Letter to the Editor

Extracorporeal life support and neurologic complications: still a long way to go

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The actual impact of neurological complications on patient outcome during extracorporeal life support (ECLS) has emerged only since a few years (1,2) despite the use of such a temporary heart/lung support for more than four decades.

The recent appraisal of the rather high incidence and ominous prognosis of these adverse events in ECLS patients have now alerted attending physicians and personnel upon continuous surveillance and early recognition. Nonetheless, it is increasingly evident that the mechanisms underlying the occurrence are not simply linked to embolization, bleeding, or low-flow related brain hypoxia (3-5) which were thought to represent the sole source of injury of the brain in ECLS patients.

Following a study addressing the neurologic complications in the neonatal population (6), other two studies realized by analysing the Registry of the Extracorporeal Life Support Organization (ELSO), have recently investigated and clearly shown the entity of neurologic adverse events in veno-arterial (V-A) and veno-venous (V-V) ECLS configurations in adult patient populations (7,8). Incidence rates of brain injury were 15% in V-A and 7% in V-V patients, respectively, with an in-hospital survival of 10% in the first group, and 25% in the second, underlining the ominous prognosis once a neurological event occurs in the ECLS patients (7,8). These studies analyzed also the type of brain damage, according to the ELSO reporting system (embolism, hemorrhage, seizures, brain death) but also, more importantly, the trends of the overall CNS complications and of the single type-related rates of such adverse events during a 20-year period whose assessment provided interesting findings (7,8).

The difference of neurologic complication rates between V-A and V-V is not surprising. However, the two studies, as also highlighted by the comments provided by Pappalardo, Hirose, and Perico herewith enclosed (9-11), have provided several relevant clues for further interpretation and discussion. Interestingly, the incidence of CNS events in V-A ECLS patients steadily declined in the recent years, whereas no substantial change was observed in the V-V ECLS population (7,8). It is well-known that patients undergoing V-A ECLS, by definition and as also confirmed by the ELSO Registry data, are usually more prone to experience bleeding and hemodynamic instability after ECLS implant than V-V cases, therefore at higher risk also for brain injury. This is due to either the underlying disease, settings, and clinical conditions of the ECLS candidates or to the ECLS access (arterial cannulation certainly at higher risk of bleeding than venous access). V-A ECLS, indeed, is often applied nowadays in patients suffering from cardiac arrest, condition which is directly linked to brain hypoperfusion

and hypo-anoxia thereby representing a critical factor for brain injury, albeit prior to ECLS implant, not forgetting the unknow extent of the reperfusion injury after the circulation is restored. Another relevant aspect of V-A configuration is the direct connection of the ECLS flow to the supra-aortic vessels, posing the patient at risk for embolization due to the of particulate debris coming from the ECLS circuit/device, but also formed in the left cardiac chamber, particularly in blood stasis conditions. Nonetheless, although V-V patients showed 50% less chance to suffer from a CNS event, they also showed to be at higher risk for brain hemorrhage than V-A patients (7,8). Cerebral bleeding is certainly not a single-factor event, and several aspects and factors may play a variable role in the genesis of such a complication, ranging from coagulation disorder (12) to perfusion impairment, from local or systemic inflammatory and tissue alterations, from vascular spasm due to altered autoregulatory capacity of the brain to endothelial injury. Furthermore, the mechanisms underlying the high rate of cerebral hemorrhage experienced in V-V subjects might be different from the same event observed in V-A patients, who, instead, have higher rates of brain death and ischemic injury. The importance of altered blood gases, particularly of CO_2 clearance, in the genesis of neurologic adverse events has been underlined by several investigators (4,5,13).

It is a fact, therefore, that brain bleeding rate and lack of reduction of such a CNS event in the V-V patients represent a clear sign of no progress in this area and a call for action.

The main issue in this field, and it is indeed an admission of "clinical weakness", is represented by the lack of knowledge about the effects and changes of brain perfusion during ECLS, how the patient metabolic and blood gas states influence brain integrity, and finally about the appropriate management of anticoagulation or control and management of coagulation disorders often observed during ECLS (12). Besides the understanding of underlying mechanisms of CNS events during ECLS, monitoring and timely recognition of the adequacy of brain perfusion or the onset of maladaptive changes and cerebral injury, either perfusion or structure-related, is paramount, but mostly lacking in ECLS patients. On-line information about appropriateness of anticoagulation state and presence and extent of coagulation disorder, brain perfusion and onset of cerebral tissue injury, as well as information about vascular structural and functional integrity, are all part of the complex puzzle which constitutes the ECLS/patient interplay which is, at the moment, poorly defined and understood (12-18). As mentioned, it is likely that CNS event-related etiology is multifactorial, but we are still far from understanding why some patients develop such brain damages and some not.

More emphasis is currently applied in the search for enhanced brain monitoring (14-18), and this includes also the elucidation of not only overt brain injury, but also the impact of ECLS on more subtle and important aspects accounting for the neurocognitive status, particularly in children (19-21).

The actual appraisal of the importance and rate of CNS events is actually soliciting more research in this direction, hopefully enhancing further studies on alternatives for anticoagulation, more biocompatible ECLS systems and components, improved and continuous monitoring system for peripheral and central perfusion and integrity assessment, blood markers, and appropriate counteractions once a suspicion of ongoing or danger of injury may occur, and last but not least, understanding and depicting potential neuropsychological disorders (19,21).

