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RESEARCH ARTICLE

Predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation (V-A ECMO): A systematic review and meta-analysis

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Abstract

Background

Venoarterial extracorporeal membrane oxygenation (V-A ECMO) use to support patients in cardiac failure is increasing. Despite this increased use, predicting successful weaning from ECMO can be challenging, no uniform guidelines on weaning exist. Therefore, we completed a systematic review to evaluate prognostic factors that predict successful weaning from V-A ECMO.

Methods

Following the PRIMSA guidelines, a systematic literature search of Medline, Embase, SCOPUS and CENTRAL identified original research studies of patients requiring V-A ECMO where weaning was attempted. Data was collected on demographic factors and weaning protocol, biomarkers, haemodynamic, echocardiographic factors for the successfully weaned (SW) and not successfully weaned (NSW) groups. Two investigators reviewed studies for relevance, extracted data, and assessed risk of bias using the ROBINS-I tool. The study was registered on the international prospective register of systematic reviews (PROSPERO ID# CRD42022366153).

Results

1219 records were screened, of which 20 studies were deemed sufficient to be included in the statistical analysis based on pre-specified criteria. Factors associated with successful weaning were higher left ventricular ejection fraction (LVEF) (MD 9.0, 95% CI 4.1–13.8; p < 0.001) and left ventricular outflow tract velocity time integral (LVOT VTI) at time of

weaning, (MD 1.35, 95% CI 0.28-2.40 lactate at admission (MD -3.2, 95% CI -4.8 to -1.5, p < 0.001), and CK-MB at admission (MD -4.11, 95%CI -6.6 to -1.6, p = 0.001). Critical appraisal demonstrated moderate-high risk of bias owing to confounding and low sample sizes.

Conclusion

In patients on V-A ECMO support being assessed for weaning multi-parametric assessment is required. Moderate-high heterogeneity and low sample sizes warrant higher-quality studies to help guide decisions to wean patients from V-A ECMO.

Introduction

Veno-arterial (V-A) extracorporeal membrane oxygenation (ECMO) is increasingly being used [1,2] in acute cardiac failure to provide end-organ perfusion whilst definitive treatment, myocardial recover occurs or bridge to left ventricular assist device (LVAD) or heart transplant is completed.

Complications whilst on V-A ECMO support are common and effect mortality and increase with duration of support [3]. Therefore, minimising duration of V-A ECMO support, where possible, is sought. However, premature withdrawal of V-A ECMO support, may result in recurrence of cardiogenic shock and effect recovering organs. Minimizing complications associated with device support with the potential for hemodynamic deterioration if support is prematurely discontinued can be challenging.

The definition of successful V-A ECMO weaning has been proposed as when a patient survives for longer than 48 hours after ECMO explantation, with more, recent definitions as those having ECMO removed and not requiring further mechanical support because of recurring cardiogenic shock over the following 30 days [4,5]. Depending on the definition the proportion of V-A ECMO patients successfully weaned ranged between 30–75% [4–9].

A variety of clinical, haemodynamic, biochemical and echocardiographic variables have been proposed and used to guide clinical improvement and readiness to wean [10]. However, criteria and variables have not been completely reviewed to ascertain effectiveness [11] and meta-analyses as yet not completed. Therefore, we systematically reviewed a broad range of biomarkers, haemodynamic, echocardiographic and scoring systems to predict successful weaning from V-A ECMO.

Materials and methods

The study was conducted as previously outlined in our registered and published protocol (PROSPERO ID# CRD42022366153) and in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [12]. Ethics approval and patient consent were not required. The PRISMA checklist is provided in S1 Appendix.

Search strategy

The search strategy is detailed in a Material. A comprehensive search of three electronic databases (Medline, Embase, SCOPUS and CENTRAL) was conducted in October 2022, which were re-run in December 2023 and March 2024 prior to final analysis and further studies retrieved for inclusion. Appropriate Boolean operators were used to combine search terms that included V-A ECMO, ECMO, extra-corporeal life support, weaning, decannulation and ECLS. The reference lists of all included studies were also reviewed to identify any additional

articles, and duplicate articles were removed. Studies that were not primarily in the English language were included if they were accompanied by an English translation. There were no limitations on the publication period. The search strategy is provided in <u>S2 Appendix</u>.

Study characteristics

Inclusion criteria allowed for randomized controlled trials, cohort studies, case series and conference abstracts that (1) considered adult or paediatric populations (2) involved patients who were on V-A ECMO and (3) there was an attempt to de-cannulate/wean from ECMO. Studies using ECMO as a bridge to ventricular assist device or heart transplant were excluded. Case series were included if >5 patients. Studies had to report associations between variables within the study and weaning success. Review publications, grey literature, non-English language publications, editorials, comments, letters to the editor and animal studies were excluded. Studies only assessing baseline variables with weaning success were excluded.

Study selection

Title and abstract screening were conducted by independent investigators (P.S. or H.H. or C.D.). Likewise, full-text screening was performed by two independent investigators (P.S. or H.H. or C.D.). All conflicts were resolved by a third, senior investigator (M.D.). The systematic review platform Covidence (www.covidence.org; Veritas Health Innovation, Melbourne, Australia) was used to facilitate the screening process. Publications found to fulfil eligibility criteria underwent data extraction. Literature search and decisions are provided in S1 Table.

Data extraction

Data was extracted from studies by two independent reviewers (P.S. or H.H. or C.D. or J.G.) using Microsoft Excel. Extracted variables included but not limited to patient demographics, weaning protocol, successful weaning definition, weaning success, various prognostic factors including biomarkers, haemodynamic, echocardiographic and scoring systems. The primary outcome was weaning success defined survival post removal of mechanical circulatory support and not requiring ventricular assist device or heart transplant. Meta-analysis was planned of predictors as appropriate. Missing data was reported as not reported. Authors were attempted to be contacted for further or missing data via email. Data extraction table is provided in S2 Table.

Evaluation of risk of bias

Critical appraisal of the risk of bias for individual studies was conducted using the ROBINS-I Tool (Risk of Bias in Non-Randomized Studies - of Interventions) [13]. Each included study was scored by two independent investigators (P.S. or J.G. or H.H.). Any discrepancies between the two reviewers were resolved by discussion and mutual agreement. Studies of poor-quality following risk of bias assessment were not be excluded from being included in our synthesis. Where a poor-quality study has contributed to a synthesized effect estimate, we explored the impact of study quality by performing sensitivity analysis by removing the poor-quality study to observe the impact that bias has had on the synthesized effect. Risk of bias assessment is provided in §3 Table.

Statistical analysis

Meta-analysis was completed as per the Cochrane Handbook for Systematic Reviews of Interventions when the outcomes were reported by two or more trials [14]. Statistical analysis was

performed using Review Manager (version 5.3, The Cochrane Collaboration, Oxford, UK). For continuous outcomes, mean, standard deviation (SD) and sample size were extracted from each of the groups. Where studies reported median and ranges or interquartile range, derived mean and standard deviation as described by Wan et al. were calculated [15]. Mean differences with 95% confidence interval (CI) were used for continuous outcomes. An inverse variance method was applied for mean difference. Heterogeneity was assessed using I² statistics and values between 50% and 90% were considered to represent substantial heterogeneity. A random effects meta-analysis model and exploring heterogeneity with sensitivity and subgroup analysis were applied where appropriate. Categorisation of reported risk factors of successful weaning from studies that reported multivariable adjustment was completed.

