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Introduction:

Sepsis is a clinical syndrome; it has been re-defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (sepsis-3). If the sepsis definition and criteria capture the wrong patients there is a risk of dilutional effect on research and a risk to miss diagnosing patients or delay treatment. By utilizing high-throughput proteomics and explainable machine learning, we look to further interrogate the unique molecular definition of sepsis to improve diagnosis and personalize patient care.

Methods:

Patients were eligible for inclusion if ≥ 18 years and admitted to the emergency department at Skåne University Hospital, Lund, Sweden with suspected sepsis. Plasma samples were withdrawn at admission and analyzed using data-independent acquisition trapped ion-mobility mass spectrometry to generate comprehensive proteome maps. Through statistical analysis, explainable machine learning, and novel feature selection methods we investigated the unique proteome signatures associated with different clinical parameters to provide a molecular definition of sepsis.

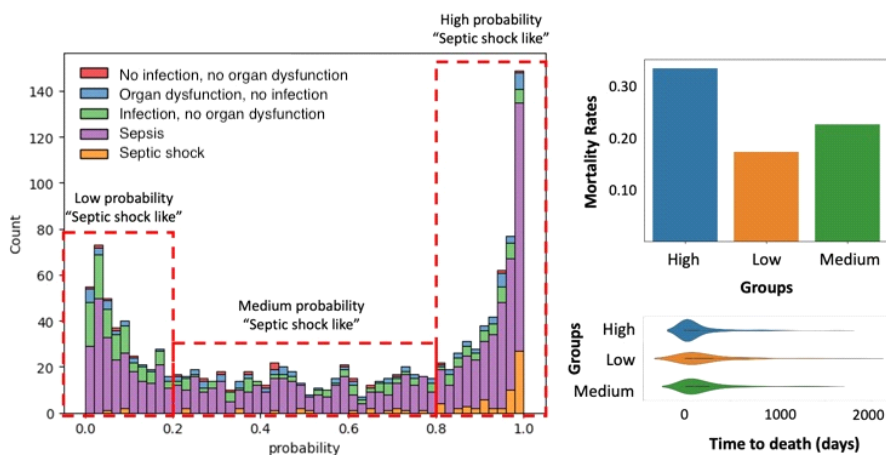
Results:

In 1380 patients, we identified panels of proteins that were predictive for septic shock. We combined each protein panel into a consensus molecular signature to train a machine learning model that predicts septic shock with high accuracy. Finally, we used this classifier to stratify patients into different probability of belonging to the same entity as septic shock and highlight how increasing risk of being proteomic septic shock like is associated with higher mortality. Figure 1.

Conclusion:

Through a combination of high-throughput mass spectrometry and explainable machine learning we identified unique biological signatures associated with the clinical manifestations of sepsis. These findings could be directly applied in the clinic as a proteomic definition of sepsis to provide more accurate sepsis diagnosis and personalized care based on the predicted risk category.

Image :



Probability of patients being septic shock like and its mortality