

The use of extracorporeal life support systems in patients with acute respiratory insufficiency

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Chapter 8.

Impact

The clinical value of this dissertation is to be found in the extensively approach to the management of the patients with severe ARDS that needs full respiratory support due to the native lungs' failure.

We approached the crucial point about the identification of the most important variable that could affects the outcome of the patients that received an ECMO support due to the respiratory insufficient. The respiratory rate during the first days of ECMO seems to be one of the key point factors to keep under tight control to apply the lungs rest strategy. In this study we highlighted that despite a safe value of mechanical power applied by the ventilator, the respiratory rate could be related to a better outcome in terms of ECMO weaning and mortality. Practically the threshold values that we found was 15 b/min, and the patients that have been ventilated during the VV ECMO support with less the 15 b/min are associated with a statistically significant lower mortality. The logical consequence is that we suggest setting on the ventilator, during an ECMO for respiratory insufficient a respiratory rate lower that 15 b/min.

Moreover, we thought about which is the possible monitored variable that could be used to define which is the support given by the ECMO in terms of CO₂ elimination, that means work of breathing or mechanical power applied, and we concentrated our effort to study the CO₂ removal done by the membrane lung (the oxygenator) and by the native patient's lungs. If the measurement of the CO₂ removal by the lungs ($V'CO_{2NL}$) is well established with the clinical use of the volumetric capnometer, it is not well assessed for the measurement of the CO₂ removal done by the membrane or artificial lung ($V'CO_{2ML}$). For this reason, we tested a brand new

volumetric capnometer, in an experimental animal setting, designed and engineered especially for the ECMO. The result of our experimental tests confirmed the value of the new device that can provides the measurement of the $V'CO_2ML$ continuously during the ECMO support. This finding suggest that the clinical implementation of such device is available and trustable, so it was integrated in a commercial device that is already available on the market (Landing monitor, Eurosets srl, Italy).

Starting from this satisfactory result of the new device for the continuous monitoring of the $V'CO_2ML$, we went deeply inside the question about which is the partition between the native lungs and the membrane lung during the ECMO support. Particularly, we studied the CO_2 removal during the weaning phase from ECMO, this because in a clinical setting it's fondant to understand which the contribution of the native lungs, as indirect representation of the lung's potential performance and recovery from the respiratory failure. Our pilot study concluded that if the clinicians keep monitored day by day, or better continuously, the ratio between $V'CO_2 NL$ and the total $V'CO_2$ (equal to sum of $V'Co_2ML$ plus the $V'CO_2NL$) it could be possible to be identified a sort of threshold that is correlated with a successful weaning. This threshold is approximately 50% that describe the moment when the workload for CO_2 elimination is done equally by the ECMO e by the patient's lungs. The remarkable data is that the ratio is not statistically correlated with the ventilatory settings or ECMO settings, obviously this was a pilot study and that such important message should be confirmed with a prospective study with a more robust sample size.

After these studies we moved to understand which could be the possible or more frequent or not well-established complication of ECMO support in patient with respiratory failure. So, we analysed the risk of haemolysis during prolonged ECMO support, particularly we tried to identify which component or variables of the extracorporeal support could help the clinicians to reduce or better prevent the haemolysis phenomenon. We analysed 35 consecutive ECMO patients and we tried to discover which are the variables correlated with an important haemolysis. Our results showed that the CRRT machine directly conned tot the ECMO circuit is correlated with an arising of haemolysis sings combined with oxygenator aging. The evident clinical relapse seems to be that if we would like to prevent the arising of haemolysis (and its consequences) we could avoid the connection of the CRRT machine to the ECMO circuit and to check daily the aging of the oxygenator un terms of dead space volume.

Finally, we dedicated our attention to the neurological complication, one of the most dangerous complication during ECMO for respiratory support. Particularly, we analysed the correlation of the cannula's configuration, in terms of comparison between two single lumen cannulas versus the double-lumen cannula configuration. We prepared a retrospective analysis of 6'834 patients included into the ELSO registry, of which the 63.9% with single-lumen cannula configuration and 36.1% with double-lumen cannula configuration. Our main finding was that the choice of the configuration does not affect the incidence and prevalence of the major neurological complications such intracranial bleeding, seizure, acute ischemic stroke or brain death. The clinical relance of this last study is a different conclusion

respect previous reports, in which seems that the double-lumen configuration was associated with an increase incidence of intracranial bleeding. So, the choice of cannulation system could be based only on clinical input and needs, without the risk of improving the probability of neurological complications.

As relevant messages of this thesis we could summarized that the patients with severe respiratory insufficient that need an ECMO support should be ventilated with a respiratory rate lower than 15 b/min; they should be monitored with a volumetric capnometer for the native lungs and membrane lung and when the ratio of total CO₂ elimination and the lungs elimination reach the 50% , it could considered as a positive prognostic index for the weaning from ECMO; the haemolysis during ECMO could be prevent avoiding the direct connection of the dialysis machine to the ECMO circuit and monitoring the oxygenator dead space; the neurological complications, particularly the intracranial bleeding incidence, is not correlated with the use of the single double-lumen jugular cannula.