Results

Systematic search and study selection

The search strategy of relevant references yielded a total of 2199 references (Fig 1). After the removal of 980 duplicates, the remaining 1219 references were screened by title and abstract. A total of 62 publications were deemed to be eligible for full-text screening, of which 28 studies were excluded with reasons. A total of 34 articles were included in the final analysis, of which 20 studies were deemed sufficient to be included in the statistical analysis. Risk of bias assessment is summarised in Fig 2. The remaining 14 studies examined differing prognostic predictors that were not able to be meta-analysed together. The sample sizes ranged from 12 to 265 patients, with a pooled sample size of 1903 patients. Twenty-six publications were retrospective

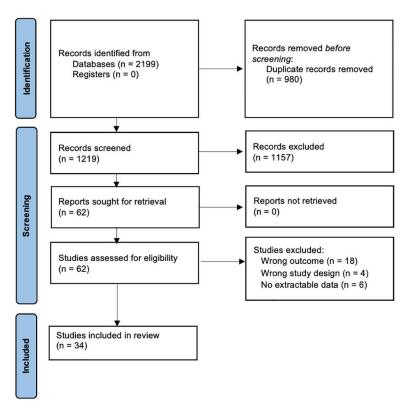


Fig 1. PRISMA flow diagram illustrating the number of studies identified by the search and the stages in which they were chosen and eliminated.

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Fig 2. Risk of bias of the included studies (ROBINS-I).

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cohort studies, seven were prospective cohort studies, and one not recorded. Cardiogenic shock was the primary indication for V-A ECMO in ten publications, myocarditis in two, cardiomyopathy in two, cardiac arrest in four, pulmonary embolism in one, post cardiac surgery in two, congenital heart disease in one, acute respiratory distress syndrome in one, and eleven not recorded. Geographically, fourteen publications were from Asia, eight were from North America, eleven were from Europe, and one was from the Middle East. A summary of the baseline characteristics of included papers and clinical variables is provided in Table 1.

Biomarkers. Markers of organ damage were inversely associated with weaning success— Fig 3. Lower levels of creatinine kinase (CK-MB) (MD -4.1, 95%CI -6.6 to -1.6, p = 0.001; I²

(Continued)

Table 1. Characteristics of included studies.	racterism	,	I	-							11.11				•	
Author	Country Enrolment period	Enrol- ment period	Type of Total study number of ber of patier	f nts	Suc- cessful weaned	Unsuc- cessful wean	Age Suc- cess wean	Unsuc- cess wean	Male Suc- cess wean	Unsuc- cess wean	Suc- cess wean	Unsuc- cess wean	Heart failure (co- morbidity)	Indication for V-A-ECMO	Successful weaning definition	Wean- ing success (%)
Aissaoui 2011 [16]	France	2007–	Pro- spective cohort	38	25	13	49 ± 14	67 ± 11	25	∞	NR	NR	8	CMP (47%), FM (6%), Post-cardiotomy shock (22%), Post-transplantation (10%), Other (16%)	ECMO remoV-Al and no further MCS because of recurring CS over the following 30 days	20/38 = 53%
Akin 2017 [17,29]	Nether- lands	2014-	Pro- spective cohort	13	10	8	56 ± 17	41 ± 16	6	_	NR	NR	0	PE (38%), Post-cardiotomy shock (23%), CS post-AMI (15%), Myocarditis (15%), Intoxication (8%)	Successful V-A-ECMO explantation within 48 h	10/13 = 77%
Aksoy 2024 [18]	Turkey	2010–	Retro- spective cohort	55	27	28	2.3	1.6	19	20	NR	NR	NR	Post-op complications following congenital heart surgery, including: low cardiac output syndrome, inability to wean from bypass, ECPR.	Wean trial when adequate myocardial contraction and haemodynamically stable; initiated with flow rate to 25%	27/55 = 49%
Chen 2022 [<u>19</u>]	Taiwan	NR	Retro- spective cohort	47	31	16	69 ± 16	39 ± 18	15	6	NR	NR	NR	NR	Weaning from ECMO and surviV-Al beyond 48 h	31/47 = 66%
Colombo 2019 [20]	Italy	2013– 2017	Retro- spective cohort	25	18	7	N.	NR	NR.	NR	NR	NR	NR	CPR (71%), CS post-AMI (17%), Myocarditis (7%), PE (4%), Takotsubo (2%), Intoxication (2%)	Device remoV-Al without requirement for re-cannulation over the following 30 days	18/25 = 72%
Cusanno 2022 [9]	France	2016– 2021	Retro- spective cohort	57	36	21	46 ±	57 ± 17	NR	NR	26 ± 6	25 ± 7	37	Ischemic CS (35%), Refractory CA (28%), Other (37%)	NR	36/57 = 63%
Daftari 2010 [<u>21</u>]	USA	2000– 2008	Retro- spective cohort	27	16	11	NR	NR	NR	NR	NR	NR	27	Heart failure (100%)	NR	16/27 = 59%
Dunton 2023 [22]	USA	2016– 2021	Retro- spective cohort	265	140	125	59.1 ± 13.6	59.4 ±	95	100	30.8 ±	30.4 ± 7.4	75	CPR, cardiogenic shock, post cardiotomy shock	Survival to decannulation	140/265 = 53%
Finnigan 2020 [<u>23]</u>	United Kingdom	NR	NR	14	NR	NR	NR	NR	N.	NR	NR	NR	NR	Post cardiac surgery support (57%), Respiratory support (43%)	NR	NR.
Frederiksen 2018 [24]	Denmark NR	NR	Retro- spective cohort	29	15	14	N.	NR	Ä	NR	NR	NR	NR	NR	ECMO weaning and being alive 24h later without hemodynamic MCS	15/29 = 52%
Gonzalez Martin 2021 [25]	Spain	2013- 2020	Retro- spective cohort	85	52	33	NR	NR	N.	NR	NR	NR	0	CS (47%), ECPR (9%), Electrical storm (9%), Post- cardiotomy CS (33%), Other (1%)	Survival >24 h after explant and no mortality from car- diogenic shock/heart failure or cardiac arrest during admission	52/85 = 61%
Huang 2018 [26]	Taiwan	2014- 2015	Retro- spective cohort	46	28	18	59 ± 16	48 ± 15	18	15	NR	NR	8	CS/Cardiac arrest post AMI (50%), Dilated cardiomyopathy (15%), VT/VF Arrest (11%), Myocarditis (8%), PE (4%)	ECMO removal and no mortality and/or MCS because of recurring CD over the following 48 h	28/46 = 61%

Author	Country Enrol-	Enrol-	Type of	Total	Suc-	Unsuc-	Age		Male		BMI		Heart	Indication for V-A-ECMO	Successful weaning	Wean-
		ment period	study	num- ber of patients	cessful			Unsuc-	Suc- cess wean	Unsuc- cess wean	Suc- 1 cess c	Unsuc-	failure (comorbidity)		definition	ing success (%)
Hutchins 2023 [27]	USA	2015– 2021	Retro- spective cohort	199	103	96	14.6	16.2	29	71	NR 1	NR	NR	Cardiogenic shock	Successful decannulation was defined as survivall without relapse to mechan- ical circulatory support or heart transplant within 30 days	103/199 = 51.8%
Joseph 2019 [28]	USA	NR	Retro- spective cohort	30	NR	NR	NR	NR	NR 1	NR	NR 1	NR	NR	NR	NR	NR
Kellnar 2024 [29]	Germany 2021.	2021–	Pro- spective cohort	12	7	72	53.0 [1QR (1QR 47.0; 560.0)	58.0 (IQR 57.5; 67.0)	NR 1	NR	26.9 (IQR (25.2; 230.0)	24.9 (IQR 23.7; 26.9)	NR	Cardiogenic shock	Not requiring further mechanical circulatory support within 30 days	7/12 = 58%
Kim 2021 (A) [30]	South Korea	2016– 2018	Pro- spective cohort	92	64	28	60 ± 12	59 ± 12	48	21	24 ± 3	25 ± 4	NR	CS post-AMI (48%) Ischemic cardiomyopathy (48%), Other (4%)	ECMO removal and not requiring further MCS over the following 30 days	64/92 = 70%
Kim 2021 (B) [31]	South Korea	2016– 2019	Pro- spective cohort	79	50	29	63 ± 13	58 ± 12	41	23	25 ± 3	25 ± 4	NR I	Post-MI CMP (52%), Idiopathic dilated CMP (18%), Fulminant myocarditis (4%), Stress-induced CMP (4%)	Successful removal of V-A-ECMO and no further mechanical circulatory support in the following 30 days	63%
L'Acqua 2019 Italy [32]	Italy	2012– 2018	Retro- spective cohort	86	49	49	NR.	NR	NR 1	NR	NR 1	NR	NR	NR	Patient weaned from V-A ECMO	49/98 = 50%
Lee 2023	South Korea	2017– 2019	Retro- spective cohort	55	38	17	NR	NR	NR 1	NR	NR 1	NR	NR	NR	NR	38/55 = 69%
Lim 2019 [34]	South Korea	2010– 2018	Retro- spective cohort	122	72	50	57.8 ± 15.0	NR	Ä.	NR	NR 1	NR	NR	NR	NR	72/122 = 59%
Matsumoto 2018 [35]	Japan	1995– 2014	Retro- spective cohort	37	22	15	44 ± 432	40 ± 31	13 8	∞	21 ± 3 2	22 ± 4	NR	Myocarditis (100%)	ECMO removal	22/37 = 59%
Mongkolpun Belgium 2019 [36]	Belgium	NR	Retro- spective cohort	22	12	10	NR	NR	NR 1	NR	NR 1	NR	NR	CS post-AMI (64%), post- cardiotomy (14%), Myocardi- tis (14%), PE (8%)	ECMO removal and HD Stabilization without the need to increase the Vaso- pressor dose within 24 h	12/22 = 55%
Naruke 2010 Japan [37]	Japan	1996– 2008	Retro- spective cohort	25	18	7	54 ± 114	49 ± 18	∞	rv.	NR	NR	8	Myocarditis (52%), CS post- AMI (36%), ACHF (12%)	ECMO weaning	18/25 = 72%

