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Impact of COVID-19 Progression in Patients With Hypertension

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BACKGROUND

Coronavirus disease (COVID-19) due to SARS-CoV-2 infection is aggravated by some comorbidities, with arterial hypertension being one of the most common. Hypertensive patients are more vulnerable to developing severe COVID-19 complications through different joint mechanisms. The main objective is to find biomolecules and metabolic pathways through a multiomic approach that may explain the relationship between hypertension and unfavorable COVID-19 disease progression.

METHODS

One hundred and three patients with COVID-19 were classified according to disease severity (mild, severe and critical) and divided into hypertensive (n=26) and non-hypertensive (n=77). To evaluate the impact of hypertension and COVID-19 severity, the severe and critical groups were grouped together in unfavorable group (n=63) (Figure 1). Serum samples were collected at the time of admission (acute phase) and four to eight weeks later (recovery phase), and multiomics studies of proteins, metabolites and lipids were performed. Statistical analyses were carried out by Metaboanalyst 5.0 and SPSS Statistics 25.0.

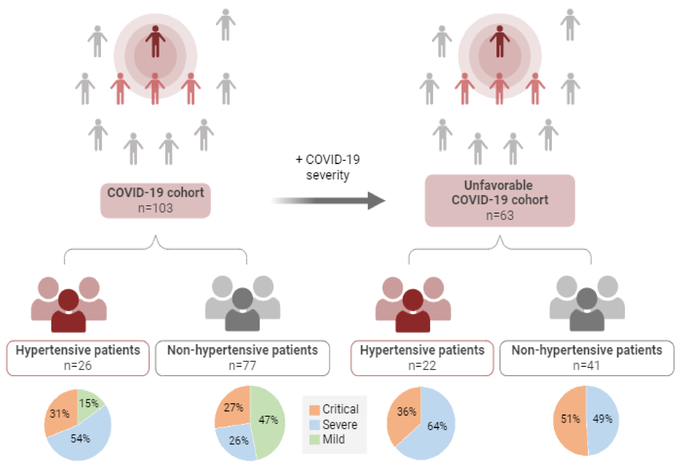


Figure 1. Study cohorts. Created by BioRender.

The most prominent compounds related to unfavorable COVID-19 status in hypertensive patients were **gelsolin**, **myo-inositol** and **phosphatidylcholines**, involved in different pathways, such as the **immune system**, **inflammation**, **oxidative stress** and **lipid metabolism.**

RESULTS

Hypertension was present in 25% of COVID-19 patients as a previous comorbid disease. Hypertension was significantly related to COVID-19 severity (p=0.008); 85% of the hypertensive patients belonged to the unfavorable COVID-19 group (severe and critical). The profile of biomolecules changed depending on the study phase, with the number of significant molecules in the acute phase (n=43) being greater than those in the recovery phase (n=25) (Figure 2).

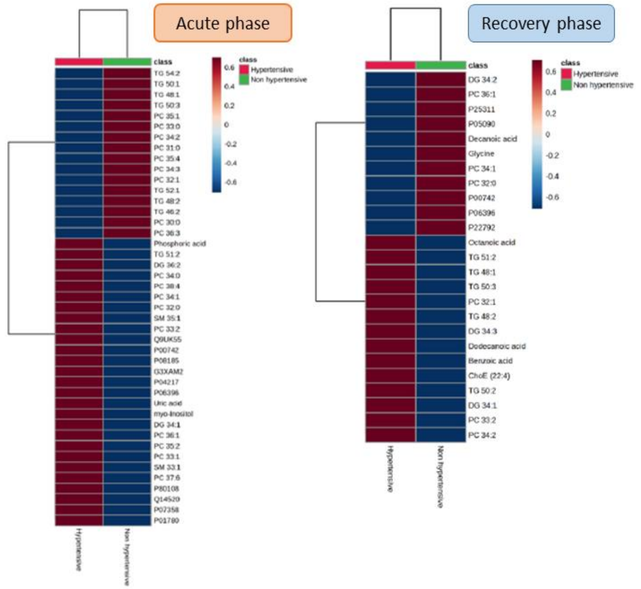


Figure 2. Biomolecules significantly determined by the non-parametric Mann-Whitney test and Metaboanalyst 5.0.

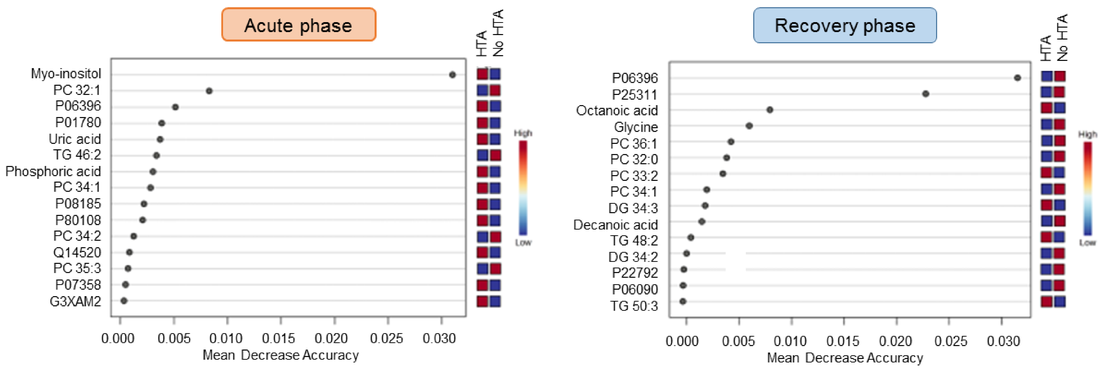


Figure 3. Random forest of 15 significant proteins, metabolites and lipids. The graphics were performed using Metaboanalyst 5.0. HTA: hypertension.

In the acute phase, myo-inositol (AUC=0.695), phosphatidylcholine 32:1 (PC 32:1) (AUC=0.643) and gelsolin (P06396) (AUC=0.696) were the molecules with the best ability to distinguish between hypertensive and non-hypertensive patient. In the recovery phase, gelsolin (AUC=0.674), zinc-alpha-2-glycoprotein (P25311) (AUC=0.711) and octanoic acid (AUC=0.699) presented the best discriminatory power (Figure 3).

Gelsolin, which has a key role in both acute phase and recovery phase, in the acute phase resulted to be significantly decreased in the unfavorable group compared to mild group (0.763±0.367 vs. 1.082±0.622, p=0.002). Of note, within the unfavorable group, hypertensive patients had increased relative amount of plasma gelsolin compared to non-hypertensive patients (0.919±0.388 vs. 0.681±0.332; p=0.03) (Figure 4).

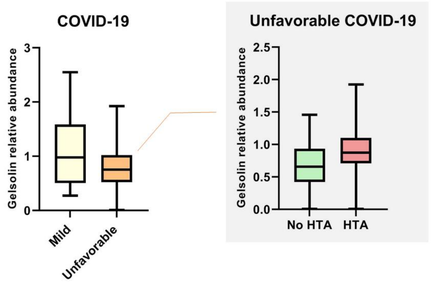


Figure 4. Relative abundance of gelsolin in COVID-19 cohort and unfavorable COVID-19 cohort. HTA: hypertension.

CONCLUSIONS

The study confirmed hypertension as a frequent comorbid disease in patients with unfavorable COVID-19 progression, which significantly increases the severity of the disease. Gelsolin, myo-inositol and some lipid species were those molecules that could be determinants in COVID-19 progression and could explain the clinical worsening of COVID-19 patients through different pathways such as immune system processes, inflammation, oxidative stress and lipid metabolism.

FUNDING

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