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## Effects of a physiotherapeutic program in patients on veno-venous extracorporeal membrane oxygenation. A 8 year single center experience

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**Effects of a physiotherapeutic program in patients on veno-venous extracorporeal  
membrane oxygenation**

**a 8 year single center experience**

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**ABSTRACT**

**BACKGROUND:** To date, there is no agreement on the timing to perform a physical session in patients on Venous-Venous Extracorporeal Membrane Oxygenation (VV-ECMO) .

We aimed to assess whether early physiotherapy (within the first week from ECMO start) could affect in-ICU mortality

**METHODS:** our retrospective observational study included 101 adults supported on VV ECMO from 2009 to 2016, consecutively admitted at our ECMO referral Center in Florence (Italy). Clinical data right before ECMO start were collected for all patients. The level of mobilization using the ICU mobility scale was recorded on the first session and at discharge.

**RESULTS:** Early physiotherapy (within the first week) was more frequently initiated in patients with lower BMI ( $p=0.013$ ) and it was associated with lower duration of ECMO support ( $p=0.03$ ), mechanical ventilation ( $p=0.001$ ) and length of stay ( $p=0.001$ ). In-ICU mortality was not different between the two subgroups.

**CONCLUSIONS:** In patients on VV-ECMO support, physiotherapy is feasible and safe and that early physiotherapy, initiated within the first week from ECMO start, is associated with shorter duration of ECMO support and ICU length of stay.

**Key words:** ARDS, ECMO, physiotherapy, prognosis

**ABBREVIATION LIST**

ARDS: Acute Respiratory Distress Syndrome

ICU: intensive care unit

VV-ECMO: venous-venous extracorporeal membrane oxygenation

## INTRODUCTION

In recent years, Venovenous Extracorporeal Membrane Oxygenation (VV-ECMO) has emerged as a supportive treatment in ARDS refractory to conventional therapy <sup>(1,2)</sup>.

Though physical therapy has been routinely incorporated into the care of the critically ill worldwide, patients on ECMO support are usually considered too unstable for active physical therapy. High volume ECMO programs have extended this practice in selected ECMO patients, being facilitated by advances in extracorporeal technology and cannulation techniques <sup>(3)</sup>.

Nevertheless, there is no agreement on the timing to begin a physical session in patients on VV-ECMO support, considering the challenges/difficulties these patients present for mobilization, among whom the cannulation strategy (femoro femoral versus bicaval) .

The aim of the present investigation was to test the hypothesis that early physiotherapy (first session within the first week from ECMO start) could affect in-ICU mortality in 101 patients with refractory ARDS on VV ECMO support, admitted to our ECMO referral Center from 2009 to 2016.

## METHODS

In this observational study we enrolled all consecutive patients with refractory ARDS <sup>(4)</sup> on venovenous ECMO support admitted to our ICU (a tertiary ECMO referral center) from Oct 1<sup>st</sup>, 2009 to December 31<sup>th</sup>, 2016 submitted to physiotherapy. Data were prospectively recorded in clinical registry and retrospectively analyzed. All patients (or their next of kin) signed a written informed consent for using and storing their clinical data. The study was approved by the Institutional Review Board of our hospital <sup>(5)</sup>.

### *Data collection*

Clinical data right before ECMO start were collected for all patients and the sequential organ failure assessment (SOFA) and the simplified acute physiology *score* (SAPS II) score were calculated <sup>(6)</sup>.

### *Physiotherapy*

To record the level of mobilization achieved by patients receiving ECMO, the following ordinal scale was used: (1) no mobilization or passive range of motion of extremities, (2) turning in bed (including active-assisted range of motion of extremities), (3) sitting in bed with the head of bed elevated, (4) sitting on the edge of the bed with feet on floor, (5) out of bed sitting in a chair, (6) standing out of bed, (7) marching in place, and (8) ambulating . This mobilization scale was adapted from an early version of a validated ICU Mobility Scale <sup>(7)</sup>. These scores were recorded at the first physiotherapy session and at ICU discharge.

All ECMO recipients are evaluated daily (six days out of seven) to assess their suitability for participation in physical therapy. This comprises evaluation by physical therapists, nurses, and intensive care physicians. Reasons for deferring therapy, assessed on an individual basis and at the discretion of the treatment team, comprise clinically significant hemorrhage, unstable arrhythmia, severe thrombocytopenia, hemodynamic instability requiring high-dose vasopressors, severe hypoxemia despite oxygen supplementation, sedation precluding active participation by the patient and use of neuromuscular blockade. During physiotherapy sessions, particular attention is provided to the integrity of the ECMO cannula and tubing. Changes in ECMO sweep gas flow rates, ECMO blood flow rates and supplemental oxygen, may be performed as needed, based on clinician judgment. Hemodynamic and respiratory statuses (continuous pulse oximetry) are monitored throughout. Physical therapy sessions may be interrupted or terminated, based on the judgment of the participating clinicians, in presence of clinical variations such as the development of hemodynamic instability, hypoxemia, chest pain or dyspnea.