The application of different sedation strategy, the actual understanding if hypothermia may help to avoid or reduce severe brain damage in case of cardiac arrest or low-flow state, the conclusive proof of the effects on improper management of gas exchange on ECLS (particularly in the CO_2 reduction and management), and at last but not least, the recognition of further potential determinants of CNS integrity or injury, will certainly improve patient outcome and favor patient selection for ECLS, avoiding futile run, or improve ECLS management with obvious impact on early, but also on late outcome (19,21). Indeed, it is now increasingly evident that ECLS patients, based on the current ECLS management, may undergo substantial insult which are recognizable only after hospital discharge with appropriate counselling and evaluation, making therefore a neurocognitive surveillance a mandatory action in such a field, particularly in pediatric patients (19).

In summary, Pappalardo and colleagues rightly state that "*In other words*, *we wait for neurological complications*, *rather than to timely identify them*" in ECLS patients (9). Unfortunately, we should also work hard to understand why they do occur and how the local and systemic factors may act on the brain environment so as to induce or predispose for such adverse events, but we are still too far from this understanding. Once we will elucidate the mechanisms underlying brain injury and reaction to adaptive or maladaptive changes during ECLS, and be able to manage more effectively the ECLS management (particularly anticoagulation), then we will be able to timely and effectively prevent or substantially reduce conditions or factors predisposing to cerebral insult, thereby ultimately improving early and long-term ECLS patients' survival and quality of life.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Kasirajan V, Smedira NG, McCarthy JF, et al. Risk factor for intracranial hemorrhage in adults on extracorporeal membrane oxygenation. Eur J Cardiothorac Surg 1999;15:508-14.
2. Mateen, FJ, Muralidharan R, Shinohara RT, et al. Neurologic injury in adults treated with extracorporeal membrane oxygenation. Arch Neurol. 2011;68:1543-9.
3. Lorusso R, Vizzardi E, Pinelli L, et al. Posterior reversible encephalopathy syndrome in a patient submitted to extracorporeal membrane oxygenation for acute fulminant myocarditis. Int J Cardiol 2014;172:e329-30.
4. Muellenbach RM, Kilgestein C, Kranke P, et al. Effect of veno-venous extracorporeal membrane oxygenation on cerebral oxygenation in hypercapnic ARDS. Perfusion 2014;29:139-41.
5. Kredel M, Lubnow M, Westermaier T, et al. Cerebral tissue oxygenation during the initiation of veno-venous ECMO. ASAIO J 2014;60:694-700.
6. Polito A, Barret CS, Wypij D, et al. Neurologic complications in neonates supported with extracorporeal membrane oxygenation. An analysis of the ELSO Registry data. Intensive Care Med 2013;39:1594-601.
7. Lorusso R, Barili F, Mauro MD, et al. In-hospital neurologic complications in adult patients undergoing venoarterial extracorporeal membrane oxygenation: Results from the Extracorporeal Life Support Organization Registry. Crit Care Med 2016;44:e964-72.
8. Lorusso R, Barili F, Mauro MD, et al. Neurologic injury in adults supported with veno-venous ECMO for respiratory failure: findings from the Extracorporeal Life Support Organization Registry. Crit Care Med 2017;45:1389-97.
9. Pappalardo F, Montisci A. Neurologic complications during V-V extracorporeal membrane oxygenation: still counting… J Thorac Dis 2017. [Epub ahead of print].
10. Hirose H, Cavarocchi NC. Neurologic complications during veno-venous ECMO. J Thorac Dis 2017. [Epub ahead of print].
11. Persico N, Bourenne J, Roch A. Editorial on "Neurologic injury in adults supported with veno-venous extracorporeal membrane oxygenation for respiratory failure: findings from the Extracorporeal Life Support Organization database". J Thorac Dis 2017. [Epub ahead of print].
12. Khalbenn J, Wittau N, Zieger B, et al. Identification of acquired coagulation disorders and effects of target-controlled coagulation factors substitution on the incidence and severity of spontaneous intracranial bleeding during veno-venous ECMO therapy. Perfusion 2015;30:675-82.
13. Luyt CE, Bréchot N, Demondion P, et al. Brain injury during venovenous extracorporeal membrane oxygenation. Intensive Care Med 2016;42:897-907.
14. Peek GJ, Killer HM, Sonsowski MA, et al. Modular extracorporeal life support for multiorgan failure patients. Liver 2002;22;69-71.
15. Roth C, Schrutka L, Binder C, et al. Liver function predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery. Crit Care 2016;20:57.
16. Bembea MM, Felling R, Anton B, et al. Neuromonitoring during extracorporeal membrane oxygenation: a systematic review of the literature. Pediatr Crit Care Med 2015;16:558-64.
17. Lorusso R, Taccone FS, Belliato M, et al. Brain Monitoring in adult and pediatric ECMO patients: the importance of early and late assessments. Minerva Anest 2017. [Epub ahead of print].
18. Wong JK, Smith TN, Pitcher HT, et al. Cerebral and lower limb near infra-red spectroscopy in adults on extracorporeal membrane oxygenation. Artif Organs 2012;36:659-67.
19. Mehta A, Ibsen LM. Neurologic complications and neurodevelopmental outcome with extracorporeal life support. World J Crit Care Med 2013;2:40-7.
20. Nasr DM, Rabistein AA. Neurologic complications of extracorporeal membrane oxygenation. J Clin Neurol 2015;11:383-9.
21. Risnes I, Hefdal A, Wagner K, et al. Psychiatric outcome after severe cardio-respiratory failure treated with extracorporeal membrane oxygenation: a case-series. Psychosomatics 2013;54:418-27.

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