

CLINICAL OUTCOME OF PATIENTS UNDERGOING EXTRACORPOREAL MEMBRANE OXYGENATION AFTER MULTIDISCIPLINARY TRAINING

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ABSTRACT

Objective: to verify the influence of multidisciplinary team training on the clinical outcome of adult patients undergoing extracorporeal membrane oxygenation. Method: observational study, conducted in an Adult Intensive Care Unit of a hospital in the southern zone of São Paulo, from 2012 to 2020. Survival analysis was performed by the Kaplan-Meier method and the probability of in-hospital mortality was analyzed by a multiple logistic regression model. Results: 72 patients were included, 54 (75%) after the training period. A reduction in mortality from 83.3% to 57.4% was observed after training ($p=0.047$), with an increase in 90-day survival of 31% after training. Conclusion: the impact of training on in-hospital death rate and 90-day survival is an incentive for hospital managers to adopt the training model with their teams to ensure better quality care.

DESCRIPTORS: Extracorporeal Membrane Oxygenation; Professional Training; Mentoring; Intensive Care Units; Critical Care.

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INTRODUCTION

The use of extracorporeal Membrane Oxygenation (ECMO) as a therapy for respiratory and cardiac failure has quadrupled after the first decade of the XXI century⁽¹⁻³⁾. The Extracorporeal Life Support Organization (ELSO) also points out an increase of centers specialized in this therapy, mostly in North America, Europe, and Asia, as compared to South America. Currently, Brazil has approximately 30 reference centers, a number that is not consistent with the demands of the Brazilian population⁽³⁾. It is noteworthy that the support in question is still in the process of expanding its use in the country.

During the covid-19 pandemic, declared by the World Health Organization as of March 2020, ECMO has become a prominent option for patients with respiratory failure caused by the SARS-CoV-2 virus. According to ELSO, from the start of the pandemic until February 2021, 4,891 patients have undergone ECMO⁽⁴⁾. Associated with the contraindication of the use of ECMO by institutions without trained teams due to the risk of failure of the therapy, this panorama reinforces the concern in promoting adequate training of the multidisciplinary team to prevent serious adverse events⁽⁴⁻⁶⁾.

Despite this context, literature is scarce regarding the impact of training multidisciplinary teams to care for patients with ECMO on patients' clinical outcomes⁽⁶⁻⁷⁾. A recent American study showed that the hospital discharge rate of patients submitted to ECMO increased significantly after training of the multidisciplinary team, from 37.7% to 52.3%⁽⁶⁾. Additionally, a Korean study verified that mortality in up to 28 days of these patients fell from 71.7% to 53.3% after training implementation⁽⁸⁾.

In Brazil, a study was found that demonstrated the impact of training of the multidisciplinary team on the clinical outcomes of patients on ECMO, focusing on surgical aspects⁽⁷⁾. Thus, the aim of this study is to verify the influence of multidisciplinary team training on the clinical outcome of adult patients undergoing ECMO.

METHOD

This is an observational before-and-after study, carried out in an Adult Intensive Care Unit (ICU), with general characteristics of an extra-large hospital, located in São Paulo. The sample consisted of all medical records of patients over 18 years old admitted to the mentioned ICU, undergoing ECMO in the period from 2012 (beginning of use of the technology in the institution) to 2020.

In the institution, the professionals who aid patients on ECMO are physicians, nurses and intensive care physiotherapists, cardiac, thoracic, and vascular surgeons. Until the second half of 2015, these professionals performed assistance based on specific institutional training in relation to ECMO, however, without a multidisciplinary group specifically trained for this therapy. Throughout the second half of 2015, a team of intensive care physicians, nurses, and physical therapists underwent targeted training to ensure more specific and safer care. The training consisted of a 60-hour course, implemented by the Heart Institute of the Faculty of Medicine, University of São Paulo, in partnership with a Canadian institution (Stollery Children's Hospital), both ELSO reference centers.

In early 2016, the multidisciplinary team was put into practice to systematize the care of adult patients undergoing ECMO. To this end, the flow of professionals involved in this therapy was standardized. These professionals standardized kits of materials for cannulation, maintenance, and decannulation of ECMO. Institutional flowcharts related to safety procedures were also improved, both for the patient and the ECMO system, in addition to the creation of instruments for recording data related to the conduct of ECMO.

