comorbidity Index update category, <i>n</i> (%)					<0.001
≤2	8,273 (93)	415 (97)	3,010 (95)	4,848 (92)	
≥3	588 (6.6)	12 (2.8)	148 (4.7)	428 (8.1)	
Consciousness on admission, <i>n</i> (%)					<0.001
Alert	5,132 (58)	275 (64)	1,515 (48)	3,342 (63)	
Disturbance	3,729 (42)	152 (36)	1,643 (52)	1,934 (37)	
Ambulance use, <i>n</i> (%)	5,334 (60)	190 (45)	2,184 (69)	2,960 (56)	<0.001
Hospital volume (per year), <i>n</i> (%)					<0.001
Low (0.75–17.4)	2,769 (31)	93 (22)	1,019 (32)	1,657 (31)	
Medium (17.5–41.4)	3,005 (34)	170 (40)	1,063 (34)	1,772 (34)	
High (≥41.5)	3,087 (35)	164 (38)	1,076 (34)	1,847 (35)	

Table S5.

Duration of Observational Period, Timing of Intervention After Starting Venoarterial Extracorporeal Membrane Oxygenation Among Age Category on Surviving Patients Only†

	Patient age				<i>p</i>
	Overall	Young	Adult	Elderly	
	(<i>n</i> =8,861)	(≤18 years) (<i>n</i> =427)	(19–60 years) (<i>n</i> =3,158)	(≥60 years) (<i>n</i> =5,276)	
Observational period	41 (25,68)	59 (32,115)	40 (24,64)	41 (25,67)	<0.001
Timing of leg intervention*	7 (4,22)	9 (5,16)	6.5 (3,32)	9.5 (5,22)	0.75

† Data was given as median day (IQR). * Timing of fasciotomy or amputation after starting VA-ECMO.

Table S6.

Sensitivity Analysis of Risk Factors for Severe Lower Extremity Ischemia Following Venoarterial Extracorporeal Membrane Oxygenation on Surviving Patients Only

Risk factor	Cause-specific hazard ratio	95% Confidence interval	<i>p</i>
Age (years)			
19–59	Reference		
≤18	3.78	1.44–9.94	0.007
≥60	0.60	0.33–1.09	0.096
Sex			
Female	Reference		
Male	0.94	0.53–1.68	0.843
Body mass index (kg/m ²)			
Normal weight (18.5–24.9)	Reference		
Underweight (<18.5)	0.86	0.35–2.11	0.750
Overweight (≥25.0)	1.35	0.74–2.47	0.329
Comorbid conditions			
Diabetes mellitus	1.05	0.51–2.14	0.893
Atherosclerotic disease	0.93	0.47–1.83	0.826
Episode of arrest at admission	0.90	0.42–1.96	0.799
VA-ECMO duration (per day)	0.96	0.89–1.04	0.344
Consciousness on admission			
Alert	Reference		
Disturbance	2.60	1.47–4.61	0.001
VA-ECMO, venoarterial extracorporeal membrane oxygenation			

Table S7

Sensitivity Analysis With Clearer Indications for Venoarterial Extracorporeal Membrane Oxygenation

Risk factor	Cause-specific hazard ratio	95% Confidence interval	<i>p</i>
Age (years)			
19–59	Reference		
≤18	3.33	1.06–10.43	0.039
≥60	0.53	0.27–1.03	0.065
Sex			
Female	Reference		
Male	1.06	0.55–2.03	0.854
Body mass index (kg/m ²)			
Normal weight (18.5–24.9)	Reference		
Underweight (<18.5)	1.89	0.80–4.51	0.148
Overweight (≥25.0)	1.33	0.66–2.67	0.429
Comorbid conditions			
Diabetes mellitus	1.57	0.71–3.49	0.266
Atherosclerotic disease	0.34	0.10–1.11	0.074
Episode of arrest at admission	1.09	0.47–2.52	0.846
VA-ECMO duration (per day)	0.96	0.91–1.02	0.157
Consciousness on admission			
Alert	Reference		
Disturbance	2.45	1.24–4.82	0.010
VA-ECMO, venoarterial extracorporeal membrane oxygenation			

Table S8

Sensitivity Analysis With Excluding Patients Who Did Not Receive Anticoagulants at the Start of Venoarterial Extracorporeal Membrane Oxygenation

Risk factor	Cause-specific hazard ratio	95% Confidence interval	<i>p</i>
Age (years)			
19–59	Reference		
≤18	3.13	1.26–7.81	0.014
≥60	0.62	0.36–1.06	0.079
Sex			
Female	Reference		
Male	0.96	0.56–1.66	0.888
Body mass index (kg/m ²)			
Normal weight (18.5–24.9)	Reference		
Underweight (<18.5)	1.48	0.68–3.22	0.322
Overweight (≥25.0)	1.32	0.75–2.30	0.337
Comorbid conditions			
Diabetes mellitus	1.08	0.55–2.11	0.826
Atherosclerotic disease	0.62	0.30–1.27	0.194
Episode of arrest at admission	0.75	0.37–1.49	0.404
VA-ECMO duration (per day)	0.99	0.96–1.03	0.613
Consciousness on admission			
Alert	Reference		
Disturbance	1.73	1.00–2.98	0.049
VA-ECMO, venoarterial extracorporeal membrane oxygenation			

Table S9

Sensitivity Analysis With Excluding Patients Who Underwent Cardiac Surgery

Risk factor	Cause-specific hazard ratio	95% Confidence interval	<i>p</i>
Age (years)			
19–59	Reference		
≤18	3.25	1.38–7.66	0.007
≥60	0.62	0.38–1.01	0.053
Sex			
Female	Reference		
Male	1.03	0.63–1.68	0.922
Body mass index (kg/m ²)			
Normal weight (18.5–24.9)	Reference		
Underweight (<18.5)	0.70	0.32–1.57	0.391
Overweight (≥25.0)	1.16	0.71–1.90	0.551
Comorbid conditions			
Diabetes mellitus	1.27	0.72–2.24	0.412
Atherosclerotic disease	0.63	0.33–1.20	0.161
Episode of arrest at admission	0.70	0.36–1.38	0.307
VA-ECMO duration (per day)	0.97	0.92–1.02	0.190
Consciousness on admission			
Alert	Reference		
Disturbance	2.05	1.28–3.30	0.003
VA-ECMO, venoarterial extracorporeal membrane oxygenation			