Growing body of evidence supporting the use of Bivalirudin as alternative anticoagulation during extracorporeal membrane oxygenation.

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Letter on the article : Bivalirudin vs. heparin in paediatric and adult patients on extracorporeal membrane oxygenation: A meta-analysis. Li MJ, et al. Br J Clin Pharmacol. 2022 Jan 30.

Dear Editor,

We congratulate Li et al. for their meta-analysis investigating the value of an alternative strategy of anticoagulation for patients supported by extracorporeal membrane oxygenation (ECMO)[1]. The authors divided the ECMO patients according to the use of unfractionated heparin or bivalirudin. A previous systematic review has been conducted[2] and bivalirudin use has increased in perioperative cardiothoracic practice[3]. However, the present study represents one of the first attempts to address quantitatively the benefits of bivalirudin over standard anticoagulation. The authors pooled data from 9 retrospective studies and analysed results on almost 1000 patients[1].

We applaud the authors for their balanced interpretation of the results; indeed, they suggested that bivalirudin may be a potential alternative to heparin in paediatric and adult patients requiring ECMO. We agree that the inclusion of retrospective studies warrant caution in drawing conclusions, but we would like to make some remarks.

The first one is that the authors have probably missed some relevant studies according to their inclusion criteria. In our opinion, at least five potentially eligible studies[4-8]*_ENREF_6*deserved inclusion as they compared the use of bivalirudin and heparin in patients undergoing ECMO. These studies are listed in Table 1.

First author, Year	Study Design Population	Some Outcomes of interest
Giuliano K et al. 2021	Retrospective Adult ECMO	Bleeding, transfusions, thrombosis, mortality
Kaushik S et al. 2021	Retrospective Pediatric ECMO	Bleeding, hemolysis, thrombosis, mortality
Macielak S et al 2019	Retrospective Adult ECMO	Bleeding, thrombosis
Ljajikj E et al 2017	Retrospective Adult ECMO and LVAD	Bleeding, transfusions, mortality
Pappalardo F et al. 2014	Retrospective Adult ECMO	Bleeding, transfusions, thrombosis, mortality

Table 1. Five studies comparing bivalirudin and heparin anticoagulation that may have deserved inclusion in the meta-analysis by Li et al. ECMO: extracorporeal membrane oxygenation. LVAD: Left Ventricular Assist Device.

It happens to miss relevant studies in systematic reviews[9], and our intention is just to make aware the community of a greater number of data available. Moreover, even if all the studies were of retrospective design and thus likely to be biased (selection and reporting bias very likely), the greater number of studies may help in conducting a Trial Sequential Analysis. Although such analyses do not overcome the limitations due to the retrospective study design, their results may inform on the robustness of the meta-analysis findings[10], eventually supporting the idea of conducting prospective studies with randomized design.

In summary, we commend the authors for their balanced conclusions mainly prompted by the design of the included studies. The inclusion of the five missed studies may confirm (or not?) the author's findings, and a Trial Sequential Analysis may add further valuable information on the topic.

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