IDENTIFICATION OF KEY BIOMARKERS FOR THE PREDICTION OF CRITICAL COVID-19 OUTCOMES

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BACKGROUND

- Understanding the mechanistic pathways responsible for the uncontrolled immune response driven by SARS-CoV-2 infection is essential to shedding light on the COVID-19 pathophysiology.
- This study aims at extending the current knowledge of acute illness through the identification of upset molecules in the host immunometabolism. These new molecules might, in turn, reveal potential biomarkers for the prediction of disease severity.

METHODS

- A multicenter case-controlled study including 273 participants recruited during the first wave (March-May 2020) of COVID-19 pandemic into a well-characterized COVID-19 cohort.
- The proteomic, lipidomic and metabolomic profile was determined in blood samples collected at the acute phase of the infection from SARS-CoV-2 infected individuals.

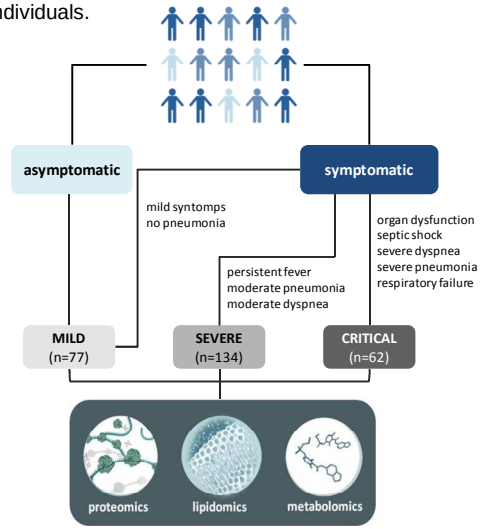


Figure 1. Flow-chart of the clinical strategy followed to categorize patients of the COVID-19 study cohort and the multi-omic analysis.

Novel **biomarker panel** (AHSG, ITIH3, glutamic acid and ChoE (18:0)) accurately **differentiates mild from critical COVID-19** outcomes

RESULTS

- The multi-omics analysis revealed specific molecules related to complement and coagulation cascades, platelet activation, cell adhesion, acute inflammation, energy production (Krebs cycle and Warburg effect), amino acid catabolism and lipid transport as fingerprints of the acute disease (**Figure 2A, B**).
- Among all the significantly disturbed molecules, the random forest analysis determined fetuin-A (AHSG), inter-α-trypsin inhibitor (ITIH3), glutamic acid and ChoE (18:0) as the four biomarkers with the highest potential in predicting disease severity (**Figure 2C**).

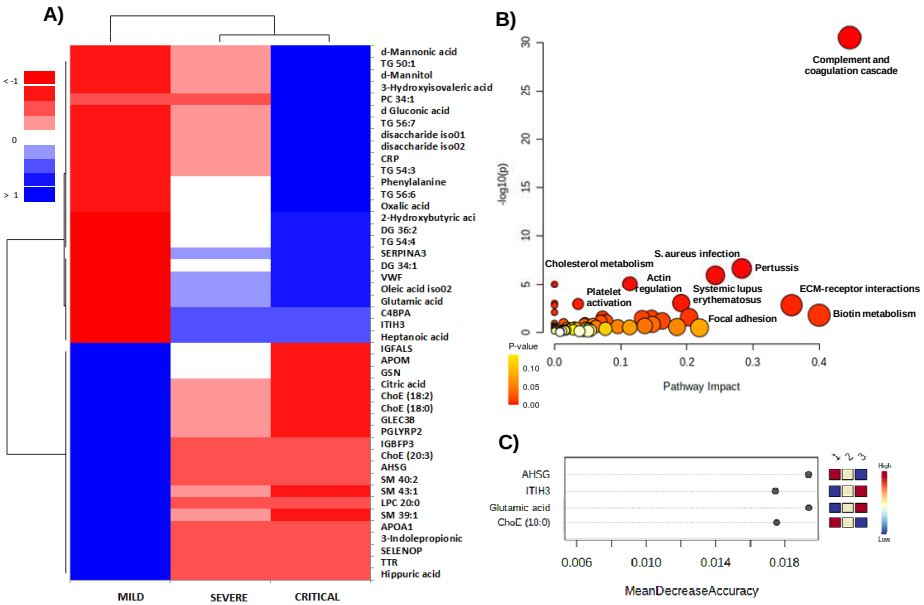
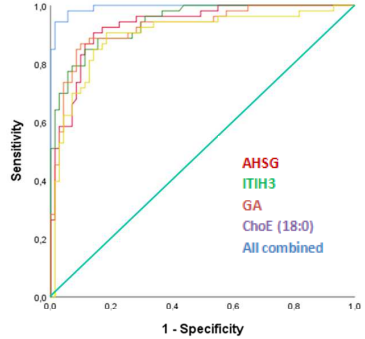


Figure 2. **A)** Multi-omic profile of the COVID-19 patient's cohort, **B)** Pathway enrichment analysis involving the most significantly altered proteins, lipids and metabolites according to the disease severity, **C)** Random forest analysis showing the molecules with the highest classification accuracy .

CONCLUSIONS

- The novel biomarker panel composed of AHSG, ITIH3, glutamic acid and ChoE (18:0) is capable of predicting the most adverse COVID-19 outcomes with high accuracy (AUC: 0.994, 85.9% specificity and 100% sensitivity).



- The newly revealed biomarkers might provide valuable tools for the rapid identification of clinical progression to severe illness in the early stage of SARS-CoV-2 infection, with potential applicability in the clinical management of the pandemics for patient's stratification purposes.

ADDITIONAL KEY INFORMATION

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