(Continued)

Table 1. (Continued)

Table 1. (Continued)

Author	Country Enrol-	Enrol-	Type of	Total	Suc-	Unsuc-	Age		Male		BMI	<u> </u>	Heart	Indication for V-A-ECMO	Successful weaning	Wean-
				ıts	nd led			Unsuc-		Unsuc- S		Unsuc-	(co-dity)			ing success (%)
Naruke 2012 [38]	Japan	NR	Retro- spective cohort	30	NR	NR			Ä Z				NR	Z.	V-A-ECMO weaned of without severely dete- riorated cardiac output indicated by ETCO2 < 10 mmHg or LVET < 100 ms	NR
North 2018 [41]	USA	2012- 2017	Retro- spective cohort	09	42	18	NA L	NR	Z Z	NR	NR NR		NR	NR	-	42/60 = 70%
Ouazani 2019 [42]	USA	NR	Pro- spective cohort	12	6	3	Ä.	NR	NR N	NR	NR NR		NR	NR	ECMO removal without requiring any further MCS	9/12 = 75%
Punn 2019 [39]	USA	2010- 2018	Pro- spective cohort	63	25	38	58 ± 21	32 ± 40	16 2	20	NR NR		NR	Congenital heart defect (63%), wean within 48 hours of Myocarditis (15%), Idiopathic assessment and survived dilated cardiomyopathy without ventricular assist (14%), Sepsis (2%), Others transplantation	wean within 48 hours of assessment and survived without ventricular assist devices or orthotopic heart transplantation	25/63 = 40%
Sawada 2021 Japan		2013- 2017	Retro- spective cohort	50	24	26	76 ± 6	64 ± 29	20 1	17 2	23 ± 6 23	3 ± 6		CS post-AMI (54%), FM (24%), CMP (10%), other heart disease (12%)	ECMO removal and survival beyond 30 days without needs for further MCS	24/50 = 48%
Stull 2013 [41]	USA	2010– 2013	Retro- spective cohort	23	15	8	Ä.	NR	X X	NR	NR NR		NR	ARDS (100%)	NR	15/23 = 65%
Sugiura 2019 Japan [42]		2012– 2016	Retro- spective cohort	55	28	27	64 ± 0	68 ± 16	21 2	25 2	25 ± 4 25	25 ± 5 N	NR	CS post-AMI (100%)	ECMO removal	28/55 = 51%
Sugiyama 2019 [43]	Japan	2011–	Retro- spective cohort	74	37	37	NK I	NR	NA NA	NR	NR NR		NR	NR	Patient survives more than 48 h after the removal of cannulas of ECMO	37/74 = 50%
V-ArodomV- Thailand 2018 Anichkul 2023 [44]	Thailand	i	Retro- spective cohort	57	46	11	NK L	NR	NA NA	NR Z	NR NR		NR	Cardiogenic shock	NR	46/57 = 81%
Voigt 2022 [45]	Germany 2017- 2020	2017– 2020	Retro- spective cohort	40	16	24	51 ± 0	60 ± 15]	10 1	18 2	28 ± 6 27	9 +	NR	Cardiac arrest (40%), Cardio- genic shock (60%)	V-A-ECMO decannulation and subsequent discharge	16/40 = 40%
Watanabe 2023 [46]	Japan	2010-	Retro- spective cohort	41	17	24	70.6 ± (13.2	68.0 ± 14.5	12 1	17	NR NR		NR	Z	Survival for more than 24 hours after V-A-ECMO withdrawal without requiring reintroduction	17/41 = 41%

ACHE, acute on chronic heart failure; AMI, acute myocardial infarction; ARDS, acute respiratory distress syndrome; CA, cardiac arrest; CMP, cardiomyopathy; CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; ECMO, extracorporeal membranous oxygenation; FM, fulminant myocarditis; MCS, mechanical cardiac support; NR, not reported; PE, pulmonary embolism; VF, ventricular fibrillation; VT, ventricular tachycardia.

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Heart Rate

Successfully Weaned **Not Successfully Weaned** Mean Difference Mean Difference Study or Subgroup SD Total Weight Mean Total Mean SD IV, Random, 95% CI IV, Random, 95% CI Year -12.00 [-58.86, 34.86] 2010 Naruke 2010 106 44 18 118 57 2.0% Aissaoui 2011 95 16 20 115 19 13 17.1% -20.00 [-32.48, -7.52] 2011 Matsumoto 2018 106.036 37.07 22 98 37.07 15 6.6% 8.04 [-16.29, 32.36] 2018 Punn 2019 121.2 26.8 25 125.7 15.7% -4.50 [-17.87, 8.87] 2019 26 38 Sawada 2021 24 10.37 82 17.77 84 26 25.3% -2.00 [-10.15, 6.15] 2021 **Hutchins 2023** 91.6 17.4 103 91 16 96 33.3% 0.60 [-4.04, 5.24] 2023 Total (95% CI) 195 100.0% -4.14 [-10.99, 2.71] Heterogeneity: $Tau^2 = 31.10$; $Chi^2 = 10.15$, df = 5 (P = 0.07); $I^2 = 51\%$ -25 Test for overall effect: Z = 1.18 (P = 0.24) Successfully Weaned Not Successfully Weaned

Systolic Blood Pressure (mmHg)

	Succ	essfully Weane	d	Not Su	ccessfully Wear	ned		Mean Difference			Mea	n Diff	erence		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, Ra	ndom	,95% CI		
Naruke 2010	84	31	18	85	4	7	12.1%	-1.00 [-15.62, 13.62]	2010			_	_		
Matsumoto 2018	84	11.85185185	22	86	17.7777778	15	13.9%	-2.00 [-12.27, 8.27]	2018		- 2	-	_		
Kim 2021 (A) JASE	100.3	10.3	64	97.3	15.4	28	15.2%	3.00 [-3.24, 9.24]	2021			+	-		
Sawada 2021	114	25.18518519	24	100	25.92592593	26	12.3%	14.00 [-0.17, 28.17]	2021				•		
Watanabe 2023	122.5	24.5	17	79.1	41.9	24	9.8%	43.40 [22.99, 63.81]	2023				_	•	_
Hutchins 2023	116	21.6	103	93.4	22.3	96	15.3%	22.60 [16.49, 28.71]	2023				_		
Lee 2023	109.4	12.3	38	81.6	17.2	17	14.3%	27.80 [18.74, 36.86]	2023				-	-	
Kellnar 2024	111.7786	16.5338	7	80.9155	29.6661	5	7.1%	30.86 [2.12, 59.61]	2024			- 1-			
Total (95% CI)			293			218	100.0%	15.65 [5.44, 25.86]					•		
Heterogeneity: Tau ² =	168.11; Chi	² = 51.12, df = 7	(P < 0.00	0001); I ² =	86%							_		+	
Test for overall effect:			,	,						-50 Success	-25 fully Wear	0 ned 1	25 Not Succes	50 sfully W	/eane