Primary outcome was in-ICU mortality. Secondary outcomes were length of stay and duration of mechanical ventilation.

### *Statistical analysis*

Data have been stored in a dedicated data-base and analyzed with SPSS for Windows 20.0 (SPSS Inc., Chicago, IL). A p value less than 0.05 has been considered statistically significant.

Categorical variables are reported as frequencies and percentages; continuous variables are reported as mean  $\pm$  standard deviation (SD). For continuous variables, between-groups comparisons have been performed with Student's t-test. Categorical variables have been compared with chi-square. Univariate analysis (chi-squared or Fisher's exact test for categorical data; Student's t test or Mann-Whitney U test for continuous data) was used to identify candidate variables for multivariable analysis which included those variables that resulted statistically significant at univariate analysis (BMI) and those considered clinically relevant (time from ECMO start to first physiotherapy session). Pearson's linear regression analysis was used to detect the relationship between both time from ECMO start and first physiotherapy session and length of stay and other variables (the coefficient of determination is reported). Multivariable logistic regression was performed in order to identify predictors of ICU mortality. Hosmer-Lemeshow goodness-of-fit test and Nagelkerke pseudo- $R^2$  are reported.

## **RESULTS**

In our series, 101 patients (101/160, 63.1%) were submitted to physiotherapy while on ECMO support and during ICU stay.

### *Survivors vs no survivors*

In this group, 26 patients died during ICU stay (26/101, 25.7%). When compared to not survivors (Table 1), patients who survived showed a significantly higher BMI ( $p=0.040$ ) and shorter period on ECMO support ( $p=0.012$ ). Dual lumen cannula was more frequently implanted in survivors ( $p=0.001$ ) who also showed a higher incidence of H1N1 infection ( $p=0.048$ ).

### *Early vs delayed physiotherapy*

To better assess time from ECMO start to first physiotherapy session, we compared patients who initiated physiotherapy within the first week since ECMO implantation and those who started this treatment afterward (Table 2). Early physiotherapy (within the first week) was more frequently initiated in patients with lower BMI ( $p=0.013$ ), higher SAPS II score ( $p=0.006$ ) and with cystic fibrosis ( $p=0.045$ ) and it was associated with lower duration of ECMO support ( $p=0.03$ ), mechanical ventilation ( $p=0.001$ ) and length of stay ( $p=0.001$ ). The type of cannulation (femoro-femoral vs dual lumen cannula) did not influence early physiotherapy. In-ICU mortality was not different between the two subgroups.

At linear regression analysis, time from ECMO start to first physiotherapy session showed a significant relation with length of stay ( $r^2=0.48$ ,  $p<0.001$ ), ECMO duration ( $R^2=0.48$ ,  $p<0.0001$ ) and SAPS II ( $r^2=0.45$ ,  $p<0.001$ ).

### *Multivariable logistic regression analysis*

In our series BMI was an independent predictor of in-ICU mortality (OR 0.899, 95%CI 0.823-0.981,  $p=0.017$ ), adjusted for time from ECMO start to first physiotherapy session (OR 1.016, 95%CI 0.988-1.044  $p=0.267$ ). Homer-Lemeshow chi square 7.557,  $p=0.478$  Nagelkerke 0.123.

IMS scores are shown in Table 3 at first physiotherapy session and at discharge. At first physiotherapy session, most patients (66/101, 65.3%) were able to perform exercise in bed, while at discharge the 37.3% (28/75) were able to actively participate to physiotherapy. No patient-related or circuit-related complications were observed as a result of physical therapy treatment sessions in any of the patients. All survived patients were transferred to a rehabilitation unit.

## DISCUSSION

The main findings of the present investigation, performed in 101 patients with severe ARDS on VV ECMO, are follows: a) physiotherapy is feasible and safe; b) early physiotherapy, initiated within the first week from ECMO start, is associated with shorter duration of ECMO support and ICU length of stay.

