

CORRESPONDENCE

Open Access



Comment on: Association between intrarenal venous flow from Doppler ultrasonography and acute kidney injury in patients with sepsis in critical care: a prospective, exploratory observational study

Nikolaus Schreiber^{1,2}, Michael Kolland¹, Philipp Eller², Alexander R. Rosenkranz¹ and Alexander H. Kirsch^{1*}

Dear Editor,

With great interest we read the recent article by Fujii et al. [1], which brings forth valuable insights in the domain of volume assessment in critically ill patients. The authors conclude that distinct intrarenal venous flow (IRVF) patterns are indicative of renal venous congestion and that they do not correlate with central venous pressure (CVP) but are associated with subsequent acute kidney injury (AKI) in critically ill patients with sepsis. While recognizing the strengths inherent in this study, we strongly believe that there are several limitations that warrant a more comprehensive discussion.

Firstly, the findings diverge from the outcomes published in the study conducted by Spiegel et al., where no discernible correlation between major adverse kidney events at 30 days (MAKE30) and IRVF patterns was established [2]. The authors of the current study justify their findings based on the temporal aspect; they posit

that while Spiegel et al. evaluated IRVF during an early juncture in the disease progression, Fujii et al. examined IRVF patterns subsequent to the initial phase of resuscitation, 24 h after sepsis onset. Furthermore, it is worth noting that the patient cohort in the study by Spiegel et al. exhibited a higher degree of heterogeneity and, contrary to the cohort of Fujii et al., did not exclusively include mechanically ventilated patients. This aspect merits attention since mechanical ventilation does alter venous congestion [3]. Accordingly, the cohort of Fujii et al. exposed noteworthy statistically significant differences in positive end-expiratory pressure (PEEP) levels among patients with distinct continuous and discontinuous IRVF patterns (even in this small sample). Specifically, individuals exhibiting a non-continuous IRVF pattern demonstrated elevated PEEP levels in contrast to those with a continuous pattern. Interestingly, the authors did not adjust their statistical models for this variable, neither for their primary outcome of central venous pressure (CVP) (ANCOVA adjusted for APACHE-II), nor for their secondary outcomes (generalized estimating equation with inclusion of APACHE II score and baseline KDIGO stage). Surprisingly, this aspect is not discussed, leaving open the possibility that the discontinuous IRVF might merely stem from higher PEEP values. This holds especially true considering recently published results encompassing over 25,000 patients in the MIMIC-III database, which strongly imply a robust correlation

This comment refers to the article available online at <https://doi.org/10.1186/s13054-023-04557-9>.

*Correspondence:

Alexander H. Kirsch
alexander.kirsch@medunigraz.at

¹ Department of Internal Medicine, Division of Nephrology, Medical University of Graz, Auenbruggerplatz 15, 8036 Graz, Austria

² Department of Internal Medicine, Intensive Care Unit, Medical University of Graz, Graz, Austria



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

between elevated PEEP values, venous congestion, and AKI [4].

Secondly, and arguably of utmost significance, Fujii et al. omitted the consideration of fluid responsiveness at the timepoint of IRVF-assessment and nevertheless conclude that their findings deliver a potential rationale to guide post-resuscitation fluid therapy and removal in sepsis. They arbitrarily defined the initial resuscitation phase as the first 24 h hours after sepsis onset. Strong prerequisites for the right time to start fluid withdrawal have been proposed based on simple physiological principles: Beside adequate tissue perfusion, patients must not be preload responsive, because if a patient is on the steep part of the Frank–Starling curve, fluid withdrawal can lead to a decrease in cardiac output [5]. The fulfillment of these prerequisites is necessary to justify more comprehensive evaluation of venous stasis to initiate and guide fluid withdrawal. The absence of any consideration of fluid responsiveness highly damped our enthusiasm for the present study findings.

In summary, this study provides only a preliminary exploration into the complex cardio-pulmo-renal interactions it seeks to investigate, especially in the context of fluid responsiveness and venous congestion. It illustrates that assessment of fluid status remains challenging and will likely never be based on a single parameter. Ultrasonography represents an attractive tool in assessing fluid status due to its non-invasiveness as well as rapid and near universal availability in the ICU setting [1, 2, 5]. However, this study (and our raised concerns) should remind readers that most studies on ultrasound-guided volume assessment in critically ill patients are relatively small, often exploratory, and susceptible to various sources of bias.

Therefore, these findings need replication in adequately powered studies with increased sample size and thoughtful covariate selection for appropriate adjustment of statistical models to finally gain robust and generalizable results that may become routine part of clinical care.

Abbreviations

AKI	Acute kidney injury
ANCOVA	Analysis of covariance
APACHE II	Acute physiology and Chronic Health Disease Classification System II
CVP	Central venous pressure
IRVF	Intrarenal venous flow
MAKE30	Major adverse kidney events at 30 days
MIMIC III	Multiparameter intelligent monitoring in intensive care
PEEP	Positive end-expiratory pressure
KDIGO	Kidney disease improving global outcomes

Acknowledgements

Not applicable.

Author contributions

NS wrote the manuscript. MK, PE, ARR and AHK critically reviewed and substantially revised the manuscript. All authors read and approved the final manuscript.

Funding

No funding.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors have no competing interests to declare.

Received: 16 August 2023 Accepted: 23 August 2023

Published online: 29 August 2023

References

1. Fujii K, Nakayama I, Izawa J, Iida N, Seo Y, Yamamoto M, et al. Association between intrarenal venous flow from Doppler ultrasonography and acute kidney injury in patients with sepsis in critical care: a prospective, exploratory observational study. *Crit Care*. 2023;27(1):278.
2. Spiegel R, Teeter W, Sullivan S, Tupchong K, Mohammed N, Sutherland M, et al. The use of venous Doppler to predict adverse kidney events in a general ICU cohort. *Crit Care*. 2020;24(1):615.
3. Gattinoni L, Marini JJ, Collino F, Maiolo G, Rapetti F, Tonetti T, et al. The future of mechanical ventilation: lessons from the present and the past. *Crit Care*. 2017;21(1):183.
4. Geri G, Ferrer L, Tran N, Celi LA, Jamme M, Lee J, et al. Cardio-pulmonary-renal interactions in ICU patients. Role of mechanical ventilation, venous congestion and perfusion deficit on worsening of renal function: Insights from the MIMIC-III database. *J Crit Care*. 2021;64:100–7.
5. DeBacker D, Ostermann M, Monnet X. The nuts and bolts of fluid de-escalation. *Intensive Care Med*. 2023 Jul 19;

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

