The discovery of biological subphenotypes in ARDS: a novel approach to targeted medicine? *j intensive care* 9, 14 (2021).

Background:

•The search for specific pharmacotherapies that effectively treat ARDS has been fruitless, despite decades of promising preclinical research.

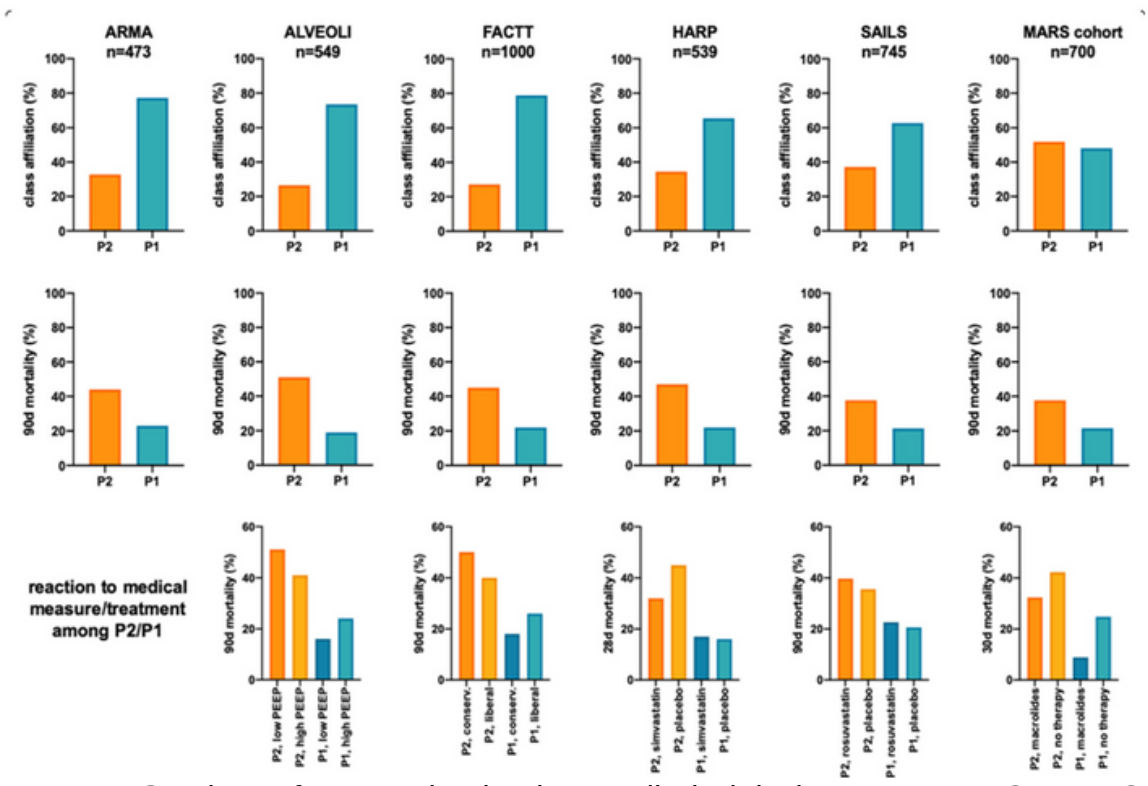
•In an attempt to overcome this obstacle and to further understand the biology of human ARDS through studies of human samples obtained from observational and interventional clinical studies have led to the identification of **promising prognostic biomarkers** in humans and identified molecular sub-phenotypes of human ARDS that may have therapeutic implications.

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Sub-phenotypes in ARDS

The discovery of biological sub-phenotypes in ARDS: a novel approach to targeted medicine?[1]



Analysis of large ARDS cohorts from randomized controlled trials (ARMA, ALVEOLI, FACTT, HARP, SAILS and MARS), have identified the presence of distinct biological subphenotypes among ARDS patients:

•**A hypoinflammatory (or uninflamed; named P1**)

•**A hyperinflammatory (or reactive; named P2).** The hyperinflammatory subphenotyope is clearly associated with shock state, metabolic acidosis, and worse clinical outcomes1.

In secondary analyses of the completed randomized controlled trials2, these two ARDS sub-phenotypes responded differently to PEEP, fluid management and, of most interest, simvastatin therapy. “Hyperinflammatory” subphenotype was identified with elevated plasma levels of interleukin-6, interleukin-8, and tumor necrosis factor α and reduced levels of bicarbonate and protein C3.

B. Taylor Thompson et al3, in their review article, noted that classification of the severity of ARDS and use of traditional clinical variables or severity-of-illness scores, such as the Acute Physiology, Age, and Chronic Health Evaluation (APACHE) III score, could not identify patients with this treatment-responsive subtype, but a relatively simple assessment of three to five biomarkers was able to identify this sub phenotype.

EXPERT COMMENT

“Sub-phenotyping of ARDS into “hypo-” and “hyper”- inflammatory categories provides a new promising approach for therapeutic development through the concept of predictive and prognostic enrichment, potentially resulting in a more targeted treatment. Nevertheless, there are crucial gaps yet to overcome, namely a more in-depth understanding of the underlying driving biological factors and a reliable biomarker for early differentiation between subpheno- types at the bedside. Once these hindrances have been resolved, subphenotyping will most likely be the key factor in all future pursuits in ARDS treatment.”

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With warm regards,

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Reference

1. Wildi, K., Livingstone, S., Palmieri, C. *et al.* The discovery of biological subphenotypes in ARDS: a novel approach to targeted medicine?. *j intensive care* **9,** 14 (2021). https://doi.org/10.1186/s40560-021-00528-w
2. Calfee, C. S. et al. Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. Lancet Respir. Med. 6, 691–698 (2018).
3. Thompson, B. T., Chambers, R. C., & Liu, K. D. (2017). *Acute Respiratory Distress Syndrome. New England Journal of*