Critical Care

CORRESPONDENCE

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Difference of 11 years between two periods of VV-ECMO does not impact mortality in large centres: we are not sure

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Fanelli et al. conclude that in patients with acute respiratory distress syndrome (ARDS) who received extracorporeal membrane oxygenation (ECMO), the observed unadjusted 60-day mortality was higher in cases of COVID-19 than influenza H1N1 pneumonia [1]. This difference in mortality was not significant after multivariable adjustment; older age and longer hospital length of stay before ECMO emerged as important covariates that could explain the observed difference [1]. The authors state that the current study has several limitations including the possible effect of change of standard of care on outcomes compared over a period of more than 10 years [1]. However, they state that selected academic ECMO centers with high volume and experience in extracorporeal support should guarantee a high standard of care in treating both COVID and influenza H1N1 patients [1]. We would like to comment.The statement that the outcome of ECMO should be the same in 2009 versus 2021 in selected academic ECMO centers is contradicted by the literature [2]. Numerous studies have shown that an enormous evolution has occurred in techniques over a decade [2]. A relatively recent meta-analysis which compares mortality rates over a period of 15 years (from 2000 up to 2015) clearly showed a reduced mortality after adjustment for confounding variables [2]. The meta-regression model in this study showed that the year of study realization was an independent risk factor for mortality ($b=-0.176$; $p=0.003$) [2, 3]. Undoubtedly findings would be similar for the period between 2009 and 2021, an 11 year period in which ECMO has evolved enormously [2, 3]. A meta-analysis by Vaquer et al. demonstrated that the impact of cannula size is an independent factor for mortality ($b=-0.075$; $Q=7.04$; $n=4$; $p=0.008$) [2]. In the study by Fanelli, veno-venous (VV) ECMO blood flow and sweep gas flow were similar in the two groups, except for higher blood flows at day 1 and 14 in the COVID-19 group [1] possibly confirming the role of increased cannula size with increased flow over the years [2]. Another recent study confirmed that a larger drainage cannula diameter was also associated with a reduced risk of death on ECMO [HR 0.88 (0.80–0.96), $p=0.005$] [4]. Progressive technological evolution of VV-ECMO equipment, with improved biocompatibility and reduced complication rates, could have had a potential positive impact on patient evolution [3]. Finally, centre experience has also been associated with improved outcomes in previous reports [3].

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Authors reply

Difference of 11 years between two periods of VV-ECMO does not impact mortality in large centres: we are not sure. Authors' reply

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We thank Dr. Honore and colleagues for their comments to our study on extracorporeal membrane oxygenation (ECMO) support for COVID-19 and H1N1 patients with ARDS [1]. They raise few points that we want to address. Over the last decade, the care of critical ARDS patients on ECMO support has indeed evolved. Dr Honore and colleagues argue that the outcome of ARDS patients treated with ECMO has improved overtime given the technological improvement of extracorporeal support. Recent evidences show that greater attention has been paid on limiting driving pressure to minimize the risk of ventilator induced lung injury [5]. Ultraprotective ventilation was already implemented in our H1N1 ECMO cohort, as shown by a median driving pressure of 10 (see electronic supplement), which was lower compared to COVID-19 patients. In addition, the use of prone positioning has become a standard of care after 2013 [6] but, it has been implemented in patients on ECMO support only in the last few years and was frequently used in COVID-19 patients. This might have influenced our findings, as two recent large meta-analysis on retrospective studies showed a possible association with reduced mortality [7, 8]. Moreover, in our H1N1 cohort hospital mortality was around 30%, similar to the rate reported in the EOLIA trial [9] and did not improve over time. Dr Honore and colleagues speculate that higher blood flow at day 1 and 14 in COVID-19 group might be related to the use of larger cannula over time, which was reported to be associated with higher mortality. In our study, the hazard ratio of death at 60 days was estimated accounting for blood flow and sweep gas at day 1 of extracorporeal support. The hazard ratio of death at 60 days decreased from 1.76, (95% CI 1.17–2.64) to 1.54 (95% CI 0.82–2.90) accounting for blood flow and sweep gas at day 1 of extracorporeal support; only adjusting for confounders, mainly age and hospital length of stay before ECMO support, the hazard ratio decreased noticeably to 1.39, 95% CI 0.78–2.47, suggesting that patients characteristics at baseline primarily accounted for the higher risk of death of COVID-19 patients. Furtheremore, Dr Honore and colleagues argue that center experience affects patients outcome. This is certainly reasonable, however in the current study the H1N1 and COVID-19 cohorts were enrolled at the same ECMO centers and the hazard ratio of death at 60 and 90 days were all estimated stratifying by center-level. We are aware that it is impossible to conclusively resolve in one study all the factors influencing the outcome of ECMO patients, especially over twelve years study period. Nonetheless, we believe that our study provides useful insights for clinicians who deal with the difficult task of defining the indication for ECMO and shows that outcome depend on patient selection rather than the different viral etiology.

Abbreviations
ARDS: Acute respiratory distress syndrome; ECMO: Extracorporeal membrane oxygenation; VV-ECMO: Veno-venous ECMO.

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PMH, RA designed the paper; PMH, SR, PD, TP, BVC, KK, LBG, SA, AG, RA, participated in drafting and reviewing; PMH, SR, PD, TP, BVC, KK, LBG, SA, AG, RA, read and approved the final version of the manuscript.

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