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Comments on "Smoking patterns and outcomes of severe SARS-CoV-2 infection: a retrospective cohort study"

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Dear Editor,

We have read with interest the recently published paper by Beronja *et al*. reporting the clinical outcomes in a group of patients hospitalized for COVID-19, being current smokers or not, and concluding that a history of cigarette smoking (past or active) is an independent factor for negative prognosis in COVID-19 patients [1]. Since the publication of the first data coming from China during the first months of the COVID-19 pandemic, it appeared clear that among hospitalized patients for COVID-19, those who were active smokers were less represented with respect to former and non-smokers, while one would have expected the opposite, being mainly previous smokers or never-smokers, those mainly hospitalized among SARS-CoV-2 infected subjects [2-4].

Those first and subsequent observations have led to the conclusion that cigarette smoke might contain a somehow "protective" factor (nicotine?) for the development of severe complications in SARS-CoV-2 infected subjects up to hospitalization [5-7].

At variance with these considerations, as also underlined by Beronja *et al*., over the years, other studies have reported that cigarette smoking was associated with poorer clinical outcomes in COVID-19 patients [8].

The main observation regards the fact that the authors strongly underline that current smokers were more often admitted to the intensive care unit (ICU) than non-smokers, also showing a higher mortality rate [1]. This cannot be in conflict with the reported lower percentages of active smokers among hospitalized patients for COVID-19, since, although less represented among hospitalized subjects for COVID-19, once hospitalized, current smokers could have worse outcomes than non-active smokers [9]. On the other hand, it is well known that ICU admission is higher among smokers, whatever the cause of hospitalization [10], and thus the observations of the authors are probably expected also in COVID-19 patients, although there are data showing the opposite [11].

In this regard, the data of the authors also report a proportion of hospitalized patients with COVID-19 that is higher among non-active smokers than in current smokers (182/307 *vs*. 125/307, *i.e*., 59.3% of non-active smokers *vs*. 40.7% of current smokers), although the authors did not highlight these data in their discussion [1].

What is important to consider is the difference between the percentages of current smokers and non-active smokers between subjects hospitalized for COVID-19 and the percentages of those SARS-CoV-2 infected subjects that, once hospitalized, show a severe progression of the disease leading to ICU admission. The presence of multiple comorbidities prior to hospitalization for COVID-19 is thus a fundamental aspect to understand the outcomes of those patients [9].

Furthermore, the authors reported that the percentage of SARS-CoV-2 vaccinated patients among current smokers was half that of non-current smokers (8.8% *vs*. 16.6%), and maybe this could have favored the rise of clinical complications in non-vaccinated actively smoking patients, as also reported previously [12].

Finally, Beronja *et al*. reported that among hospitalized patients, the majority were females (68.7%). This result, also considering that in the authors' country, female smokers are fewer than males [13], is quite different from what has been reported previously in all studies on COVID-19 hospitalized patients showing a higher prevalence of males among hospitalized patients with COVID-19 [14], but the reasons for such an unexpected higher female prevalence have not been fully elucidated by the authors [1].

The unhealthy effects of cigarette smoking are well known and do not need to be questioned further, and cigarette smoking should always be discouraged. Nonetheless, the data from epidemiological studies must push research to investigate, without any preconceived position, what the possible mechanisms are leading to the observed low prevalence of current smokers among hospitalized patients with COVID-19.

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