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CORRESPONDENCE

Bi-level HFNC: A promising approach for optimizing and individualize respiratory support?

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We read with great interest the study by Shamohammadi et al. [1] entitled "Digital twins of acute hypoxemic respiratory failure and sepsis patients suggest potential benefits of bi-level high flow nasal cannula therapy." This innovative in silico analysis provides compelling mechanistic evidence supporting bi-level high-flow nasal cannula (Bi-flow HFNC) to optimize respiratory support in acute hypoxemic respiratory failure (AHRF) and sepsis, addressing a critical area of debate in respiratory intensive care. We commend the authors for their work and wish to underscore how Bi-flow HFNC may circumvent major limitations inherent to conventional uni-flow HFNC.

Uni-flow HFNC constitutes a cornerstone therapy in AHRF, exerting its effects primarily via anatomical dead space CO_2 washout and flow-dependent positive end-expiratory pressure (PEEP). Nevertheless, substantial inter-individual heterogeneity in physiological response has been documented. Prior digital twin simulations by the same investigators [2] revealed that while "responders" exhibit reduced respiratory drive with escalating flows, "non-responders" display a paradoxical increase in inspiratory effort and deterioration of patient self-inflicted lung injury (P-SILI) indices, attributable to adverse changes in lung mechanics.

A pivotal drawback of uni-flow HFNC is that attempts to maximize dead space washout through higher delivered flows can, counterintuitively, regional overdistension, and augmented work of breathing in susceptible patients (i.e., AECOPD, ARDS). Mauri et al. [3] demonstrated that titrating flow from 20 to 60 L/min improved oxygenation relative to standard oxygen therapy yet increased inspiratory effort in a subset of subjects, accompanied by elevation of end-expiratory lung volume (EELV) across both dependent and non-dependent lung zones—consistent with overdistension rather than homogeneous recruitment. Likewise, Li et al. [4] reported a plateau in oxygenation and ROX index beyond flows equivalent to 1.34–1.67 × peak tidal inspiratory flow (PTIF), suggesting that supraphysiological flows predominantly augment expiratory resistance without incremental washout benefit.

These data may explain the ongoing lack of consensus regarding optimal flow titration and reinforce the principle that "more is not invariably better."

By contrast, Bi-flow HFNC, as modeled by Shamohammadi et al. [1], permits independent modulation of inspiratory and expiratory flows, affording higher inspiratory support to decrease resistive workload while reducing expiratory flow to mitigate overdistension without impairing CO_2 clearance. Preliminary physiological data in healthy volunteers by Huh et al. [5] corroborate this concept, demonstrating superior reduction in inspiratory effort (quantified via nasopharyngeal pressure–time product) with Bi-flow compared to uni-flow HFNC, alongside preservation of baseline EELV and negligible changes in respiratory rate. However, certain aspects, such as the precise timing

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and synchronization of flow delivery with the patient's respiratory cycle, warrant further investigation.

In conclusion, the capacity of Bi-flow HFNC to decouple inspiratory assistance from expiratory unloading represents a physiologically rational strategy to overcome response heterogeneity and mitigate iatrogenic lung injury risk in uni-flow non-responders, potentially enabling personalized respiratory support. These observations strongly advocate for prospective clinical trials to validate the efficacy and safety profile of Bi-flow HFNC.

We thank the authors for their insightful contribution and hope these remarks enrich the ongoing scientific discourse and catalyze further investigation in this promising domain.

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References

1. Shamohammadi H, Mauri T, Bates DG et al (2025) Digital twins of acute hypoxemic respiratory failure and sepsis patients suggest potential benefits of bi-level high flow nasal cannula therapy. Intensive Care Med. https://doi.org/10.1007/s00134-025-08172-w
2. Shamohammadi H, Saffaran S, Tonelli R et al (2025) Digital twins suggest a mechanistic basis for differing responses to increased flow rates during high-flow nasal cannula therapy. Intensive Care Med Exp. 13(1):66. https://doi.org/10.1186/s40635-025-00773-5. (**Published 2025 Jun 26**)
3. Mauri T, Alban L, Turrini C et al (2017) Optimum support by high-flow nasal cannula in acute hypoxemic respiratory failure: effects of increasing flow rates. Intensive Care Med 43(10):1453–1463. https://doi.org/10.1007/s00134-017-4890-1
4. Li J, Scott JB, Fink JB, Reed B, Roca O, Dhand R (2021) Optimizing high-flow nasal cannula flow settings in adult hypoxemic patients based on peak inspiratory flow during tidal breathing. Ann Intensive Care. 11(1):164. https://doi.org/10.1186/s13613-021-00949-8. (**Published 2021 Nov 27**)
5. Huh JW, Seo WJ, Ahn JH et al (2025) Physiological effects of bi-level high-flow nasal cannula in healthy individuals: a proof of concept trial. Front Med (Lausanne). 12:1538832. https://doi.org/10.3389/fmed.2025.1538832. (**Published 2025 May 9**)