

# Risk Factors of COVID-19 Symptoms in Old Subjects

Tomoyuki Kawada

Department of Hygiene and Public Health, Nippon Medical School, Tokyo, Japan

Dear Editor,

I read with great interest the study by Del Ser et al. [1] that explored the risk factors for severe COVID-19 in older people. Regarding the APOE  $\epsilon 4$  allele, some queries were previously presented [2]. I want to discuss the risk of smoking and disease severity with special reference to statistical validity.

The authors described that more intense smoking was significantly associated with severe COVID-19 symptoms by applying linear regression analysis with the Poisson distribution. The age- and sex-adjusted odds ratio (95% confidence interval) of smoking intensity for severity of COVID-19 symptoms was 0.95 (0.91–0.99). I accept that the mean value of the smoking severity index was about 2-fold higher in the moderate/severe group than in the mild group; however, the multivariate statistical results presented an inverse relationship between smoking intensity and severity of COVID-19 symptoms.

Regarding smoking, COVID-19 infection, and disease progression, Simons et al. [3] conducted a meta-analysis by overviewing past epidemiological studies. Compared with never smokers, current smokers presented a reduced risk of COVID-19 infection, presenting a relative risk (95% confidence interval) of 0.74 (0.58–0.93). In contrast, the risk of hospitalization, disease severity, and mortality of COVID-19 in current smokers did not reach levels of significance.

A previous meta-analysis found that the risks of hospitalization, severe disease, and mortality of COVID-19

in former smokers might be significantly high [3]. The risk of disease progression in current smokers should be specified by further studies.

## Acknowledgments

I greatly appreciate technical support by members of the Department of Hygiene and Public Health, Nippon Medical School.

## Conflict of Interest Statement

The author has no conflicts of interest to declare.

## Funding Sources

There was no funding for this letter.

## References

- 1 Del Ser T, Fernandez-Blazquez MA, Valenti M, Zea-Sevilla MA, Frades B, Alfayate E, et al. Residence, clinical features, and genetic risk factors associated with symptoms of COVID-19 in a cohort of older people in Madrid. *Gerontology*. 2021;67(3):281–9.
- 2 Hubacek JA, Dlouha L, Dusek L, Majek O, Adamkova V. Apolipoprotein E4 allele in subjects with COVID-19. *Gerontology*. 2021; 67(3):320–2.
- 3 Simons D, Shahab L, Brown J, Perski O. The association of smoking status with SARS-CoV-2 infection, hospitalization and mortality from COVID-19: a living rapid evidence review with Bayesian meta-analyses (version 7). *Addiction*. 2021;116(6):1319–68.