Pulse Pressure

	Succ	essfully Weane	d	Not Su	ccessfully Wear	ned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Aissaoui 2011	52	12	38	39	19	13	15.5%	13.00 [1.99, 24.01]	2011	
Punn 2019	33.6	14.6	25	26.6	13.7	38	24.3%	7.00 [-0.19, 14.19]	2019	-
Sawada 2021	50	30.37037037	24	45	14.81481481	26	11.8%	5.00 [-8.42, 18.42]	2021	- •
Lee 2023	32.8	8.1	38	18.4	8.7	17	31.5%	14.40 [9.53, 19.27]	2023	-
Watanabe 2023	60.1	17.6	17	35.2	21	24	14.0%	24.90 [13.04, 36.76]	2023	
Kellnar 2024	50.6221	21.1265	7	24.3595	30.6717	5	2.9%	26.26 [-4.85, 57.37]	2024	
Total (95% CI)			149			123	100.0%	13.09 [7.65, 18.53]		•
Heterogeneity: Tau ² =	18.29; Chi	$^2 = 8.92$, df = 5 (1	P = 0.11	$ ^2 = 44\%$						to 15 1 15 15
Test for overall effect:	Z = 4.71 (F	o < 0.00001)								-50 -25 0 25 50 Successfully Weaned Not Successfully Weane

Fig 3. Forrest plot of comparison of haemodynamic parameters on V-A ECMO Weaning.

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= 24%), lactate at admission (MD -3.2, 95% CI -4.8 to -1.5, p < 0.001; I² = 90%), and lower levels of alanine aminotransferase (ALT) (MD -36.7, 95%CI -65.5 to 7.9, P = 0.01; I² = 0%) at the time of weaning were associated with weaning success. Too few studies reported NT-ProBNP or Troponin to enable analysis.

Haemodynamics. Patients with higher pulse pressure (MD 13.1, 95%CI 7.7–18.5, p < 0.001; $I^2 = 44\%$) and systolic blood pressure (MD 15.7, 95%CI 5.4–25.9, p < 0.001; $I^2 = 86\%$) were associated with weaning success—Fig 4.

Echocardiography. Patients with higher left ventricular ejection fraction (LVEF) at time of weaning (MD 9.0, 95% CI 4.1–13.8; p < 0.001; $I^2 = 85\%$), left ventricular outflow tract velocity time integral (LVOT VTI) (MD 1.35, 95% CI 0.28–2.40, p = 0.01; $I^2 = 0\%$), E/Ea (MD –2.72, 95% CI –4.45 to –0.98, p = 0.002; $I^2 = 29\%$) were associated with weaning success—Fig 5.

Multi-variable adjusted: Risk predictors. Thirteen studies provided multi-variable adjusted analysis to identify predictors of successful weaning. Covariates tested varied widely between studies; only lack of renal failure or CRRT during ECMO, and post-weaning lactate, reported by more than one study as predictors of successful ECMO weaning—<u>Table 2</u>.

Lactate (initial)

	Succ	essfully Wean	ed	Not Su	ccessfully Wea	ned		Mean Difference		Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI	
Aissaoui 2011	7.3	5.4	38	7.3	6.1	15	7.2%	0.00 [-3.53, 3.53]	2011		
Matsumoto 2018	1.35	2.5926	22	2.8	6.68	15	7.2%	-1.45 [-5.00, 2.10]	2018	-	
L'Acqua 2019	8	4.9	49	11.9	4.9	49	10.8%	-3.90 [-5.84, -1.96]	2019		
Sugiura 2019	11.8	4.74074074	27	13.8	3.85185185	27	9.9%	-2.00 [-4.30, 0.30]	2019		
Kim 2021 (B) (JACimaging)	3.3	3.037	50	5.8	4.5185	29	11.0%	-2.50 [-4.35, -0.65]	2021		
Sawada 2021	1.2	0.59259259	24	1.6	0.96296296	26	13.6%	-0.40 [-0.84, 0.04]	2021		
Chen 2022	6.5	5.2	31	9	6.1	16	7.3%	-2.50 [-6.00, 1.00]	2022	· · ·	
Voigt 2022	7.7	4.5	16	11.5	4.9	24	8.4%	-3.80 [-6.75, -0.85]	2022	-	
Hutchins 2023	1.69	2.06	103	6.6	6.47	96	12.2%	-4.91 [-6.26, -3.56]	2023		
Watanabe 2023	1.9	1.2	17	13.1	7.4	0		Not estimable	2023		
Aksoy 2024	3.7	2.3	27	6.2	2.6	28	12.3%	-2.50 [-3.80, -1.20]	2024	(-4- -	
Total (95% CI)			404			325	100.0%	-2.46 [-3.83, -1.09]		•	
Heterogeneity: Tau ² = 3.54; C		The state of the s	.00001); I	° = 85%						-10 -5 0 5	10
Test for overall effect: Z = 3.52	2 (P = 0.0)	004)								Successfully Weaned Not Successfully W	

CK-MB Max (IU/L)

	Success	fully We	aned	Not Succe	ssfully We	aned		Mean Difference		Mean Diff	erence
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Y	'ear	IV, Random	1,95% CI
Matsumoto 2018	7.7	4.42	22	14.91	9.38	15	19.9%	-7.21 [-12.30, -2.12] 2	018		
Sugiura 2019	2.5	9.64	28	7.2	6.34	27	26.3%	-4.70 [-9.00, -0.40] 2	019	-	
Voigt 2022	2.6	3.2	16	5.27	5.1	24	53.7%	-2.67 [-5.24, -0.10] 2	022	-	
Total (95% CI)			66			66	100.0%	-4.11 [-6.58, -1.64]		•	
Heterogeneity: Tau ² =	1.24; Chi ² =	2.63, df	= 2 (P =	0.27); $I^2 = 24$	%				_	-10 -5 0	5 10
Test for overall effect:	Z = 3.26 (P	= 0.001)									Not Successfully Wean

BUN

	Suc	cessfully Weans	ed	Not Su	ccessfully Wear	ned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Matsumoto 2018	32.5	17.7777778	22	34	14.07407407	15	23.1%	-1.50 [-11.79, 8.79]	2018	-
Sawada 2021	31	22.2222222	24	34	14.81481481	26	22.3%	-3.00 [-13.56, 7.56]	2021	-
Chen 2022	19.6	11	31	16.2	15.1	16	29.6%	3.40 [-4.95, 11.75]	2022	- • -
Aksoy 2024	27.3	18.4	27	38.2	18.1	28	25.0%	-10.90 [-20.55, -1.25]	2024	-
Total (95% CI)			104			85	100.0%	-2.74 [-8.89, 3.42]		•
Heterogeneity: Tau ² =	15.14; Ch	$i^2 = 4.87$, df = 3 (P = 0.18)	$I^2 = 38\%$						
Test for overall effect: 2	Z = 0.87 (P = 0.38)								-20 -10 0 10 20 Successfully Weaned Not Successfully Weaned