Finally, there was a standardization of nursing care and interventions specific to the context of ECMO, with nursing professionals dimensioning for patients using ECMO of 1:1.

The data were collected by the authors through review of electronic medical records. After patients were included in the study, they were divided into two groups: individuals who underwent ECMO from January 2012 to December 2015, which were considered the pre-training group, while patients who underwent ECMO from January 2016 to the end of December 2020 were considered the post-training group.

The outcome variables were the occurrence of in-hospital death and 90-day survival. Sample characterization variables and potential antecedent variables collected were related to demographic characteristics, clinical characteristics, and ECMO characteristics. Demographic characteristics were gender and age. Clinical characteristics were origin, morbidities, outcome, vasoactive drug use, mechanical ventilation, renal replacement therapy, pressure injury, length of ICU stay, hospital stay and mechanical ventilation, Simplified Acute Physiology Score 3, Sequential organ failure assessment score and Nursing activities score on ICU admission and on the day ECMO was started. Finally, ECMO characteristics were modality, cannulation type, cannulation site, time between ICU admission and ECMO installation and support use, and gasometric parameters collected immediately before therapy installation.

Data were entered into the Research Electronic Data Capture® (REDCap®)⁽⁹⁾ platform and imported into Microsoft Excel® 2007 spreadsheet. The Statistical Package for the Social Science (SPSS) software, version 26, was used for the analyses. Descriptive analysis was performed using absolute and relative frequencies for qualitative variables and means and standard deviations for variables.

Decisions for the most appropriate tests to compare demographic, clinical, and ECMO-related characteristics between the pre- and post-training groups were based on data distributions. For numerical variables, when the variable had a normal distribution, Student's t test was used. When the distribution of the variable was asymmetric, the Mann-Whitney test was used. For categorical variables, we used the chi-square test or Fisher's test, the latter when there was a variable with few individuals in some category(ies).

For the survival analysis of patients, the Kaplan-Meier method was used together with the log-rank test. The probability of in-hospital mortality was analyzed by a multiple logistic regression model, in which variables with $p < 0.20$ were included in the univariate analysis between the group death versus no death. Values of $p < 0.05$ were considered significant for all analyses performed.

Data collection was carried out by the REDCap® platform after the project was approved by the institution's Research Ethics Committee, under opinion number 3345313.

RESULTS

We included 72 patients, 18 (25%) admitted in the pre-training period and 54 (75%) in the post-training period. Tables 1 and 2 describe, respectively, the demographic and clinical profile of patients and the variables related to ECMO in the periods before and after training.

Table 1 - Demographic and clinical profile of patients undergoing ECMO before and after multidisciplinary training. São Paulo, SP, Brazil, 2021