Our population includes ECMO patients with acute respiratory failure from different etiologies (ranging from influenza to cystic fibrosis) thus mirroring the real world in an ECMO referral Center. Interestingly, in these patients, physiotherapy per se was associated with lower in-ICU mortality. This finding is in agreement with that reported by Munshi et al <sup>(8)</sup> who observed that physiotherapy was associated with lower mortality rate, even when controlled for baseline clinical data and severity of disease. We confirm this association in a larger cohort of patients (101 vs 50 patients) all on VV ECMO support (patients on ECMO mixed modality were also included in the series by Munshi et al <sup>(8)</sup>). Factors accounting for the benefits of physiotherapy on mortality rate can only be hypothesized according to our data, since severity of disease (as inferred by SOFA and SAPS II score) are comparable between the two groups.

Interestingly patients submitted to physiotherapy showed a significant higher BMI which is known to favorably affect early mortality in VV ECMO <sup>(8-11)</sup>. The association between BMI and physiotherapy has not been investigated in previous papers on this topic <sup>(3, 12-14)</sup>, so our finding is

difficult to be compared. In our series patients submitted to physiotherapy had a higher BMI than those who were not, since obesity is known to predispose to respiratory complications. Interestingly the cannulation type (femor-femoral versus dual lumen cannula) did not influence physiotherapy in our center nor timing of physiotherapy. As previously reported (5), at our center since 2012 the dual lumen cannula is the preferred type, also because it allows early mobilization. Nevertheless the feasibility and safety of mobilization was reported also for patients on femoral cannulation (and VA support) (9).

In the present investigation we assessed for the first time the clinical impact of early (within the first week from ECMO start) physiotherapy, taking into account important variability among centers in timing of early mobilization. An International Survey on early mobilization and sedation during VV ECMO support (394 ECMO centers, 209 responders) reported that 41% of the responders initiated physiotherapy within 72 hours of cannulation whereas no physical therapy was engaged by the 16% (15). At our Center, one third of ECMO patients initiated physiotherapy within the first week from cannulation. The benefits of this strategy consisted in reduced mechanical ventilation days, ECMO support duration and length of stay. Two may be the main barriers for early mobilization in ECMO patients: the severity of disease and the type of cannulation.

A multidisciplinary daily (six out of seven days) assessment of the clinical conditions of the single patient, the kind of monitoring during the first sessions, as well as its continuance while on ECMO support and throughout ICU stay are pivotal for an efficacious physical therapy in these patients.

#### *Limitation of the study*

Our study is a single center investigation but it described 8 year experience of physiotherapy in a ECMO referral center with a high percentage of enrollment. Furthermore, we included patients with refractory ARDS from different etiologies (I.e including cystic fibrosis) thus mirroring the real world of an ECMO referral center. In our series, only three patients walked. This is due to the fact that most patients were transferred from the ICU to the Rehabilitation Unit where

they continue their rehabilitation program. The possibility that less sick patients are more likely to receive physiotherapy earlier and that the better outcomes may be attributed also to this rather than the physiotherapy per se cannot be completely ruled out. However in our series we documented an equivalent SOFA or SAPS score. Further studies performed in larger series of patients could better assess the clinical impact of this factor.

### *Conclusion*

The findings of our investigation, performed in 101 adults on VV ECMO, strongly suggest that physiotherapy per se is feasible and safe and that early physiotherapy (within the first week since ECMO start) has a clinical impact being associated with reduced duration of ECMO support, mechanical ventilation and length of stay. A multidisciplinary, daily approach is, according to our experience, a pivotal factor for an efficacious physical treatment.

**Acknowledgment: none**

***Ethical Approval: The study was approved by the Institutional Review Board of our hospital***

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***On behalf of all authors, the corresponding author states that there is no conflict of interest.***

## WHAT IS KNOWN

- Though physical therapy has been routinely incorporated into the care of the critically ill worldwide, patients on ECMO support are usually considered too unstable for active physical therapy. High volume ECMO programs have extended this practice in selected ECMO patients, being facilitated by advances in extracorporeal technology and cannulation techniques .
- Nevertheless, there is no agreement on the timing to begin a physical session in patients on VV-ECMO support, considering the challenges/difficulties these patients present for mobilization, among whom the cannulation strategy (femoro femoral versus bicaval).

## WHAT IS NEW

- In 101 ARDS treated with ECMO support, physiotherapy proved to be feasible and safe. Moreover the cannulation type (femor-femoral versus dual lumen cannula) did not influence physiotherapy in our center nor timing of physiotherapy .
- In the present investigation we assessed for the first time the clinical impact of early (within the first week from ECMO start) physiotherapy, taking into account important variability among centers in timing of early mobilization
- Early physiotherapy (within the first week since ECMO start) has a clinical impact being associated with reduced duration of ECMO support, mechanical ventilation and length of stay in ARDS patients on ECMO. A multidisciplinary, daily approach is, according to our experience, a pivotal factor for an efficacious physical treatment.