pH

	Succ	essfully Wean	ed	Not Su	ccessfully Wea	ned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Aissaoui 2011	7.33	0.1	38	7.35	0.15	13	11.9%	-0.02 [-0.11, 0.07]	2011	-
Matsumoto 2018	7.45	0.08148148	22	7.36	0.13333333	15	12.6%	0.09 [0.01, 0.17]	2018	-
L'Acqua 2019	7.33	0.1	49	7.26	0.2	49	13.3%	0.07 [0.01, 0.13]	2019	
Sugiura 2019	7.12	0.3037037	27	7.01	0.28888889	27	8.0%	0.11 [-0.05, 0.27]	2019)
Sawada 2021	7.46	0.05185185	24	7.47	0.1037037	26	14.2%	-0.01 [-0.05, 0.03]	2021	-
Chen 2022	7.4	0.1	31	7.4	0.1	16	13.5%	0.00 [-0.06, 0.06]	2022	-
Cusanno 2022	7.45	0.05925926	36	7.45	0.07407407	21	14.5%	0.00 [-0.04, 0.04]	2022	+
Watanabe 2023	7.44	0.08	17	7.11	0.2	24	11.9%	0.33 [0.24, 0.42]	2023	-
Total (95% CI)			244			191	100.0%	0.06 [-0.00, 0.13]		•
Heterogeneity: Tau ² =	0.01: Chi ²	= 56.72. df = 7	(P < 0.00	0001); I ² =	88%					-JJJJ-
Test for overall effect:									1	-0.5 -0.25 0 0.25 0.5 Successfully Weaned Not Successfully Weaned

'ALT (IU/L)

	Suc	cessfully Wean	ed	Not St	ccessfully Wear	ned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Sugiura 2019	46.5	64.07407407	27	88.5	55.92592593	27	80.5%	-42.00 [-74.08, -9.92]	2019	
Sawada 2021	41	169.6296296	24	56	61.48148148	24	15.9%	-15.00 [-87.18, 57.18]	2021	+
Chen 2022	270.7	1,107.4	31	225.1	689.3	31	0.4%	45.60 [-413.58, 504.78]	2022	
Aksoy 2024	169	310	27	190	294	28	3.2%	-21.00 [-180.79, 138.79]	2024	
Total (95% CI)			109			110	100.0%	-36.68 [-65.46, -7.91]		•
Heterogeneity: Tau ² =	AND ALTON PERSON AND	AND COMPANY CONTRACTOR OF THE PARKET	P = 0.89;	$ ^{2} = 0\%$						-1000 -500 0 500 1000
Test for overall effect: 2	Z = 2.50 (P = 0.01)								Successfully Weaned Not Successfully Weaned

Fig 4. Forrest plot of comparison of laboratory parameters on V-A ECMO.

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Fractional Shortening

	Suc	cessfully Wean	ed	Not St	iccessfully Wear	ned		Mean Difference			Mean	Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, Ran	dom, 95	%CI	
Daftari 2010	20.5	28.81481481	16	11.8	18.2962963	11	6.6%	8.70 [-9.08, 26.48]	2010		_	+-		
Matsumoto 2018	14	8.14814815	22	15.5	11.11111111	15	28.7%	-1.50 [-8.07, 5.07]	2018		-	-		
Punn 2019	31	16.8	25	23.5	15.5	38	22.1%	7.50 [-0.73, 15.73]	2019			-	-	
Sawada 2021	18	7.40740741	24	11	7.40740741	26	42.6%	7.00 [2.89, 11.11]	2021			-		
Total (95% CI)			87			90	100.0%	4.78 [-0.04, 9.60]				•		
Heterogeneity: Tau ² =	9.82; Chi	' = 5.18, df = 3 (F	= 0.16);	l ² = 42%						-50	25	-	25	50
Test for overall effect:	Z = 1.94 (P = 0.05)									essfully Weane	d Not	Successfull	ly Weaned

TAPSE

	Succ	essfully Wean	ed	Not Su	ccessfully Wea	aned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Frederiksen 2018	16	2.2222222	15	8	3.7037037	14	19.7%	8.00 [5.76, 10.24]	2018	
Huang 2018	8.7	4	28	6.9	2.1	18	20.8%	1.80 [0.03, 3.57]	2018	-
Kim 2021 (A) JASE	9.8	5.9	64	10.3	4.8	28	19.6%	-0.50 [-2.79, 1.79]	2021	
Kim 2021 (B) (JACimaging)	12.8	4.37037037	50	11.3	4.37037037	29	20.3%	1.50 [-0.50, 3.50]	2021	 • • • • • • • • • • • • • • • • • • •
Cusanno 2022	18	5.18518518	36	16	3.7037037	21	19.5%	2.00 [-0.32, 4.32]	2022	-
Total (95% CI)			193			110	100.0%	2.55 [-0.09, 5.19]		•
Heterogeneity: Tau ² = 7.90; Ch			.00001); I	2 = 87%						-10 -5 0 5 10
Test for overall effect: Z = 1.89	(P = 0.0)	6)								Successfully Weaned Not Successfully Weaned

LVOT VTI

	Succ	essfully Wean	ed	Not Suc	cessfully Wea	aned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Frederiksen 2018	11.3	3.6	15	9.4	4.4	14	13.0%	1.90 [-1.04, 4.84]	2018	 -
Punn 2019	7.1	3.8	25	5.8	4.1	38	28.7%	1.30 [-0.68, 3.28]	2019	
Kim 2021 (B) (JACimaging)	8.5	4.8888889	50	7.4	5.7037037	29	18.3%	1.10 [-1.38, 3.58]	2021	
Kim 2021 (A) JASE	10.8	4.1	64	9.4	4.6	28	28.8%	1.40 [-0.58, 3.38]	2021	
Cusanno 2022	15	5.56	31	14	5.86	21	11.1%	1.00 [-2.18, 4.18]	2022	1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1
Total (95% CI)			185			130	100.0%	1.34 [0.28, 2.40]		•
Heterogeneity: Tau2 = 0.00; C	$hi^2 = 0.22$	df = 4 (P = 0.9)	(9); $I^2 = 0$	%						1 1 1 1
Test for overall effect: Z = 2.47	7 (P = 0.0)	1)								Successfully Weaned Not Successfully Weaned

E/Ea

	Succ	essfully Wean	ed	Not Su	ccessfully Wea	ned		Mean Difference			Mea	an Dif	ferenc	е	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, R	andor	n, 95%	CI	
Aissaoui 2011	8.7	3.4	38	9.4	4.6	13	27.6%	-0.70 [-3.42, 2.02]	2011		_	-	_		
Kim 2021 (A) JASE	12.7	12.4	64	14.6	7.6	28	14.6%	-1.90 [-6.04, 2.24]	2021			•	_		
Kim 2021 (B) (JACimaging)	9.6	8.66666667	50	14.4	5.5555556	29	22.5%	-4.80 [-7.94, -1.66]	2021		-	- 1			
Cusanno 2022	7.7	4.4444444	36	11	4	21	35.3%	-3.30 [-5.54, -1.06]	2022			-			
Total (95% CI)			188			91	100.0%	-2.72 [-4.45, -0.98]			•	-			
Heterogeneity: Tau ² = 0.90; C	hi² = 4.20	df = 3 (P = 0.2)	24); 12 = 29	9%						-10	-5	-		+	10
Test for overall effect: Z = 3.0	7 (P = 0.0)	02)									essfully Wear	ned	Not S	uccessful	ly Weaned