Variables	Total (n=72)	Before the training (n=18)	After the training (n=54)	p
	n (%)	n (%)	n (%)	
Gender male	48 (66,7)	11 (61,1)	37 (68,5)	0,564 ^a
Age (years old), Mean ±SD	49,6±15,8	45,6±14,7	51,0±16,1	0,214 ^b
Comorbidity				
SAH	26 (36,1)	6 (33,3)	20 (37)	0,777 ^a
HF	20 (27,8)	6 (33,3)	14 (25,9)	0,543 ^a
DM	17 (23,6)	2 (11,1)	15 (27,7)	0,207 ^c
COPD	11 (15,3)	3 (16,7)	8 (14,8)	>0,999 ^c
SAPS 3, Mean ±SD	51,4±15,2	51,7±11,2	51,3±11,2	0,920 ^d
SOFA, Mean ±SD	10,9±2,8	11,7±2,5	10,7±2,8	0,144 ^b
Source				
Emergency Room	14 (19,4)	3 (16,7)	11 (20,3)	>0999 ^c
Surgical Center	17 (23,6)	2 (11,1)	15 (27,7)	0,207 ^c
Medical/Surgical	6 (8,3)	2 (3,7)	4 (7,4)	0,031 ^c
External	18 (25,0)	4 (22,2)	14 (25,9)	>0999 ^c
Semi-Intensive Care	11 (15,3)	5 (27,8)	6 (11,1)	0,128 ^c
Hemodynamics	6 (8,3)	-	6 (11,1)	-
Vasoactive drugs				
Noradrenaline	68 (94,4)	17 (94,4)	51 (94,4)	>0,999 ^c
Adrenaline	43 (59,7)	11 (61,1)	32 (59,2)	0,890 ^a
Dobutamine	34 (47,2)	8 (44,4)	26 (48,1)	0,785 ^a
Vasopressin	13 (18,1)	5 (27,8)	8 (14,8)	0,289 ^c
Milrinone	9 (12,5)	2 (11,1)	7 (12,9)	>0,999 ^c
Sodium nitroprusside	26 (36,1)	9 (50)	17 (31,4)	0,157 ^a
ICU time (days), Mean ±SD	19,8±19,3	17,5±22,5	20,5±18,3	0,349 ^b
Length of stay (days), Mean ±SD	39,6±54,1	25,2±22,1	44,5±60,6	0,499 ^b
MV Time (days), Mean ±SD	14,1±18,0	12,9±22,4	14,6±16,6	0,593 ^b
RRT	42 (58,3)	12 (66,7)	30 (55,6)	0,408 ^a
NAS ICU admission, Mean ±SD	105,0±33,2	93,5±36,5	108,8±31,5	0,063 ^b
NAS ECMO start, Mean ±SD	126,6±10,3	126,9±5,3	126,5±11,6	0,725 ^b
Pressure Injury	28 (38,9)	4 (22,2)	24 (44,4)	0,094 ^a

SD: standard deviation, DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, ECMO: extracorporeal membrane oxygenation, SAH: Systemic arterial hypertension, HF: Heart failure, AKI: Acute kidney injury; NAS: Nursing activities score, SAPS: Simplified Acute Physiology Score, SOFA: Sequential Organ Failure Assessment Score, RRT: Renal Replacement Therapy, ICU: Intensive Care Unit, MV: Mechanical ventilation: chi-square test, b: Mann Whitney test, c: Fisher's exact test, d: t-test.

Source: Authors (2021)

Table 2 - Variables related to ECMO of patients before and after multidisciplinary training. São Paulo, SP, Brazil, 2021

Variable	Total	Before training	After training	p
	(n=72)	(n=18)	(n=54)	
ECMO Modality				
VA, n(%)	39(54,2)	9(50,0)	30(55,5)	0,682 ^a
VV, n(%)	33(45,8)	9(50,0)	24(44,4)	
Type of cannulation				
Peripheral, n(%)	60(83,3)	16(88,9)	44(81,5)	0,718 ^b
Central, n(%)	12(16,7)	2(11,1)	10(18,5)	
Time between admission and start of ECMO (days), Mean \pm SD	7,4 \pm 13,7	10,7 \pm 11,5	6,3 \pm 14,3	0,014 ^c
Time in ECMO (days), Mean \pm SD	9,4 \pm 15,3	9,5 \pm 21,3	9,4 \pm 13,0	0,193 ^c
Gasometric parameters pre-ECMO				
Lactate (mg/dL), Mean \pm SD	53,0 \pm 48,9	52,0 \pm 41,4	53,3 \pm 51,5	0,790 ^c
pH, Mean \pm SD	7,22 \pm 0,2	7,23 \pm 0,2	7,22 \pm 0,2	0,932 ^d
PaCO ₂ , Mean \pm SD	57,0 \pm 28,4	53,5 \pm 24,3	58,1 \pm 29,8	0,649 ^c
PaO ₂ , Mean \pm SD	111,3 \pm 64,2	79,9 \pm 28,1	121,8 \pm 69,5	0,018 ^c
HCO ₃ , Mean \pm SD	23,4 \pm 11,6	21,6 \pm 6,0	24,0 \pm 12,9	0,687 ^c
Decannulation, n(%)	31(43,1)	4(22,2)	27(50,0)	0,039 ^a

SD: Standard Deviation, ECMO: extracorporeal membrane oxygenation, ARF Acute Respiratory Failure, PaCO₂: Partial Pressure of Carbon Dioxide, PaO₂: Partial Pressure of Oxygen, ICU: Intensive Care Unit, VA Venous, VV: Ven venous.

