



Letter to the Editor

Letter to the Editor: Effects of levosimendan on weaning from mechanical ventilation: A systematic review and meta-analysis

ARTICLE INFO

Keywords:

Levosimendan
Mechanical ventilation
Meta-analysis
Weaning
Mortality

The recent article by Li et al., “Effects of levosimendan on weaning from mechanical ventilation: A systematic review and meta-analysis,” presents a rigorous and commendable meta-analysis. However, there is a critical need to examine conflicts in the evidence about levosimendan’s efficacy. This commentary aims to balance their conclusions by addressing these disparities and emphasizing the importance of further research in this area.

In their conclusion, the authors state, “Levosimendan helps patients wean from mechanical ventilation earlier and reduces length of stay in both the intensive care unit (ICU) and overall hospitalization, but does not affect mortality” [1]. We would like to offer a nuanced perspective on this conclusion.

In another meta-analysis, Gayatri et al. [2] focused on the prophylactic use of inotropic agents, including levosimendan, for preventing Low Cardiac Output Syndrome (LCOS) and mortality in adults undergoing cardiac surgery. As the burden of cardiovascular disease increases, so too does the incidence of cardiac surgeries. Surgery, especially in older adults with comorbidities, often leads to perioperative complications, including LCOS, which is responsible for substantial morbidity and mortality. The prevention of LCOS is crucial for improving the outcomes and effectiveness of cardiac surgery. However, guidelines consistently report a lack of evidence supporting pharmacological LCOS prophylaxis [2]. Gayatri et al. included 29 randomized controlled trials with 3307 participants who underwent cardiac surgery and were prophylactically treated with one or multiple inotropic agents in comparison to any type of control (i.e. standard cardiac care, placebo, other inotropic agents) and found that levosimendan, compared to placebo, may reduce the risk of LCOS (risk ratio [RR] 0.43, 95 % CI 0.25 to 0.74; $I^2 = 66\%$) and possibly reduces all-cause mortality (RR 0.65, 95 % CI 0.43 to 0.97; $I^2 = 11\%$) [2]. This translates into a number needed to treat for an additional beneficial outcome of 8 to prevent one event of LCOS post-surgery and of 44 to prevent one death at 30 days.

These findings, from Li et al. and Gayatri et al., present a complex picture of levosimendan’s clinical utility. Li et al. demonstrate benefits for earlier weaning and reduced hospital stay, but report no effect on mortality, which contrasts with Gayatri’s findings that suggest levosimendan may reduce both LCOS and mortality after cardiac surgery. To

better understand these discrepancies, it is important to consider the differences in the patient populations studied. Li et al. focused primarily on adult patients with prolonged ventilation durations, while Gayatri et al. included a broader age range and surgical risk profiles. In particular, older adults with comorbid cardiovascular conditions may benefit more significantly.

Additionally, Beretta-Piccoli et al. [3] focused on the pediatric population and found that levosimendan did not effectively prevent intraoperative events; however, their findings suggested a potential benefit for prophylactic use in reducing the risk of LCOS after surgery in selected cases [3]. This highlights ongoing uncertainty around the drug’s optimal use in children and the need for further, targeted research in this subgroup. Building on this, Honore et al. [4] expanded the discussion by evaluating the broader mechanisms and safety profile of levosimendan. Their review identified significant gaps in our understanding of levosimendan’s renoprotective effects and its influence on medullary oxygenation, issues that remain unresolved across the population [4].

The conflicting findings between these studies underscore the need for well-designed, randomized controlled trials to further clarify the role of levosimendan in clinical practice. Future research should focus not only on short-term outcomes, such as LCOS prevention and weaning from mechanical ventilation, but also on long-term outcomes, including quality of life and recovery trajectories. Studies should also investigate patient selection criteria, dosing regimens, and the broader clinical indications for the use of levosimendan.

Author’s contribution

NDL & PMH designed the paper. All authors participated in drafting and reviewing. All authors read and approved the final version of the manuscript.

CRediT authorship contribution statement

Nathan De Lissnyder: Conceptualization, Writing – original draft, Writing – review & editing. **Sydney Blackman:** Writing – original draft,

<https://doi.org/10.1016/j.jcrc.2025.155414>

Received 12 November 2025; Accepted 14 December 2025

Available online 17 December 2025

0883-9441/© 2025 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Writing – review & editing. **Ilann Oueslati**: Writing – original draft, Writing – review & editing. **Alexis Lefèvre**: Writing – original draft, Writing – review & editing. **Hamza Slibani**: Writing – original draft, Writing – review & editing. **Oumayma Errais**: Writing – original draft, Writing – review & editing. **Patrick M. Honore**: Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Not applicable.

Funding

None.

Declaration of competing interest

The authors declare to have no competing interests.

Acknowledgements

None.

Data availability

Not applicable.

References

- [1] Li C, Guo F, Wang Z, Shan L. Effects of levosimendan on weaning from mechanical ventilation: a systematic review and meta-analysis. *J Crit Care* 2025 Jul 28;90: 155195. <https://doi.org/10.1016/j.jcrc.2025.155195> (Epub ahead of print. PMID: 40729830).
- [2] Gayatri D, Tongers J, Efremov L, Mikolajczyk R, Sedding D, Schumann J. Prophylactic use of inotropic agents for the prevention of low cardiac output syndrome and mortality in adults undergoing cardiac surgery. *Cochrane Database Syst Rev* 2024 Nov 27;11(11):CD013781. <https://doi.org/10.1002/14651858.CD013781.pub2> (PMID: 39601298; PMCID: PMC11600501).
- [3] Beretta-Piccoli X, Biarent D, De Bels D, Honore PM, Redant S. Prophylactic use of levosimendan in pediatric patients undergoing cardiac surgery: the jury is still out. *Crit Care* 2020 Mar 23;24(1):113. <https://doi.org/10.1186/s13054-020-2812-z> (PMID: 32204717; PMCID: PMC7092602).
- [4] Honore PM, Redant S, Moorhamers S, Preseau T, Kaefer K, Barreto Gutierrez L, Attou R, Gallerani A, Boer W, De Bels D. What should clinicians know about the renal effect and the mechanism of action of levosimendan? *Expert Opin Drug Saf* 2021 Dec;20(12):1459–61. <https://doi.org/10.1080/14740338.2021.1986483> (Epub 2021 Oct 18. PMID: 34612116).

Nathan De Lissnyder^a, Sydney Blackman^b, Ilann Oueslati^c, Alexis Lefèvre^d, Hamza Slibani^e, Oumayma Errais^c, Patrick M. Honore^{f,*}

^a VUB University, Brussels, Belgium

^b CHIREC, ULB University, Brussels, Belgium

^c ULB University, Brussels, Belgium

^d CHU Marie Curie, ULB University, Brussels, Belgium

^e Hassan 2 University, Casablanca, Morocco

^f ICU, CHU UCL Godinne Namur, UCLouvain Medical School, Belgium

* Corresponding author at: ICU Dept, CHU UCL Godinne Namur, UCL Louvain Medical School, Campus Godinne, Avenue G Thérassé 1, 5530 Yvoir, Belgium.

E-mail addresses: ilann.oueslati@ulb.be (I. Oueslati), alexis.lefevre@ulb.be (A. Lefèvre), oumayma.errais@ulb.be (O. Errais), patrick.honore@chuucnamur.uclouvain.be (P.M. Honore).