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LETTER TO THE EDITOR

Letter by Meuwese et al Regarding Article, "Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation: Results From an International, Multicenter Cohort Study"

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To the Editor:

With great pleasure, we read the well-conducted study by Schrage et al[1] in which they showed a favorable effect of left ventricular (LV) unloading via Impella as an adjunct to venoarterial extracorporeal membrane oxygenation (ECMO) on mortality. With 686 patients with cardiogenic shock being included in the analyses, this is the largest study investigating the effect of Impella in this context,[2] and, in the absence of randomized controlled trials, it provides the best current evidence available on this topic.

Compared with other unloading strategies, Impella seems to provide more potent LV unloading.[3] On the downside, however, the occurrence of complications is common and includes both local and systemic problems.[1] Given the high complication rates and uncertainty regarding which subpopulation might benefit most from LV unloading, the authors call for further studies exploring optimal patient selection. For this selection, we believe 2 factors might be of importance to consider: right ventricular function and the timing of unloading initiation.

First, poor right ventricular (RV) function, which in itself might be associated with worse prognosis, could potentially protect individuals from the development of pulmonary edema during venoarterial ECMO support. This concept was illustrated by means of simulation studies finding lower left atrial pressures during ECMO support in patients with reduced RV function.[4] As such, it could well be that patients with poor RV function have less benefit from LV unloading than those with preserved RV function, and they may only experience the increased complication rate imposed by a second device.

Second, it seems as if the clinical benefit of LV unloading might be different in patients who exhibit signs of pulmonary edema versus those who do not. In a subgroup of patients who received Impella with a certain delay after venoarterial ECMO insertion, Schrage et al found no statistically significant association between unloading and mortality. Although the lack of statistical significance could be explained by the lower numbers of patients, it is of interest that a recent meta-regression of the literature[5] also showed a relatively higher protective effect of LV unloading in studies with a higher percentage of patients with prophylactic LV unloading. This could suggest that the prophylaxis of pulmonary edema by adjunct LV unloading is advisable, rather than awaiting its occurrence. Pulmonary edema could well reflect clinical deterioration and impending multiorgan failure beyond a critical threshold after which LV unloading does not influence outcome anymore. These differential findings must naturally be interpreted with caution and considered as hypothesis generating.

All in all, we congratulate the authors with this very nice study that adds important evidence to optimal management of venoarterial ECMO. For future (randomized controlled) studies designed to investigate the effect of LV unloading and identify subpopulations at highest benefit, we suggest considering effect modification as a consequence of RV function and pulmonary congestion status.

ARTICLE INFORMATION

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Disclosures

Dr Meuwese reports no conflicts of interest. Dr Kraaijeveld reports speaker fees from Abbott, consultancy fees from Abbott and Boston Scientific, and research cooperation with Fresenius-Xenios-NovaLung. Dr Donker reports speaker fees from Getinge-Maquet and Fresenius-Xenios-NovaLung and research cooperation with Getinge-Maquet and FreseniusXenios-NovaLung.

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REFERENCES

1. Schrage B, Becher PM, Bernhardt A, Bezerra H, Blankenberg S, Brunner S, Colson P, Cudemus Deseda G, Dabboura S, et al. Left ventricular unloading is associated with lower mortality in patients with cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation: results from an international, multicenter cohort study. *Circulation.* 2020;142:2095–2106. doi: 10.1161/CIRCULATIONAHA.120.048792
2. Russo JJ, Aleksova N, Pitcher I, Couture E, Parlow S, Faraz M, Visintini S, Simard T, Di Santo P, Mathew R, et al. Left ventricular unloading during extracorporeal membrane oxygenation in patients with cardiogenic shock. *J Am Coll Cardiol.* 2019;73:654–662. doi: 10.1016/j.jacc.2018.10.085
3. Meuwese CL, de Haan M, Zwetsloot PP, Braithwaite S, Ramjankhan F, van der Heijden J, Hermens J, Cremer O, Broomé M, Donker DW. The hemodynamic effect of different left ventricular unloading techniques during veno-arterial extracorporeal life support: a systematic review and meta-analysis. *Perfusion.* 2020;35:664–671. doi: 10.1177/0267659119897478
4. Donker DW, Sallisalmi M, Broomé M. Right-left ventricular interaction in left-sided heart failure with and without venoarterial extracorporeal membrane oxygenation support-a simulation study. *ASAIO J.* 2021;67:297–305. doi: 10.1097/MAT.0000000000001242
5. van der Wal PS, van Steenwijk MPJ, Montenij LJ, Donker DW, Meuwese CL. Prophylactic versus therapeutic left ventricular unloading during extracorporeal membrane oxygenation, better safe than sorry? *J Thorac Dis.* 2020;12:6412–6415. doi: 10.21037/jtd-20-2771