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Uncovering Heterogeneity in Sepsis

Sepsis is a life-threatening condition caused by a dysregulated host response to infection. Despite progress in understanding its underlying mechanisms, there's no specific successful treatment for sepsis. Precision therapy is needed, and understanding the heterogeneity of sepsis is crucial.

Recent methods have attempted to measure sepsis heterogeneity using various computational approaches on clinical, biomarker, or gene expression data from different studies. Numerous sepsis subtypes have been proposed, but their overlap and clinical relevance remain uncertain, partly due to a lack of data within a single cohort.

This study assessed the agreement between different subtype labels, outcomes, and biological pathways in critically ill sepsis patients. The study hypothesised that subtype strategies derived from various data sources signify unrelated sepsis subtypes due to the complexity of the condition and differences in data types. However, partial overlap may exist in subtypes associated with the worst outcomes, primarily influenced by disease severity. It was also expected that subtypes based on the same data source would exhibit higher concordance.

The study included 522 critically ill sepsis patients, and four previously established subtype strategies were examined. These strategies were based on clinical data from electronic health records (α, β, γ, and δ), biomarker data indicating hyper- and hypoinflammatory responses, and transcriptomic data (Mars1–Mars4 and SRS1–SRS2).
The most common subtypes in the four strategies were γ (61%), hypoinflammatory (60%), Mars2 (35%), and SRS2 (54%). There was no apparent relationship between the different subtyping approaches. Mars2 and SRS1 were the most similar in terms of host response biomarkers, while the other subtype strategies did not show a clear relationship. Patients with multiple subtypes exhibited distinct characteristics and outcomes depending on the combination of subtypes assigned.

Findings from the analysis show that in critically ill sepsis patients, the use of different subtype strategies based on clinical, biomarker, and transcriptomic data does not result in the identification of similar patient populations. These strategies are likely to reflect distinct clinical characteristics and underlying biological factors.

Source: Intensive Care Medicine
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