LVEF

	Succ	essfully Weane	ed	Not Su	ccessfully Wear	ned		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Y	'ear	IV, Random, 95% CI
Naruke 2010	34	19	18	20	13	7	6.2%	14.00 [0.97, 27.03] 20	010	
Aissaoui 2011	37	11	20	10	7	13	9.5%	27.00 [20.86, 33.14] 20	011	
Frederiksen 2018	30	3.7037037	15	20	14.81481481	14	8.6%	10.00 [2.02, 17.98] 20	018	
Huang 2018	35	12.3	28	25.6	16.3	18	8.2%	9.40 [0.60, 18.20] 20	018	
Sugiura 2019	10	9.03703704	27	10	7.40740741	27	10.3%	0.00 [-4.41, 4.41] 20	019	
Punn 2019	42.7	17.8	25	32.9	17.9	38	8.1%	9.80 [0.80, 18.80] 20	019	
Kim 2021 (A) JASE	25.3	15.8	64	26.3	14.4	28	9.3%	-1.00 [-7.59, 5.59] 20	021	
Kim 2021 (B) (JACimaging)	24	11.85185185	50	23	16.2962963	29	9.2%	1.00 [-5.78, 7.78] 20	021	
Voigt 2022	30	2	16	23	9	24	10.6%	7.00 [3.27, 10.73] 20	022	
Cusanno 2022	35	14.07407407	36	24	8.14814815	21	9.7%	11.00 [5.23, 16.77] 20	022	
Hutchins 2023	38.5	17.4	103	25.9	17.4	96	10.1%	12.60 [7.76, 17.44] 20	023	-
Total (95% CI)			402			315	100.0%	8.96 [4.12, 13.80]		•
Heterogeneity: Tau2 = 54.04; 0	Chi ² = 66.7	74, df = 10 (P < 1	0.00001);	l ² = 85%					_	- + + + +
Test for overall effect: Z = 3.63	3(P = 0.00	003)								-20 -10 0 10 20 Successfully Weaned Not Successfully Weaned

 $Fig \ 5. \ Forest \ plot \ of \ the \ comparison \ of \ different \ echocardiographic \ parameters \ on \ V-A \ ECMO \ weaning.$

 $\underline{https:/\!/doi.org/10.1371/journal.pone.0310289.g005}$

Table 2	Rick factors predicti	ive of successful ECMO) weaning from n	nulti-variable logictic	regression models
Table 2.	Risk factors bredicti	ive of successful ECIVIV	J weaming from ii	num-variadie iogistic	regression models.

Deceling shows stories	C4				
Baseline characteristics	Study				
Normal RV function	Puerto [<u>47</u>]				
No pre-existing ischemic cardiopathy	Cusanno [9]				
Post PCI TIMI flow	Sugiura [42]				
While on ECMO					
No CRRT	Kim [<u>31</u>]				
No need for LV venting	Kim [<u>31</u>]				
10% improvement of tricuspid S' during ECMO flow study	Kim [<u>30</u>]				
Any improvement of lateral e' during ECMO flow study	Kim [<u>30</u>]				
ECMO duration	Punn [<u>39</u>]				
Implantation-weaning test delay < 7 days	Cusanno [9]				
Echo findings on weaning					
VTI	Lim [<u>48</u>], Punn [<u>39</u>]				
LV EF	Punn [<u>39</u>]				
Corrected LV ejection time/PAWP	Sawada [<u>40</u>]				
Tricuspid annular S'/RSVP >0.33	Kim [<u>31</u>]				
RV EF	Huang [<u>26</u>]				
Normal RV function	Puerto [47]				
RV free wall strain	Huang [<u>26</u>]				
RV FAC	Huang [<u>26</u>]				
Hemodynamics					
HR on day of decannulation	Liu [49]				
MAP at weaning	Lim [48]				
MAP at 4hrs	Sugiura [42]				
Post-test SBP >120 mmHg	Cusanno [9]				
CVP on day of decannulation	Huang [26]				
Post de-cannulation	. •				
Lactate at 12hrs	Chen [19]				
Lactate at 24hrs	Sugiura [42]				
Lower vasoactive-inotropic score 24hrs post cannulation	Dunton [22]				
Improvement of RV systolic function >24hrs after decannulation	Puerto [47]				

CRRT, continuous renal replacement therapy; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; FAC, fractional area change; HR, heart rate; LV, left ventricle; MAP, mean arterial pressure; PAWP, pulmonary artery wedge pressure; PCI, percutaneous coronary intervention; RV, right ventricle; SBP, systolic blood pressure; TIMI, Thrombolysis in Myocardial Infarction score; VTI, velocity time integral.

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Additional sensitivity analyses removing studies that included paediatric patients did not reveal any significant differences—\$4 Table.

Study quality. A total of 34 publications were eligible for quality assessment, of which 12 publications were of poor quality, i.e., 'critical' risk of bias (Fig 2). Many studies did not provide detailed protocols, limiting methodological assessment, appraisal of the confounding effect of intervention and bias in selection of participants into the study.

Discussion

In this systematic review of predictors of V-A ECMO weaning success 34 predominantly small observational, studies were identified. On pooled analysis, lower levels of biochemical markers of end-organ perfusion or injury (lactate, CK-MB and ALT), haemodynamic

(pulse pressure and systolic blood pressure) and echocardiographic indicators of myocardial function (LVEF, LVOT VTI, E/Ea) were associated with successful weaning form V-A ECMO.

To our knowledge this review is only the second to systematically assess predictors of V-A ECMO wean success. The first, in adult patients with specifically cardiogenic shock or cardiac arrest identified similar results to our review, with lower creatine kinase and lactate levels, and higher LVEF being predictors for successful weaning from V-A-ECMO [10] Other, non-systematic, reviews have reported also reported lower creatine kinase and lactate levels, and higher LVEF and LVOT VTI being predictors for successful weaning from V-A-ECMO [50]. Several other V-variables used in clinical practice [9] Troponin, NT-ProBNP, RV to PA coupling indices were not identified owing to limited numbers of studies and patients reported with these.

Despite significant heterogeneity, small sample sizes and a significant risk of bias, there are some conclusions that can be drawn from this review and the available literature. First, determination of likely weaning success, should consider multiple variables and not be focussed on one individual predictor. Factors associated with success (or failure), were present across clinical, biochemical, haemodynamic and echocardiographic parameters and clinicians should avoid relying on one variable over the complete picture of the patient. Second, initial severity of illness (e.g., lactate), markers of end-organ perfusion, and then recovery of such are important considerations in attempting to wean [42,51,52]. Further, absolute cut offs for specific variables, e.g., LVEF or LVOT VTI to predict weaning success vary between studies, are based empirical clinical weaning protocols [50,53] and therefore cannot yet be elucidated. Overall restitution and improvement of the overall clinical state of the patient as well as cardiac function is likely key to successful weaning rather than a specific variable or level of a variable.

Formal weaning or "ramp" studies that assess haemodynamic and echocardiographic changes to alterations to ECMO flows protocols are recommended [54] but as yet no standardised protocols exist, are only variably reported in ECMO trials, and are not formally assessed in this systematic review. However, they are critical tools to assess the response of cardiac function to reduction, and then removal, of mechanical circulatory support [9,55]. Future prospective clinical trials should publish weaning strategies and protocols to enable further assessment and comparison of strategies.

Limitations

Our review is limited by the lack of large high-quality trial, with all included studies consisting of observational studies with small sample sizes and these small trials were used to investigate widely varying interventions amongst this population group, often performed without covariate adjustment. However, we completed a comprehensive review of the literature including all commonly used variables for V-A ECMO weaning. The inclusion criteria of our study were broad and included adult and paediatric patients and any aetiology leading to V-A ECMO support. It is possible that paediatric and adult patients differ in weaning factors. Additional analysis excluding studies that included paediatric patients showed no significant change in outcomes reported. Further, V-A ECMO patients by their very nature are heterogenous and a wide array of prognostic variables are utilized by clinicians in clinical practice, a wider approach to inclusion criteria increases sensitivity and generalisability of findings. Micro-circulation indices were not assessed but are not in uniform clinical practice which was our focus. The underlying aetiology leading to requirement for V-A ECMO support was not assessed and may impact timing of weaning, weaning success and need for durable ventricular support, e.g., VAD.

Conclusions

In patients requiring V-A ECMO support, multiple biochemical, haemodynamic and echocardiographic parameters of recovery, rather than a single variable should be used to guide appropriateness for weaning. Further larger studies are required to determine optimal weaning strategies.

Supporting information

S1 Appendix. Prisma checklist. (DOCX)

S2 Appendix. Search strategy.