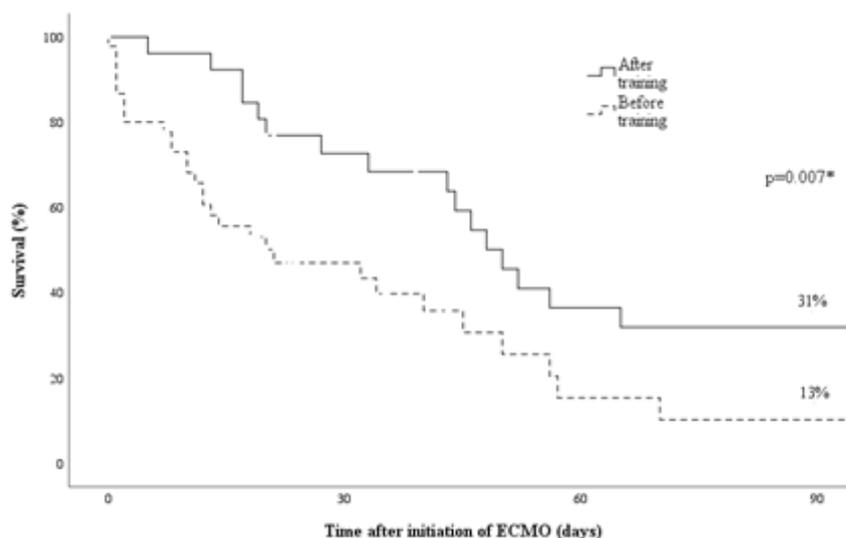
a: chi-square test, b: Fisher's exact test, c: Mann Whitney test, d: test

Source: Authors (2021)

There were no demographic and clinical differences between patients undergoing ECMO in the pre- and post-training periods, except for a statistically higher proportion of patients from the medical/surgical clinic in the post-training period, but without clinical relevance (four vs two patients) (Table 1).

Regarding ECMO characteristics, in the post-training period, it was found that ECMO was started earlier, while patients had higher PaO₂. There was also a higher proportion of decannulation of patients treated after training (Table 2).

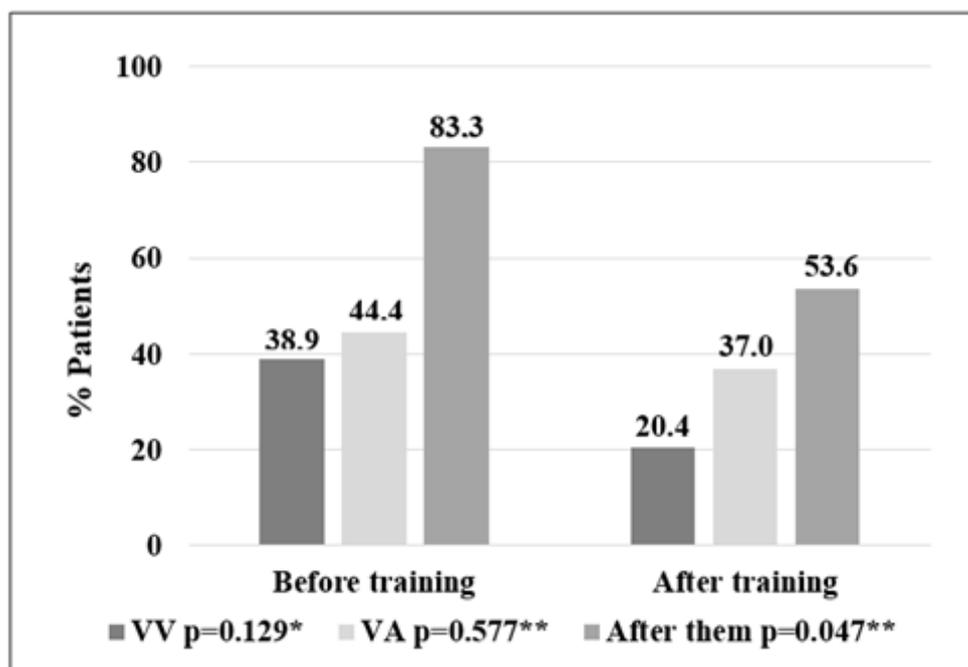
Figure 1 shows that the patients in the post-training period had a significantly higher 90-day survival rate than the survival rate of the patients in the pre-training period.



