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REPLY

Authors' reply: Non-invasive therapeutics to prevent left ventricular distension in venoarterial-ECMO patients: no room for epinephrine!

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Dear editor,

We thank Julien Guihaire and Simon Dang Van for their careful reading and thoughtful comments about our article on epinephrine infusion during VA-ECMO support.[1] As they point out, the timing and indication for epinephrine infusion are useful additional data which may help to clarify the negative outcomes that we observed with epinephrine use. At the time of VA-ECMO cannulation, 229/262 patients (87%) received epinephrine infusion, and for the 33 others (13%), epinephrine was started during the first 24 h of VA-ECMO support, suggesting the early use of epinephrine in our study population. Concerning the indication, detailed information was limited in our database, but we found that out of hospital cardiac arrest was a significantly more frequent reason for ECMO cannulation (18% vs. 10%) in the epinephrine group, whereas medical cardiogenic shock was significantly less represented (30% vs. 41%).

We agree that in patients on VA-ECMO, preventing left ventricular (LV) distention is critical in order to avoid pulmonary congestion and thrombus formation and to promote myocardial recovery.[2] Accordingly, interventional options for LV unloading while on VA-ECMO were used in 25% of the patients in our cohort, with up to 119/589 patients (20%) being supported with intra-aortic balloon pump and 26/589 (4%) with micro-axial flow pump Impella (Abiomed, Danvers, MA, USA). We have been developing a percutaneous balloon atrial septostomy programme in our institution from 2016, but the item was added only recently in our database. Of note, 12 patients benefited from the technique in the study period.

To date, the best approach to manage pulmonary congestion in patients on VA-ECMO remains a matter of debate. We strongly support the idea of a prospective study to address this important question. While we agree with Guihaire and Dang Van that inotropic support is one of the first-line non-invasive treatment for LV distension, we disagree that epinephrine is the best agent to achieve this goal. Epinephrine is a so-called inopressor so the reduction in LV distension achieved by its inotropic effects may be limited by the increased afterload created by its vasopressor effects. In fact, vasodilation is also one of the first-line non-invasive strategy for LV distension, as highlighted by the recent 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients.[3] We would argue that the dual goals of inotropy and vasodilation are more likely to be achieved with an ionodilator such as dobutamine. In our institution, moderate inotropic support is systematically maintained after ECMO cannulation to prevent LV distension as well as blood stasis and avoid intra-ventricular or aortic root thrombus formation.

As asked by Guihaire and Dang Van, we observed a lower rate of successful ECMO weaning in patients exposed to epinephrine. Indeed, only 117/262 (45%) patients were decannulated alive in the epinephrine group, compared with 210/327 (64%) in the non-epinephrine group ($P < 0.001$). Of note, our weaning protocol follows the Extracorporeal Life Support Extracorporeal Life Support Organization (ELSO) recommendations (ELSO Guidelines for Cardiopulmonary Extracorporeal Life Support Extracorporeal Life Support Organization, Version 1.4 August 2017, Ann Arbor, MI,

USA). Withdrawal of VA-ECMO is considered only if the inotropic support is minimal, to allow room for inotropic adjustment after decannulation if needed.

Finally, because we highlighted impaired splanchnic perfusion as a potential driver of epinephrine side effects, Guihaire and Dang Van wondered if mesenteric infarction was a frequent cause of death in our cohort. Only 2 deaths in each group were related to mesenteric ischemia (P = 1.0). Other main causes of death in the epinephrine and the non-epinephrine groups were persistent cardiac failure (n = 41 vs. 33, respectively; P = 0.058), multiple organ failure (n = 23 vs. 26, respectively; P = 0.83), neurological complications (n = 9 vs. 5, respectively P = 0.17), sepsis (n = 4 vs. 5, respectively; P = 1.0), haemorrhage (n = 3 vs. 9, respectively; P = 0.24), and thrombosis (n = 3 vs. 1, respectively; P = 0.33). One may suspect that some patients dying of persistent cardiac failure had also associated pulmonary oedema, but the cause of death in this group of patients was not due to refractory respiratory failure. Given the availability of other methods to reduce LV distension and pulmonary congestion, we suggest that epinephrine should be used sparingly in VA-ECMO patients until further research can be completed.

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