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Antegrade Transpulmonary Blood Flow: Essential for Surviving Veno-Arterial Extracorporeal Membrane Oxygenation

To the Editor:

Veno-arterial extracorporeal membrane oxygenation (ECMO) has become the most common form of mechanical circulatory support (MCS) for cardiogenic shock (CS) in many institutions. We read with great interest the report of Hireche-Chikaoui et al (1) published in the recent issue of *Critical Care Medicine*, which illustrates the often fatal and frequently underestimated consequences of reduced transpulmonary blood flow on veno-arterial ECMO support (2). The cases, proposed management algorithm, and comments of others (3, 4) prompted us to provide further comment.

We believe it essential to reemphasize that the overall therapeutic goals of MCS in CS are end-organ, pulmonary, and myocardial protection at the same time. One without the others risks optimizing chances of survival. Notwithstanding that veno-arterial ECMO is powerful for improving end-organ perfusion (increased aortic pressure and flow), veno-arterial ECMO increases left ventricular (LV) afterload (5, 6) which can secondarily increase LV diastolic pressure (negatively affecting myocardial perfusion), increase myocardial oxygen consumption, increase pulmonary venous pressure (inducing or worsening pulmonary edema), and decrease aortic valve opening (creating risk of aortic and ventricular thrombosis). Indirect clinical measures can warn of the presence of these critical and mechanistically linked adverse effects, and Hireche-Chikaoui et al (1) suggest an algorithm to deal with them once detected. However, we firmly believe that the key strategy should be that they are not managed but anticipated and completely avoided.

In this regard, we consider it important that veno-arterial ECMO patients have a pulmonary artery catheter (PAC) for monitoring central venous, pulmonary capillary wedge, and/or pulmonary artery diastolic pressures. Frequently, we find these pressures to be unacceptably elevated which prompts further action (detailed below). In addition, based on basic hemodynamic principles and experience, we do not agree with all steps of the treatment algorithm outlined (Fig. 3 in [1]). First, correction of hypovolemia may reestablish opening of the aortic valve in some cases, but this is rarely a persistent effect and frequently results in over-hydration; volume management should be guided by PAC pressure values. Second, the addition of inotropes increases oxygen consumption and may impair myocardial recovery and should be avoided. Third, as eluded to above, we emphasize "proactive" and "early" implementation of LV unloading to maximally protect heart and lungs (7, 8). Our experience and PAC measurements show that use of an intra-aortic balloon pump for this purpose is ineffective. In contrast, an active, percutaneous transvalvular LV assist device (e.g., Impella) directly unloads the LV and pulmonary veins, eliminates stasis in both LV and aortic root, and typically allows to decrease ECMO flow (8). These effects are critical for weaning both mechanical ventilation and MCS. Finally, in addition to being very invasive, central cannulation as suggested by Hireche-Chikaoui et al (1) suffers from exactly the same hemodynamic issues as peripheral veno-arterial ECMO and is not a remedy.

With lack of studies to establish best practices, wide variability has emerged in the management of veno-arterial ECMO patients. Thus, at present, we strongly advocate that PAC-based management with early active unloading provides the best approach for achieving the most physiologic form of mechanical support of circulatory support. Dedicated studies are needed to develop bona fide algorithms for specific patient populations and clinical scenarios.

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Can We Improve Long-Term Survival of Patients With Severe Sepsis at ICU Admission?

To the Editor:

I read with interest the article by Abu-Kaf et al (1) published in a recent issue of *Critical Care Medicine* about long-term survival of severe sepsis at ICU admission, showing 6-month, 1-year, and 3-year mortality rates significantly higher than patients with just infectious disease without sepsis. When controlling for age, Charlson Comorbidity Index, history of stroke, and congestive heart failure, sepsis was associated with an increased risk of mortality up till 24 months from discharge (1). However based on cause of death analysis; excess 6-month, 1-year, up to 2-years long-term mortality was attributed to "underlying chronic comorbidities" rather than severe sepsis per se for such relatively long period (1). I am afraid this might leave the readers with the impression that, after aggressively treating severe sepsis, there is nothing more that could be done to improve patients' long-term survival (1). This does not quite concur with de Jong et al (2) "stop antibiotics on procalcitonin guidance study"; showing that procalcitonin antibiotic guidance actually decreased the 28-days short-term mortality and 1-year long-term mortality from 27% (121/457) and 43% (196/457) in standard-care severe sepsis ICU patients to 20% (107/538) and 36% (191/538) in the procalcitonin antibiotic guided patients, respectively (2). The de Jong et al (2) speculated "decreased antibiotic resistance" or "adoption of alternative therapies" as possible explanations.

On the other hand, now Abu-Kaf et al (1) and de Jong et al (2) indicating that sepsis long-term survival could be influenced by "underlying chronic comorbidities" in the former (1) and "antibiotic-stewardship" in the latter (2), still both run in the face of an established body of literature that seem to beg to differ; showing that we can just improve sepsis variables but not influence sepsis 28-days "short-term" survival. The two Lancet publications demonstrated that procalcitonin guidance, that "reduced antibiotics consumption," was associated with similar survival compared with the standard care (3, 4). Lancet 2004, 28-days 3% mortality (4/124) in procalcitonin group was similar to the 3% mortality (4/119) in the standard-care group (3), and Lancet 2010 PROcalcitonin to Reduce Antibiotic Treatments in Acutely ill patients (PRORATA) 21% mortality (65/307) in procalcitonin group was similar to the 21% mortality (64/314) in standard-care group (4). This is also in accordance with a huge body of literature of numerous meta-analyses, and a multicentre study "procalcitonin and survival study" (5), specifically showing that procalcitonin antibiotic guidance primary endpoint death from any cause of 32% (190/604) in the procalcitonin group was similar to the 32% (191/596) in the standard-of-care group (5).

As such, if underlying chronic comorbidities could explain excess 6-month, 1-year, up to 2-years long-term mortality (1), readers might be left with the feeling of futility toward improving the long-term survival of ICU patients with severe sepsis. I strongly believe that Abu-Kaf et al (1) should have elaborated in more details, in their discussion, on such an important issue, in addition to aggressively treating severe sepsis aiming toward patients safely surviving their ICU severe sepsis, there is still more that could be done like "antibiotic guidance to reduce antibiotic resistance" (2) or considering "alternative therapies for the underlying comorbidities" as the de Jong et al (2) suggested; specifically aiming at improving their long-term survival. To light a candle....

Dr. Dahaba disclosed that he does not have any potential conflicts of interest.

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Respiratory Deterioration and Cardiac Arrest

To the Editor:

The results of the study by Shappell et al (1) published in a recent issue of *Critical Care Medicine* show that the primary reason for rapid response team (RRT) is respiratory, and patients who died had a higher frequency of respiratory abnormalities (respiratory rate [RR] abnormality, nonsurvivors vs survivors 42% vs 25 %; pulse oximetry ≤ 91%, nonsurvivors vs survivors 33% vs 18%). RR is probably the most commonly reported wrong vital sign (2, 3), and their results are probably an underestimate of respiratory deterioration. Although patients are identified and an RRT is called