*: log-rank test

Figure 1 - Comparison of survival at 90 days after initiation of ECMO before and after training of the multidisciplinary team. São Paulo, SP, Brazil, 2021
Source: Authors (2021)

The prevalence of in-hospital death, considering the whole period, was 63.9% (n=46). Although there was no significant reduction in in-hospital mortality after training, when analyzing ECMO modalities separately (Figure 2), the overall in-hospital death rate of patients undergoing ECMO after training (n=31, 54.6%) was significantly lower than that of pre-training patients (n=15, 83.3%), p=0.047.



VV: venovenous, VA: venoarterial, *: Fisher's exact test, **: chi-square test

Figure 2 - Comparison of overall in-hospital mortality according to ECMO modality before and after multidisciplinary training. São Paulo, SP, Brazil, 2021
Source: Authors (2021)

Table 3 shows that the period after multidisciplinary training was marginally considered a protective factor for in-hospital mortality in the univariate analysis but did not remain significantly associated with the outcome in the multiple analysis. The use of adrenaline, in turn, was associated with an 89% lower chance of mortality, and one more day of hospitalization was associated with a 7% lower chance of mortality.

Table 3 - Univariate and multivariate analyses referring to the multiple logistic regression model for overall in-hospital mortality. São Paulo, SP, Brazil, 2021

	Univariate			Multivariate		
	OR	CI 95%	p-value	OR	CI 95%	p-value
Period after Training	3,71	0,96-14,33	0,057	0,33	0,69-1,62	0,174
Adrenaline	7,15	2,44-20,94	<0,001	0,11	0,03-0,40	0,001
Vasopressin	3,77	0,76-18,56	0,103	0,11	0,30-0,44	0,386
Time in ICU	0,97	0,95-1,00	0,065	1,05	0,94-1,17	0,33
Time of hospitalization	0,97	0,95-0,99	0,002	0,93	0,89-0,98	0,013
MV time	0,98	0,96-1,01	0,293	1	0,92-1,09	0,869

OR: Odds Ratio, CI: Confidence Interval, ICU: intensive care unit, MV: mechanical ventilation

Source: Authors (2021)

DISCUSSION

The growing advance in the use of ECMO reflects the need for specific training of the care teams, since the conduction of the equipment requires directed skills, as well as the care provided to the person using it is considered of high complexity.

Thus, it is observed in this study that, after the team training, a greater number of individuals underwent ECMO. The literature shows this trend in the increase of patients using this procedure after team training. This movement is associated with more assertive indications, with early initiation of therapy, and consequent increase in quality and safety⁽⁶⁾.

The time between ICU admission and the start of ECMO is a very important factor in the indication of therapy. In this study, it was evidenced that, after training, this time was almost halved, confirming the influence of the training. Although there are no data in literature, the result shows that the team's training reflected in early and assertive support indication, reflecting in patient's survival gain after training.

Still on the time analysis, the period of ECMO use is a relevant parameter related to patient management. The literature differs about the time of use after training, finding similar, shorter, and even longer periods after team training. This is related to specificities of patient management in each center studied^(6-8,10).

Regarding weaning from ECMO, the literature is still divergent as to the influence of training on this indicator. It was observed in a previous study that the increase in weaning frequency was not very significant, from 37.0% to 40.0%, with $p=0.789$ (8). However, in an American study, the weaning rate increased from 42.9% to 65.2%, with $p=0.018$ (10), a finding that corroborates the present study. In a single Brazilian study, a weaning rate

above 75.0% was also found in the period after training⁽⁶⁾.

In this sense, it is evident the active participation of the team to achieve the best outcome for the patient. Thus, an increase in workload at the time of ICU admission is observed in the post-training period, although without statistical significance. There is no evidence so far to compare this finding related to training periods. However, it is essential to adjust the number of nursing professionals to a 1:1 ratio, that is, one nurse for one patient on ECMO⁽¹¹⁾.

Regarding the clinical outcome of adult patients undergoing ECMO, according to the general ELSO registry, the overall hospital discharge is around 48.8%, which is like the present study (46.4%) after team training⁽³⁾. It should be added that the pediatric/neonatal population has better outcomes when compared to adults, especially in situations of cardiac arrest (58% versus 71%)⁽³⁾.

