Multiorgan failure in SARS-CoV-2 Infection – A retrospective study

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Introduction

On May 5, 2023, over 3 years since the spread of COronaVIrus Disease 2019 (COVID-19) pandemic, the World Health Organization (WHO) Emergency Committee has established that COVID-19 currently represents an ongoing health issue which no longer a public health emergency of international concern [1]. However, this does not mean that the pandemic itself has been defeated. COVID-19 is an extremely contagious illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2], that will keep broadly circulating and evolving. Collected evidence revealed the clinical profile of COVID-19 patients as a potential predictor of their outcome. Older individuals with multimorbidity are more susceptible to develop a severe form of COVID-19 than either younger individuals or those without multimorbidity [3]. Severe COVID-19 characterized by an uncontrolled and high release of pro-inflammatory cytokines, that increases the levels of inflammatory mediators, endothelial dysfunction, coagulation abnormalities. Indeed, the infiltration of inflammatory cells into the organs contributes to COVID-19 pathogenesis [4,5].

Aims

Aim of this study is to investigate the causal relationship between poor outcome and laboratory parameters in COVID- 19 hospitalised patients, in this sense observe how SARS-CoV-2 infection affects other organs.

Methods

We retrospectively evaluated a cohort of 133 patients, aged 30 to 94 years, hospitalized at the Policlinic of Bari, Giovanni XXIII Hospital, Italy, between January 12th and April 25th, 2021. All patients were positive for SARS-CoV-2. Discharge from hospital, transferral to ordinary ward or nursing home, intensive care unit (ICU) admission, and in-hospital mortality were recorded, alongside demographic, laboratory and clinical parameters. The whole sample was summarized by median (interquartile range) for quantitative data, and absolute and relative percentage frequencies for qualitative variables. Univariable logistic regression models were performed to assess the association between all the parameters of interest and COVID-19 adverse outcome, single (in-hospital mortality) and composite (in-hospital mortality and ICU admission). Hence, a multivariable model was fitted to identify potential independent predictors of the composite outcome. The accuracy of the model was assessed through appropriate fitting indices, such as C-statistic and Hosmer-Lemeshow test [6]. Moreover, to detect multicollinearity the variance inflation factor (VIF) was used [7].

Results

Our study sample had a median age of 72 years old (59.0-83.0). Most common comorbidities were hypertension (63.7%), cardiovascular disease (41.9%), diabetes (33.6%), and cerebrovascular disease (21.5%); while as most common symptoms we observed dry cough (32.5%), dyspnoea (50.8%), and fatigue (29.8%). 18 patients died during hospitalization (13.5%), 10 required ICU admission (7.5%), 78 (58.6%) were discharged from hospital, and 27 (20.3%) transferred to either ordinary wards or nursing home. Univariable logistic regression models disclosed an association of older age with both composite [OR 1.06, 95%CI 1.02-1.09; p=0.003] and single outcome [OR 1.10, 95%CI 1.04-1.16; p=0.001]. A higher oxygen saturation was associated with a better outcome [OR 0.75, 95%CI 0.60-0.93; p=0.009 and OR 0.76, 95%CI 0.61-0.95, p=0.009]. Cerebrovascular diseases determine instead three times the risk of poor outcome [OR 3.07, 95%CI 1.10-8.61; p=0.003]. Also, chronic kidney disease (CKD) was associated with a higher risk of

an adverse outcome in COVID-19 patients [OR 4.19, 95%CI 1.46-12.07; p=0.008 and OR 3.78, 95%CI 2.26-11.28; p=0.017, respectively]. Among laboratory parameters, higher levels of neutrophils increased the risk of a poor outcome [OR 1.05, 95%CI 1.00-1.10; p=0.043]; while higher levels of lymphocytes seems associated with a better outcome [OR 0.94, 95%CI 0.88-0.99; p=0.043]. Consistently with CKD, higher levels of creatinine were associated with a higher risk of both adverse events [OR 6.20, 95%CI 2.16-17.81; p<0.001 and OR 19.90, 95%CI 5.07-78.06; p<0.001, respectively]. Higher levels of sodium (Na) were associated with a higher risk of adverse events [OR 1.15, 95%CI 1.03-1.28; p=0.014 and OR 1.14, 95%CI 1.01-1.27]. Similar findings were also observed for C-reactive protein (CRP) levels [OR 1.01, 95%CI 1.00-1.02; p=0.010 and OR 1.01, 95%CI 1.00-1.02; p=0.024]. Multivariable model was fitted to identify potential independent laboratory predictors of the composite outcome, with age, SpO2 and the significant laboratory parameters. Among these selected parameters VIF method showed that lymphocytes and neutrophils were highly correlated with other dependent variables. Therefore, they were removed from the model. Age, creatinine, and Na confirmed as independent risk factor for poorer outcome, while SpO2 revealed an independent predictor of a lower risk of adverse events (Table 1). The model can be considered accurate according to LM-Test and C-statistic [p>0.83, C-stat = 0.90].

Conclusions

Our findings confirms that COVID-19 is a multiorgan disease. In fact, the analysis of laboratory parameters has revealed a strong relationship between poorer outcomes and multiple organ dysfunction, particularly established by higher level of neutrophils, creatinine, sodium, and CRP. Alongside, also cerebrovascular diseases, chronic kidney disease and older age supported this finding. Of note, instead higher level of SpO2, and lymphocytes.

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Table 1. Multivariable regression model with previous statistically significant identified laboratory markers on composite outcome.

Variable	ICU admission + In-hospital mortality	
	OR (95%CI)	P-value
Age	1.08 (1.02-1.41)	**0.013**
SpO2	0.70 (0.49-0.94)	**0.024**
Creatinine	5.70 (1.67-32.7)	**0.025**
Na	1.19 (1.02-1.41)	**0.032**
PCR	1.01 (0.99-1.02)	0.183

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