(DOCX)

S1 Table. Literature search and decisions.

(XLSM)

S2 Table. Data extraction.

(XLSX)

S3 Table. Risk of bias.

(XLSX)

S4 Table. Paediatric sensitivity analysis.

(DOCX)

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References

- Schrage B, Becher PM, Goßling A, Savarese G, Dabboura S, Yan I, et al. Temporal trends in incidence, causes, use of mechanical circulatory support and mortality in cardiogenic shock. ESC Heart Fail. 2021;8(2):1295–303. https://doi.org/10.1002/ehf2.13202 PMID: 33605565
- Mebazaa A, Combes A, van Diepen S, Hollinger A, Katz JN, Landoni G, et al. Management of cardiogenic shock complicating myocardial infarction. Intensive Care Med. 2018;44(6):760–73. https://doi.org/10.1007/s00134-018-5214-9 PMID: 29767322
- Zangrillo A, Landoni G, Biondi-Zoccai G, Greco M, Greco T, Frati G, et al. A meta-analysis of complications and mortality of extracorporeal membrane oxygenation. Critical Care Resusc. 2013;15(3):172–8. https://doi.org/10.1016/s1441-2772(23)01792-1
- Chen Y-S, Chao A, Yu H-Y, Ko W-J, Wu I-H, Chen RJ-C, et al. Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. J Am Coll Cardiol. 2003;41(2):197–203. https://doi.org/10.1016/s0735-1097(02)02716-x PMID: 12535808

- Chang W-W, Tsai F-C, Tsai T-Y, Chang C-H, Jenq C-C, Chang M-Y, et al. Predictors of mortality in patients successfully weaned from extracorporeal membrane oxygenation. PLoS One. 2012;7(8):e42687. https://doi.org/10.1371/journal.pone.0042687 PMID: 22870340
- Cavarocchi NC, Pitcher HT, Yang Q, Karbowski P, Miessau J, Hastings HM, et al. Weaning of extracorporeal membrane oxygenation using continuous hemodynamic transesophageal echocardiography. J Thorac Cardiovasc Surg. 2013;146(6):1474–9. https://doi.org/10.1016/j.jtcvs.2013.06.055 PMID: 23993027
- Aso S, Matsui H, Fushimi K, Yasunaga H. In-hospital mortality and successful weaning from venoarterial extracorporeal membrane oxygenation: analysis of 5,263 patients using a national inpatient database in Japan. Crit Care. 2016;20:80. https://doi.org/10.1186/s13054-016-1261-1 PMID: 27044572
- 8. Pappalardo F, Pieri M, Arnaez Corada B, Ajello S, Melisurgo G, De Bonis M, et al. Timing and strategy for weaning from venoarterial ECMO are complex issues. J Cardiothorac Vasc Anesth. 2015;29(4):906–11. https://doi.org/10.1053/j.jvca.2014.12.011 PMID: 25836952
- 9. Cusanno A, Aissaoui N, Minville V, Porterie J, Biendel C, Volle K, et al. Predictors of weaning failure in case of VA ECMO implantation. Sci Rep. 2022;12(1):13842.
- Charbonneau F, Chahinian K, Bebawi E, Lavigueur O, Lévesque É, Lamarche Y, et al. Parameters associated with successful weaning of veno-arterial extracorporeal membrane oxygenation: a systematic review. Crit Care. 2022;26(1):375. https://doi.org/10.1186/s13054-022-04249-w PMID: 36471408
- 11. Lusebrink E, Stremmel C, Stark K, Joskowiak D, Czermak T, Born F, et al. Update on weaning from veno-arterial extracorporeal membrane oxygenation. J Clin Med. 2020;9(4).
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906. https://doi.org/10.1016/j.ijsu.2021.105906 PMID: 33789826
- Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919. https://doi.org/10.1136/bmj.i4919 PMID: 27733354
- 14. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019;10(10):ED000142. https://doi.org/10.1002/14651858.ED000142 PMID: 31643080
- 15. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135. https://doi.org/10.1186/1471-2288-14-135 PMID: 25524443
- Aissaoui N, Luyt C-E, Leprince P, Trouillet J-L, Léger P, Pavie A, et al. Predictors of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock. Intensive Care Med. 2011;37(11):1738–45. https://doi.org/10.1007/s00134-011-2358-2 PMID: 21965097
- Akin S, Dos Reis Miranda D, Caliskan K, Soliman OI, Guven G, Struijs A, et al. Functional evaluation of sublingual microcirculation indicates successful weaning from VA-ECMO in cardiogenic shock. Crit Care. 2017;21(1):265. https://doi.org/10.1186/s13054-017-1855-2 PMID: 29073930
- Aksoy T, Arslan AH, Ugur M, Ustunsoy H. Lactate and lactate clearance are predictive factors for mortality in patients with extracorporeal membrane oxygenation. Braz J Cardiovasc Surg. 2024;39(2):e20230091. https://doi.org/10.21470/1678-9741-2023-0091 PMID: 38426430
- Chen T-Y, Chang C-H, Hsu J-Y, Sheu J-J, Kuo H-C, Hsu M-H, et al. Comparison of the predictive ability of lactate and central venous blood gas in pediatric venoarterial mode extracorporeal membrane oxygenation outcome. Pediatr Neonatol. 2022;63(5):474–83. https://doi.org/10.1016/j.pedneo.2022.03.011 PMID: 35697593
- Colombo CNJ, Dammassa V, Pozzi M, et al. Echocardiographic predictors of VA ECMO weaning in patients with cardiogenic shock. Eur Heart J Acute Cardiovasc Care. 2019;8:144–5.
- Daftari B. Echocardiographic predictors of successful pediatric cardiac ECMO wean. American Academy of Pediatrics National Conference and Exhibition. 2010.
- Dunton K, Weeks PA, Gulbis B, Jumean M, Kumar S, Janowiak L, et al. Evaluation of vasoactive-inotropic score and survival to decannulation in adult patients on venoarterial extracorporeal life support: an observational cohort study. ASAIO J. 2023;69(9):873–8. https://doi.org/10.1097/MAT.0000000000001982 PMID: 37155964
- 23. Finnigan L, Jones H, Lotto R, Horan M, Dhannapuneni R, Guerrero R et al. Cerebral blood flow velocity during weaning of V-A ECMO in pediatrics. Perfusion. 2020;13(35):93–282.
- Frederiksen CA, Nielsen R, Frederiksen AS, et al. Echocardiographic predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation. Eur Heart J. 2018;39.

