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Anais

1133 - The rs1799752/ACE1, rs12329760/TMRPSS2, rs2236757/IFNAR2 and rs368234815/IFNL4 polymorphisms are associated with COVID-19 mortality in non-white patients

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Introduction: Although advanced age, male gender, and some comorbidities impact the variation observed in the clinical symptoms of COVID-19, these factors alone do not explain the inter-individual variability in disease severity. In this context, some studies have shown genetic polymorphisms contribute to the COVID-19 severity; however, results are still inconclusive. Objective: To investigate the association between rs2285666/ACE2, rs12329760/TMRPSS2, rs2109069/DPP9, rs2304256/TYK2, rs1990760/IFIH1, rs2236757/IFNAR2, rs3775291/TLR3, rs368234815/IFNL4, and rs1799752/ACE1 polymorphisms and mortality due to COVID-19. Methods: This study used DNA samples the Biobank of Hospital de Clínicas de Porto Alegre, COVID-19 Collection [(DOI: 10.22491/hcpa-biobanco-amostras; https://biobanco-covid-19.hcpa.edu.br/samples); GPPG 2020-0218]. COVID-19 patients (n=652) were categorized into survivors (n=469) and non-survivors (n=183). Genotyping was performed by real-time PCR. Results: Of the 652 patients included, 52% were men and the mean age was 58.6 years. In the total sample, none of the 9 polymorphisms differed between survivors and non-survivors (all P values > 0.050). Stratification analyses by ethnicity: 1) In non-white patients: The frequency of the rs1799752/ACE1 Ins/Ins genotype was higher in non-survivors compared to survivors (7.1% vs. 0.0%; P=0.015). This association was maintained in the recessive (P=0.020) and additive (P=0.025) models. Presence of the rs223675/IFNAR2 A allele and rs12329760/TMPRSS2 T allele were also associated with risk of death [OR 2.236, 95% CI 1.099-4.548 (P=0.038) and OR 2.066, 95% CI 1.022-4.178 (P=0.046)]. Interaction analysis between ACE1 and TMPRSS2 polymorphisms showed that having 3 or 4 mutated alleles increases the risk of death by COVID-19 (OR 5.405, 95% CI 1.233-23.699; P=0.040). Risk of death was also increased in the presence of 3 or 4 mutated alleles of the IFNAR2 and IFNL4 polymorphisms (OR 2.844, 95% CI 1.232 6.566; P=0.023). The other polymorphisms did not differ between groups. 2) White patients: none of the 9 polymorphisms was associated with COVID-19 mortality. Conclusion: The rs1799752/ACE1, rs12329760/TMRPSS2, rs2236757/IFNAR2 and rs368234815/IFNL4 polymorphisms are associated with risk of death by COVID-19 in non-white patients.