In view of that, a study with 1,265,508 ICU patients, which compared overall mortality among individuals with and without ECMO use, showed a mortality rate of 12.6% among those not submitted to ECMO and 63.4% among those submitted to therapy, higher than that found in this study after training⁽¹²⁾. In addition, mortality was associated with a significant degree of severity, verified by prognostic scores such as SAPS and Acute physiology and chronic health evaluation (APACHE)⁽¹³⁾.

In the literature, it is observed that, after training of the multidisciplinary team, a reduction in mortality occurs^(6-8,10). A study that compared mortality before and after training showed a reduction from 91.3% to 66.7%, corroborating the findings of the present study⁽⁸⁾. A Brazilian study observed that, after training, mortality decreased from 100.0% to 60.0%⁽⁶⁾. In this context, the influence of training on patient outcome is evident.

Still on the condition of the outcome, it is observed in this study a survival of 31.0% after 90 days of initiation of therapy. In comparison with the literature, the survival rate presented is lower, since in other studies it is observed that the survival rate after 28 days of initiation of ECMO is 53.3%, in 90 days approximately 50.0%, and after one year decreases to 37.8%⁽⁶⁻⁸⁾.

However, when mortality related to the type of ECMO is observed, the degree of reduction differs⁽¹⁵⁾. In a study that compared clinical outcome according to type of ECMO after team training, it was found that there is a lower tendency for VA ECMO-related mortality reduction (78% to 60%) than for VV ECMO (73% to 40%)⁽¹⁴⁾.

In addition, a study on the learning curve of a team of specialists related to the conduct of VA ECMO showed that only after 50 patients do the first signs of impact on clinical outcomes occur⁽¹⁵⁾. Another study that analyzed the learning curve of the VA ECMO team found that after 60 to 65 cases, a positive impact on outcomes occurs. Therefore, in case of VA ECMO, the learning curve is slower, which is justified by the severity presented by SAPS II in relation to VV ECMO⁽¹⁶⁾.

The analysis of the post-training period as a protective factor for in-hospital mortality is of extreme value to consolidate the importance of the educational component in this context. However, the literature is divergent about this factor, since in an American study the post-training period was considered a protective factor in the multivariate analysis for in-hospital mortality probability (Odds ratio: 0.11; 95% CI: 0.03-0.46; $p=0.003$)⁽⁸⁾. However, in a Korean study, the post-training period was not considered protective in the analysis of in-hospital mortality (Hazard ratio: 3.43; 95% CI: 0.55-21.43; $p=0.186$), corroborating the present study⁽¹⁰⁾.

Although the period after training in this study has not been established as a protective factor for mortality, the systematization of activities performed by professionals involved in ECMO patient care after training should be highlighted, since they are aimed at reducing or avoiding complications inherent to the procedure⁽¹⁷⁾. In this sense, in a Brazilian study,

the bleeding rate after team training decreased approximately by 50.0%⁽⁶⁾.

Thus, there should be investment in training and capacity building of multidisciplinary teams in ECMO, as well as continuity of training, so that the process remains effective over time. Currently, ELSO recommends the practice of periodic training in institutions that perform this procedure, especially because of the current covid-19 pandemic, in which therapy is indicated for cases of respiratory failure unresponsive to conventional treatments⁽⁸⁾.

Finally, a limitation of this study is the sample size, since this therapy in Brazil is still in the solidification phase, due to the need for adequate infrastructure and specialized human resources. We also emphasize the retrospective nature of the research, which has difficulties related to data collection, as it depends on the quality of documentation performed by professionals. Therefore, studies with larger samples and associated with other ECMO centers are needed to address the impact of multidisciplinary team training on the respective clinical outcomes, especially in Brazil, where information on ECMO is still scarce.

CONCLUSION

After training the multidisciplinary team, there was a reduction in overall in-hospital mortality and a consequent increase in survival over 90 days after initiation of therapy.

These results serve as an incentive to hospital managers to train their multidisciplinary teams in the management of the patient on ECMO, in order to ensure better quality care in a country where the use of ECMO is increasingly advanced as a result of the covid-19 pandemic.

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