IJAO The International Journal of Artificial Organs

Letter to the editor

The International Journal of Artificial Organs
1–2

DOI: 10.1177/03913988221145502
journals.sagepub.com/home/jao
SAGE

Levosimendan's ability on veno-arterial extracorporeal membrane oxygenation weaning: Evidence says yes!

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Date received: 1 November 2022; accepted: 29 November 2022

Dear Editor,

We read with great interest the work "Levosimendan's effect on veno-arterial extracorporeal membrane oxygenation weaning"[1] by Hau et al., recently published in IJAO. They demonstrated an absent improvement in veno-arterial (VA) ECMO weaning and a longer ECMO duration in the group of patients treated with levosimendan. This data is countercurrent compared to our recently published meta-analysis: we analyzed 10 observational retrospective studies, including 987 patients. We demonstrated more successful weaning from VA-ECMO in the levosimendan group,[2] data in line with the previous meta-analysis.[3,4] We also performed again a random effect meta-analysis adding Hau et al.'s data and including information from another recent study by Chen et al.,[5] and our results were not significantly altered (Figures 1 and 2).

We agreed with the explanation Hau et al. gave: levosimendan was more easily administered in patients with a severely impaired left ventricular function, delaying the start

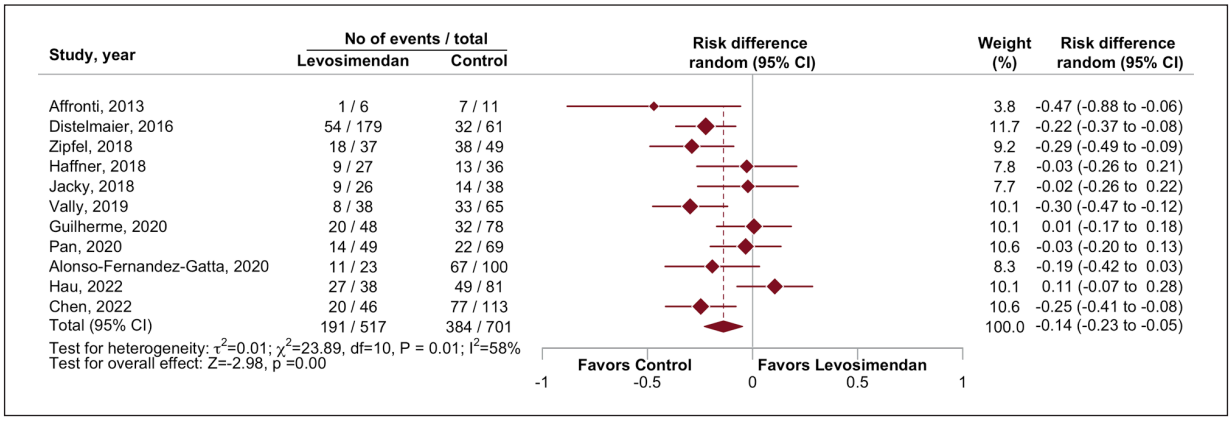

Figure 1. Mortality in VA ECMO patients treated with Levosimendan versus controls: levosimendan administration was associated with a reduced risk of mortality in overall ECMO recipients (191/517 [36.9%] in the levosimendan group versus 307/588 [54.8%] in the control group, RD = −0.14; 95% CI [−0.23 to −0.05].

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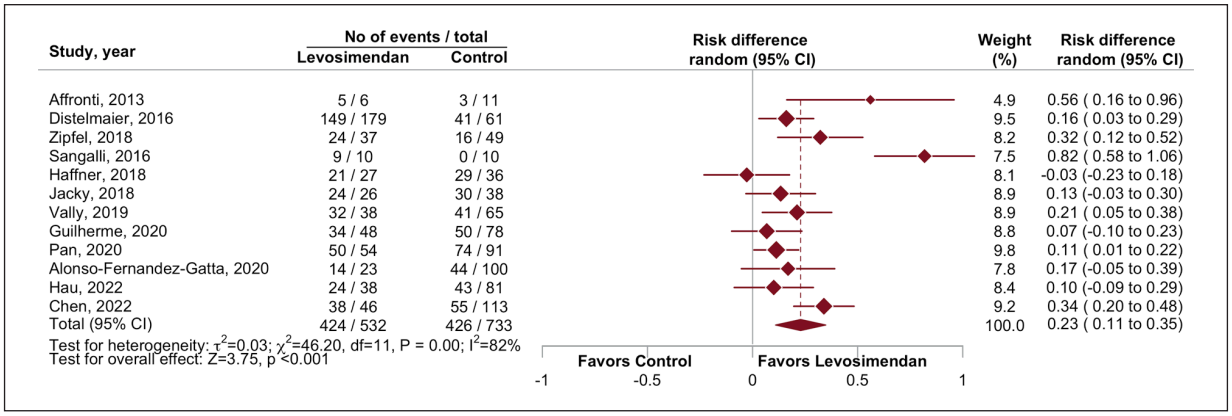

Figure 2. Weaning success in VA ECMO patients treated with Levosimendan versus controls: levosimendan administration was associated with a higher weaning success in overall ECMO recipients (424/532 [79.7%] in the levosimendan group versus 426/733 [58.1%] in the control group, RD = 0.23; 95% CI [0.11 to 0.35].

of the weaning from ECMO, which was not taken into consideration until reaching at least 20% of left ventricular ejection fraction. We believe that their explanation is extendible to other observational studies.[6,7] In observational studies, levosimendan is used in patients with poorer left ventricular function, not in a standardized way. This evidence may explain the longer ECMO duration in the levosimendan group. Even in our meta-analysis, including only observational studies, we demonstrated a non-significantly increased ECMO duration in the levosimendan group. Putting this data altogether, we may speculate that observational studies may underpower levosimendan efficacy in ECMO weaning. Observational studies with small samples may therefore lose statistical significance, which becomes apparent when increasing the number of patients is considered, as in meta-analysis. Thus, Hau et al. may not achieve an advantage in weaning from ECMO due to a small study sample, even though they demonstrated a 10% higher ECMO weaning success rate in the levosimendan group. In light of this, the two ongoing randomized trials, LEVOECMO (NCT04728 932) and Weanlevo (NCT04158674), will be able to provide more certain answers. We expect that in randomized trials, the advantageous effect on weaning will be even more pronounced, confirming levosimendan's beneficial effects in VA ECMO patients.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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