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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 COVID-19 pandemy, it appeared clear that among hospitalized patients for COVID-19, those that were active smokers were less represented with respect to former and no smokers, while one should 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 successive observations have lead to the conclusion that cigarette smoke might contain a somehow "protective" factor (nicotine?) on 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., during 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 ICU than non-smokers, showing also a higher mortality rate [1]. This cannot be in conflict with the reported lower percentages of active smokers between hospitalized patients for COVID-19 since, although less represented among hospitalized subjects for COVID-19, once hospitalized current smokers could have worst 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].

To this regard, also the data of the authors report a proportion of hospitalized patients with COVID-19 that is higher among non-active smokers that 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 highlighten 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 from 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 different multiple comorbidities prior to hospitalization for COVID-19 is thus a fundamental aspect to understand the oucomes of those patients [9].

Furthermore, the authors reported that the percentage of SARS-CoV-2 vaccinated patients among current smokers was half that that of non-current smokers (8.8 vs 16.6 %) and maybe this could have favoured 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 lower 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 patents with COVID-19 [14], but the reasons of such unexpected higher female prevalence have not been fully elucidated by the authors [1].

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

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