- Gonzalez Martin J, Alonso-Fernandez-Gatta M, Merchan Gomez S, Gonzalez Cebrian M, Diego-Nieto A, Martin-Herrero F, et al. Echocardiographic recovery changes in patients supported with veno-arterial extracorporeal membrane oxygenator and weaning success. Eur Heart J. 2021;42(Supplement_1). https://doi.org/10.1093/eurheartj/ehab724.1060
- Huang K-C, Lin L-Y, Chen Y-S, Lai C-H, Hwang J-J, Lin L-C. Three-dimensional echocardiographyderived right ventricular ejection fraction correlates with success of decannulation and prognosis in patients stabilized by venoarterial extracorporeal life support. J Am Soc Echocardiogr. 2018;31(2):169–79. https://doi.org/10.1016/j.echo.2017.09.004 PMID: 29079045
- 27. Hutchins E, Rahrooh A, Feng J, Chandra N, Hsu JJ, Bui A. Abstract 13293: predicting successful ECMO decannulation—a novel machine learning approach. American Heart Association. 2023.
- Joseph A, Venturini J, Blair JEA, Paul J, Shah A, Nathan S. Prognostic value of right ventricular function in percutaneous veno-arterial extracorporeal membrane oxygenation. BMC Cardiovasc Disord. 2019;19:A45.
- Kellnar A, Naumann D, Scherer C, Lüsebrink E, Joskowiak D, Peterß S, et al. Aortic arch blood flow measurements as a predictor of successful ECMO weaning in cardiogenic shock. Heliyon. 2024;10(5):e26773. https://doi.org/10.1016/j.heliyon.2024.e26773 PMID: 38444470
- Kim D, Jang WJ, Park TK, Cho YH, Choi JO, Jeon ES, et al. Echocardiographic predictors of successful extracorporeal membrane oxygenation weaning after refractory cardiogenic shock. J Am Soc Echocardiogr. 2021;34(4):414–22 e4.
- Kim D, Park Y, Choi KH, Park TK, Lee JM, Cho YH, et al. Prognostic implication of RV coupling to pulmonary circulation for successful weaning from extracorporeal membrane oxygenation. JACC Cardiovasc Imaging. 2021;14(8):1523–31. https://doi.org/10.1016/j.jcmg.2021.02.018 PMID: 33865793
- L'Acqua C, Rossi F, Polvani G, Ceriani R, Bertera A, Agrifoglio M, et al. Preimplant outcome predictors in patients supported with veno-arterial extracorporeal membrane oxygenation. Does the right time exist? Minerva Anestesiol. 2019;85(8):915–6. https://doi.org/10.23736/S0375-9393.19.13589-4 PMID: 31339029
- Lee J, Lee S, Joo S, Park YK, Kim KM, Jung JC, et al. Abstract: pulse pressure as a potential predictive factor for successful weaning in patients supported by venoarterial extracorporeal membrane oxygenation without left ventricular venting. ASAIO J. 2023;69:17.
- Lim JY, Jung JS. Predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation support. 8th EuroELSO Congress. 2019;34(1):82–251.
- Matsumoto M, Asaumi Y, Nakamura Y, Nakatani T, Nagai T, Kanaya T, et al. Clinical determinants of successful weaning from extracorporeal membrane oxygenation in patients with fulminant myocarditis. ESC Heart Fail. 2018;5(4):675–84. https://doi.org/10.1002/ehf2.12291 PMID: 29757498
- **36.** Mongkolpun W, Bakos P, Peluso L, Annoni F, Vincent JL, Creteur J. Cutaneous blood flow as a predictor of successful weaning from VA-ECMO. Crit Care. 2019;23(P115).
- Naruke T, Inomata T, Imai H, Yanagisawa T, Maekawa E, Mizutani T, et al. End-tidal carbon dioxide concentration can estimate the appropriate timing for weaning off from extracorporeal membrane oxygenation for refractory circulatory failure. Int Heart J. 2010;51(2):116–20. https://doi.org/10.1536/ihj.51.116 PMID: 20379045
- Naruke T, Inomata T, Kawaguchi T, Mizutani T, Shinagawa H, Koitabashi T, et al. Prognostic impact of dramatic alteration of mixed venous oxygen saturation on the hemodynamic recovery from venoarterial extracorporeal membrane oxygenation. Eur Heart J. 2012;33(69).
- 39. Punn R, Falkensammer CB, Blinder JJ, Fifer CG, Thorsson T, Perens G, et al. Hemodynamic and echocardiographic predictors of mortality in pediatric patients on venoarterial extracorporeal membrane oxygenation: a multicenter investigation. J Am Soc Echocardiogr. 2023;36(2):233–41.
- 40. Sawada K, Kawakami S, Murata S, Nishimura K, Tahara Y, Hosoda H, et al. Predicting parameters for successful weaning from veno-arterial extracorporeal membrane oxygenation in cardiogenic shock. ESC Heart Fail. 2021;8(1):471–80. https://doi.org/10.1002/ehf2.13097 PMID: 33264500
- Stull C, Baram M, Pitcher H, Hirose H, Guarav K, Cavarocchi N. Predictors of a successful wean from extracorporeal membrane oxygenation (ECMO) for ARDS. Crit Care Med. 2013;41.
- 42. Sugiura A, Abe R, Nakayama T, Hattori N, Fujimoto Y, Himi T, et al. Predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation after coronary revascularization for acute myocardial infarction complicated by cardiac arrest: a retrospective multicenter study. Shock. 2019;51(6):690–7. https://doi.org/10.1097/SHK.0000000000001220 PMID: 30080744
- Sugiyama K, Takahashi M, Miyazaki K, Ishida T, Kobayashi M, Hamabe Y. Left ventricular wall findings in non-electrocardiography-gated contrast-enhanced computed tomography after extracorporeal

- cardiopulmonary resuscitation. Crit Care. 2019;23(1):357. https://doi.org/10.1186/s13054-019-2624-1 PMID: 31727121
- Varodomvanichkul C, Puwatnuttasit P, Ariyachaipanich A, Songmuang SB, Puwanant S. Left atrial strain for predicting successful extra-corporeal membrane oxygenator weaning from cardiogenic shock. J Am Coll Cardiol. 2023;81(8):686. https://doi.org/10.1016/s0735-1097(23)01130-0
- **45.** Voigt I, Mighali M, Manda D, Aurich P, Bruder O. Radiographic assessment of lung edema (RALE) score is associated with clinical outcomes in patients with refractory cardiogenic shock and refractory cardiac arrest after percutaneous implantation of extracorporeal life support. Intern Emerg Med. 2022;17:1463–70.
- **46.** Watanabe M, Ajiro Y, Hasegawa S, Hamada K, Tsukamoto K, Saito T, et al. Clinical factors associated with successful venoarterial extracorporeal membrane oxygenation weaning: a single-center retrospective cohort study. Critical Care Shock. 2023;26:115–24.
- 47. Puerto E, Tavazzi G, Gambaro A, Cirillo C, Pecoraro A, Martín-Asenjo R, et al. Interaction between VA-ECMO and the right ventricle. Hellenic J Cardiol. 2022;68:17–24. https://doi.org/10.1016/j.hjc.2022.07.003 PMID: 35863728
- **48.** Lim JY, Jung JS. Predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation support. Perfus Ger. 2019;34:88–9.
- Liu S-F, Hsu CY, Lee C-K, Kao PH-L. Clinical predictors of successful weaning VA-ECMO. J Am Coll Cardiol. 2022;S29–30.
- **50.** Brahmbhatt DH, Daly AL, Luk AC, Fan E, Billia F. Liberation from venoarterial extracorporeal membrane oxygenation: a review. Circ Heart Fail. 2021;14(7):e007679.
- 51. Asaumi Y, Yasuda S, Morii I, Kakuchi H, Otsuka Y, Kawamura A, et al. Favourable clinical outcome in patients with cardiogenic shock due to fulminant myocarditis supported by percutaneous extracorporeal membrane oxygenation. Eur Heart J. 2005;26(20):2185–92. https://doi.org/10.1093/eurheartj/ehi411 PMID: 16014643
- North M, Eckman P, Samara M, Chavez I, Schmidt C, Garberich R, et al. Peak troponin predicts successful weaning from VA ECMO in patients with acute myocardial infarction complicated by cardiogenic shock. Int J Artif Organs. 2022;45(1):68–74. https://doi.org/10.1177/0391398821991155 PMID: 33530814
- Ortuno S, Delmas C, Diehl J-L, Bailleul C, Lancelot A, Naili M, et al. Weaning from veno-arterial extra-corporeal membrane oxygenation: which strategy to use? Ann Cardiothorac Surg. 2019;8(1):E1–8. https://doi.org/10.21037/acs.2018.08.05 PMID: 30854330
- Lorusso R, Shekar K, MacLaren G, Schmidt M, Pellegrino V, Meyns B, et al. ELSO interim guidelines for venoarterial extracorporeal membrane oxygenation in adult cardiac patients. ASAIO J. 2021;67(8):827–44. https://doi.org/10.1097/MAT.00000000001510 PMID: 34339398
- 55. Aissaoui N, Caudron J, Leprince P, Fagon J-Y, Lebreton G, Combes A, et al. Right-left ventricular interdependence: a promising predictor of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock. Intensive Care Med. 2017;43(4):592–4. https://doi.org/10.1007/s00134-016-4657-0 PMID: 28011989