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**Table 1** Patients submitted to physiotherapy: comparison between survivors and not survivors

	<b>Survivors 75 patients</b>	<b>Not survivors 26 patients</b>	
Age	49.5±15	53±13	0.300#
BMI	30.1±8	25.5±15	0.006#
PreECMO mechanical ventilation (days, median, IQR)	24 (12-72)	48 (12-96)	0.775&
SOFA (median IQR)	10 (9-13)	10 (9-12.5)	0.625&
SAPS II (median IQR)	41 (24-56)	39.5 (29.75-55.5)	0.696&
<i>Causes of lung injury</i>			0.124*
Primary (n.)	67 (89%)	17 (65%)	0.048*
H1N1	34 (45%)	3 (12%)	
Bacterial	23 (31%)	10 (65%)	
Other	10 (13%)	4 (15%)	
Secondary (n.)	13 (17%)	4 (15%)	0.877*
Shock	5 (7%)	2 (8%)	
Trauma	3 (4%)	1 (4%)	
Cystic Fibrosis	5 (7%)	1 (4%)	
<i>Type of cannulation</i>			
femoro-femoral	7 (9%)	12 (46%)	0.001*
Dual lumen cannula	68 (91%)	14 (54%)	
ECMO (days) (median, IQR)	9.5 (11-26)	18 (10-31)	0.012&
MV (days) (median, IQR)	16 (11-26)	24.5 (10.75-38)	0.112&
LOS (days) (median, IQR)	21 (15-31)	48 (11.5-39)	0.732&
Physio start (days) (median, IQR)	12 (7-18)	8 (5-19)	0.481&
Physio duration (days)	6 (3-10)	5.5 (3-11.25)	0.868&

BMI: body mass index; SAPS II: simplified acute physiology score; SOFA: simplified organ failure assessment; ECMO: extracorporeal membrane oxygenation; MV: mechanical ventilation; ICU: intensive Care Unit; LOS: length of stay ; IQR: interquartile range, #: Student t test; &: Kruskal Wallis; \*= chi square

**Table 2 Time from ECMO start to first physiotherapy session**

	Within the first week n.33	After the first week n.68	
Age	51±15	50±14	0.577#
BMI	25.9±6	30.5±8	0.013#
PreECMO mechanical ventilation	48 (18-96)	24 (12-72)	0.942&
SOFA	10 (9-12)	10 (9-13)	0.366&
SAPS II	31 (24-49.5)	44 (37.5-61)	0.006&
<i>Causes of lung injury</i>			0.043*
Primary (n.)	25 (78%)	59 (87%)	0.009*
H1N1	7 (21%)	30 (44%)	
Bacterial	16	17 (25%)	
Other	2 (6%)	12 (18%)	
Secondary (n.)	8 (24%)	15 (22%)	0.045*
Shock	1 (3%)	6 (9%)	
Trauma	2 (6%)	2 (3%)	
Cystic Fibrosis	5 (15%)	1 (1.5%)	
<i>Type of cannulation</i>			
femoro-femoral	6 (18%)	13 (19%)	0.910*
Dual lumen cannula	27 (82%)	55 (81%)	
ECMO (days) (median, IQR)	7(2.5-13.5)	11 (8.75-22)	0.030&
MV (days) (median, IQR)	11 (5-17.75)	23 (13.75-33,25)	0.000&
LOS (days) (median, IQR)	12 (7.25-21)	25 (18.75-36,25)	0.001&
In-ICU mortality	12	14	0.088*

BMI: body mass index; SAPS II: simplified acute physiology score; SOFA: simplified organ failure assessment; ECMO: extracorporeal membrane oxygenation; MV: mechanical ventilation; ICU: intensive Care Unit; LOS: length of stay ; IQR: interquartile range, #: Student t test; &: Kruskal Wallis; \*= chi square

**Table 3 ICU Mobility Scale**

	<b>At first physiotherapy session 101 patients</b>	<b>At discharge 75 patients</b>
0 Passive range of motion, dependent bed mobility	35 (34.6%)	
1 Exercises in bed	66 (65.3%)	20 (26.6%)
2 Passively moved to chair		15 (20%)
3 Sitting at edge of bed		13 (17.3%)
4 Standing		8 (10.6%)
5 Transferring bed to chair		9 (12%)
6 Marching in place		10 (13.3%)
7 Walking with assistance of two or more people		
8 Walking with assistance of one person		

ICU: intensive care unit