

## **Predictors of refractory Coronavirus disease (COVID-19) pneumonia**

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Dear Editor— The pandemic of Coronavirus disease (COVID-19) is rapidly spreading and clinicians across the globe are facing it with limited scientific evidence to support their management. There is a critical lack of predictive factors that can guide clinicians in identifying patients at risk for prolonged, and thus potentially more severe, COVID-19 that needs early and aggressive therapeutic approach. This fact has urged Mo and colleagues to retrospectively characterize patients with refractory COVID-19 as compared with patients with non-refractory COVID-19 (termed “general COVID-19”)<sup>1</sup>. The authors reported that patients classified as refractory COVID-19 were more likely to be older, of male sex, have underlying comorbidities, be afebrile, have shortness of breath and anorexia, and to have laboratory abnormalities and radiological changes. In addition, refractory COVID-19 patients were more likely to receive oxygen, mechanical ventilation, expectorant, adjunctive treatment including corticosteroids, antiviral drugs and immune enhancers when compared to general COVID-19 patients. The authors have further attempted to explore predictive factors for refractory COVID-19 using a multivariate analysis showing that male sex, anorexia on admission and being afebrile are independent risk factors for the development of a refractory disease. Furthermore, out of this analysis the authors have found that patients with refractory COVID-19 were more likely to receive oxygen, expectorant, corticosteroids, lopinavir/ritonavir and immune enhancer.

In their paper, the authors compared categorical and continuous variables between the two groups of patients and these variables that differed significantly between the two groups were included in the multivariate regression analysis. In addition to comparing the frequencies by  $\chi^2$  test and continuous data by nonparametric comparative test, it is well-accepted to perform a univariate regression analysis assessing the different variables and their association with the outcome of interest (i.e. refractory vs. general COVID19) and report their odds ratio (OR) with a measure of variance (e.g. 95% CI). Based on such a univariate regression analysis,

authors can determine the variables to be included in the multivariate logistic regression model to assess independent variables associated with the outcome and their estimated adjusted ORs<sup>2,3</sup>.

In their paper, the authors included the treatment introduced at the time of patient admission and/or hospitalization in the multivariate analysis aiming to identify independent risk factors for refractory COVID-19. One potential concern is that patients who are sicker at time of admission or during hospitalization are more likely to need oxygen and receive expectorant, corticosteroids, anti-viral and immune-enhancers and thus are more likely to have refractory COVID-19 as compared with general COVID-19. Including these variables might potentially have affected the results. The authors should have included in their multivariate model only baseline and clinical characteristics and laboratory results at admission to accurately identify independent risk factors associated with refractory COVID-19.

Given the unusual and unprecedented circumstances our clinical community is experiencing, integrating the aforementioned information in the article by Mo and colleagues will provide scientific evidence to help physicians and healthcare providers across the world to tackle the escalating COVID-19 pandemic as best as we can.

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## References:

1. Mo P, Xing Y, Xiao Y et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clin Infect Dis. 2020 Mar 16. pii: ciaa270. doi: 10.1093/cid/ciaa270.
2. Galetta P, Massari M, Luzzi I, et al. An Easter outbreak of Salmonella Typhimurium DT104A associated with traditional pork salami in Italy. Euro Surveill. 2007; 12(4):E2-1.
3. Abu-Raya B, Bettinger JA, Vanderkooi OG, et al. Burden of Children Hospitalized With Pertussis in Canada in the Acellular Pertussis Vaccine Era, 1999-2015. J Pediatric Infect Dis Soc. 2018 Dec 8. doi: 10.1093/jpids/piy128.