LETTER TO THE EDITOR

Clinical and demographic characteristics of patients dying from COVID-19 in Italy vs China

To the Editor,

Coronavirus disease 2019 (COVID-19), an infectious outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] has now progressed to global pandemic.[2] Besides the compelling need to understand the novel biological pathways underlying the virulence and pathogenicity of SARS-CoV-2 in humans to enable the development of appropriate interventions and therapies,[3,4] the notable difference in mortality rates between Asian and European populations is one of the most significant issues demanding the attention of biologists, epidemiologists, and clinicians around the world. According to the most recent World Health Organization statistics (last updated April 2, 2020), the COVID-19 case fatality rate in Italy (12 430 of 105 792; 11.75%) is considerably higher than in China (3321 of 82 631; 4.02%).[2] Without adjusting for a multitude of confounders, this would translate into an over threefold higher risk of death in Italy than in China (crude odds ratio [OR], 3.18; 95% CI, 3.06-3.31; $P < .001$).

Three leading factors are reported to strongly influence the risk of dying from COVID-19: male sex, advanced age (ie, >60 years), and the presence of comorbidities such as diabetes, hypertension, chronic respiratory diseases, cancer, and cardiovascular disorders.[5] Since the frequency of these factors may vary across different populations, we compared and summarized the impact of these variables on COVID-19 mortality rates between Italy and China.

Demographical and clinical information on mortality for COVID-19 in Italy and China were retrieved from the Italian National Institute of Health[6] and the Chinese Center for Disease Control and Prevention.[7] Statistical analysis was carried out using MetaXL software Version 5.3 (EpiGear International Pty Ltd., Sunrise Beach, Australia). Odds ratios (OR) and cumulative OR were calculated with 95% confidence intervals.

The impact of the five most important co-morbidities on the risk of dying for COVID-19 in Italy compared to China is shown in Figure 1A, showing that each comorbidity generated higher adverse impact on the odds of death in Italy. Overall, the presence of any of these five comorbidities was associated with a nearly 2.4 higher risk of dying in Italian as compared to Chinese COVID-19 patients (cumulative OR, 2.39; 95% CI, 1.50-3.81). A similar effect was observed for male sex and advanced age (Figure 1B), with both demographic factors were found associated with a nearly 1.3- and 4.6-fold enhanced odds of dying from COVID-19 in Italy than in China, respectively. Overall, the presence of either of these

two factors conferred a twofold higher risk of death for Italian COVID-19 patients (cumulative OR, 2.01; 95% CI, 0.54-7.52).

The sudden emergence and rapid spread of the COVID-19 outbreak has left the world mostly unprepared. Unlike the previous two coronaviruses diseases, severe acute respiratory disease (SARS) and Middle East respiratory syndrome (MERS), which could be both efficiently contained, COVID-19 has now become pandemic,[8] and its diffusion seems hardly tamable. Though further research is needed, this is attributed to the peculiar biological characteristics of this novel SARS-CoV-2 coronavirus, as well as to its heterogeneous interplay with genetic, epigenetic and even environmental factors.[1] It has been hypothesized, and circulating on social media, that the long incubation time is directly associated with the rapid spread of SARS-CoV-2 infection. However, no differences have been recently observed between the incubation time for SARS-CoV-2, SARS-CoV, and MERS-CoV.[9] Nonetheless, the genomic epidemiology information of the SARS-CoV-2 circulating in Italy appears still limited.[10]

While the current understanding of this infectious disease is gradually evolving, one leading aspect that remains obscure is the difference in mortality rates between worldwide countries.[2] One possible explanation is differences in COVID-19 testing and epidemiologic reporting between countries. On other hand, it is proffered that disease severity may be influenced by some specific population characteristics, which would enhance individual's vulnerability to the virus. Taken together, the results of our analysis support this theory, confirming that a higher burden of comorbidities, male sex, and older age may be considered substantial determinants of enhanced risk of death in Italy compared to China. This finding is important, whereby protection of at risk individuals, such as applying more stringent measures of social distancing, should be reinforced in countries with similar demographics.[11] Overall, COVID-19 mortality risk increases with age, especially in men older than 60 and with chronic conditions such as diabetes, cancer and cardiovascular disease. A global expert group shall hence be formed, aimed to provide guidance and aid in response to COVID-19 in elderly individuals in both residential facilities and nursing home.[12] Protection high risk individuals should then include (i) minimization of direct contact with health professionals, friends, and relatives, by using digital devices, (ii) use of new technologies to intervene remotely to reduce the negative effects of social isolation, as well as (iii) providing timely population-specific health information to support patients and healthcare providers.[13]
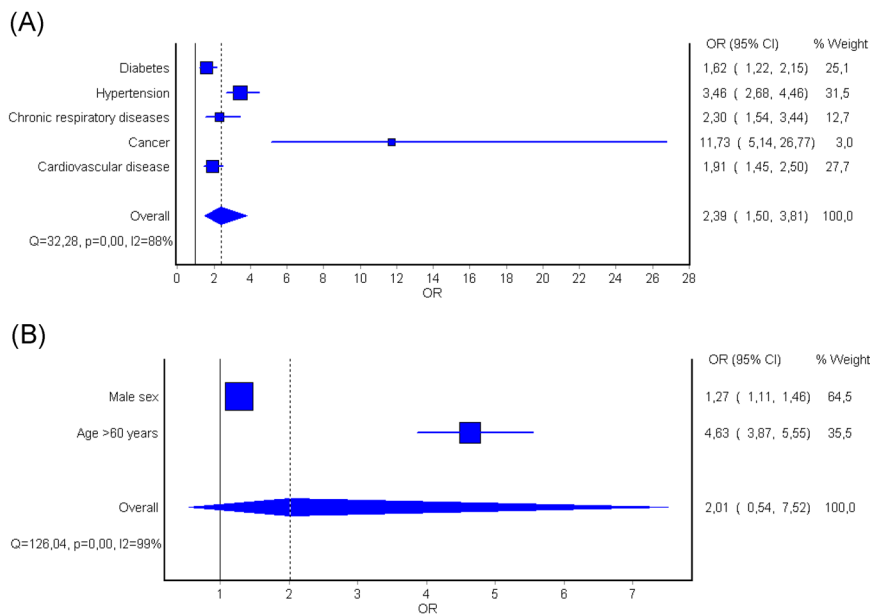
(A)

(B)

FIGURE 1 Odds ratio (OR) and 95% confidence interval (95% CI) of some clinical and demographical factors for predicting the risk of death for coronavirus disease 2019 (COVID-19) in the Italian vs the Chinese population. A, Diabetes, hypertension, chronic respiratory diseases, cancer, and cardiovascular disease. B, Male sex and age >60

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