## LETTER

# The negative impact of comorbidities on the disease course of COVID-19

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Dear Editor,

Coronavirus Disease 2019 (COVID-19) is a viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with a mortality rate of 3–7% [1]. The high mortality results from fulminant pneumonia leading to acute respiratory distress syndrome and multiple organ failure [2, 3]. Initial reports suggest that comorbidities cause a more severe course of infection and a poorer prognosis [4, 5]. Considering the fast spread and high mortality of COVID-19, it is necessary to understand the possible risk factors affecting its progression. We aimed to perform a systematic search to evaluate the potential role of all reported comorbidities on the disease course. Details of our report are provided in Supplementary file 1.

We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Scopus between 01/01/2020 and 05/11/2020. The main outcomes were mortality, intensive care unit (ICU) admission and severity. Definitions of the investigated outcomes are available in Supplementary file 2, Table 2. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to objectify the association between comorbidities and the outcomes by the random-effects model. The study was registered on PROSPERO (CRD42020176781).

Of 33,987 records screened, 61 cohort studies with 31,089 (median 162; IQR: 103–338) patients were included in the meta-analysis. The overall mortality rate was 10.0%, 19.9% of patients needed intensive, while the reported severity was 24.0%. Underlying chronic kidney disease (OR:5.3 CI 3.2–8.7), cardiovascular disease (OR:4.7, CI 2.9–7.6), cerebrovascular disease (OR:3.9, CI 1.8–8.3), chronic obstructive pulmonary disease (OR:3.7, CI 2.7–5.1), hypertension (OR:2.7, CI 1.7–4.4), malignancy (OR:2.6, CI 1.5–4.3), diabetes (OR:2.5, CI 1.7–3.6) and immunodeficiency (OR:1.6, CI 1.0–2.5) were associated with increased risk of mortality. The analysis could not prove that Hepatitis B infection or chronic liver disease were associated with mortality due to the low number of participants with comorbidities (Fig. 1, Suppl. File 2. Figs. 4–13).

Patients with a history of cerebrovascular disease (OR:3.5, CI 1.9–6.5), chronic obstructive pulmonary disease (OR:2.2, CI 1.5–3.4), cardiovascular disease (OR:2.1, CI 1.5–3.0), hypertension (OR:1.9, CI 1.5–2.5), diabetes (OR:1.8, CI 1.3–2.5), malignancy (OR:1.7, CI 1.0–2.7) needed intensive care more often. The analysis could not prove that chronic liver disease, immunodeficiency, chronic kidney disease and hepatitis B infection were associated with higher admission rate to ICU (Supp. File 1. Fig. 2.; Suppl. File 2. Figs. 4–13).

Results regarding severity are shown in Supplementary file 1, Fig. 3. Reports on comorbidities not eligible for meta-analysis are summarized in Supplementary file 2, Table 6.
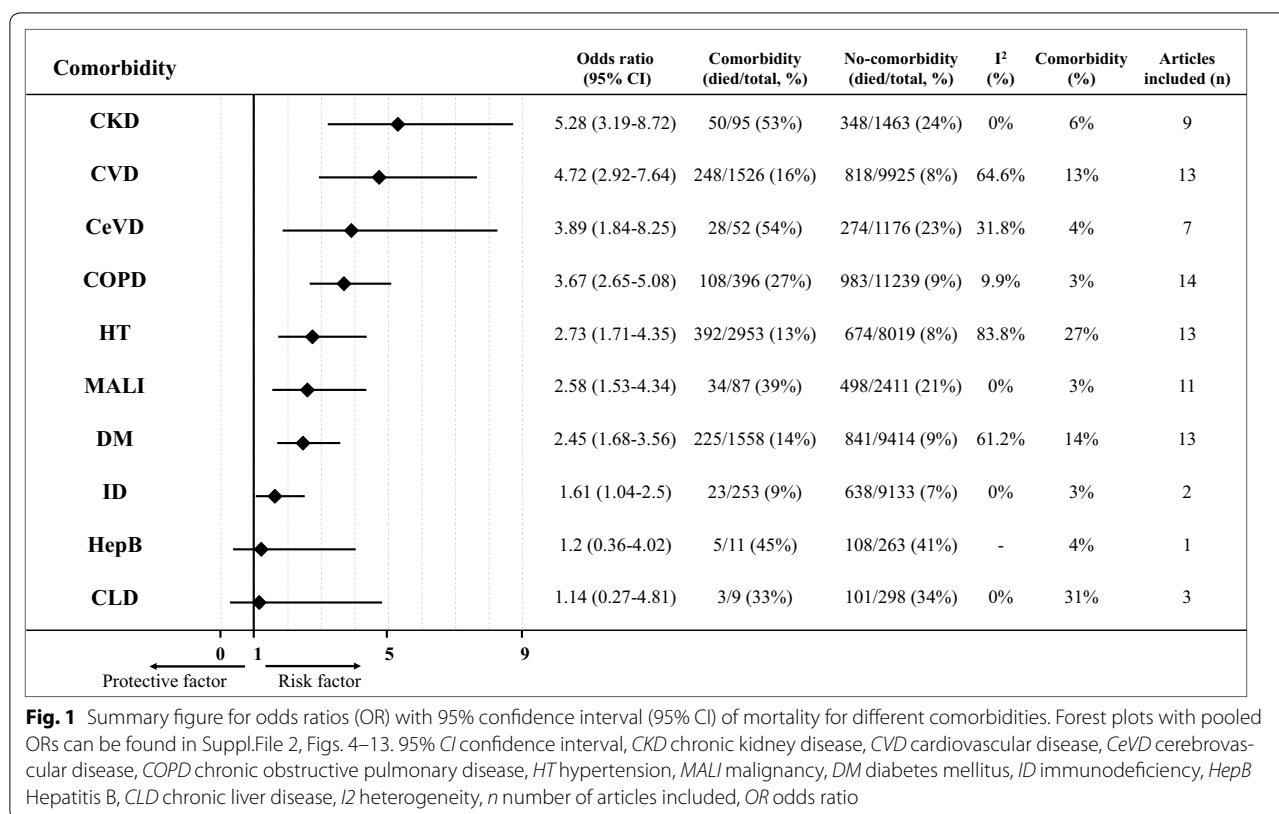
In summary, cerebrovascular disease, chronic obstructive pulmonary disease, cardiovascular disease, hypertension, diabetes mellitus, malignancy are significant risk factors for poor clinical outcome in COVID-19. Our findings emphasize the critical role of comorbidities in the course of COVID-19. These results could be used for risk stratification of patients infected with SARS-CoV-2 and should be taken into consideration when establishing a prognostic tool. Although no specific treatment has

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| Comorbidity | Odds ratio (95% CI) | Comorbidity (died/total, %) | No-comorbidity (died/total, %) | I² (%) | Comorbidity (%) | Articles included (n) |
|---|---|---|---|---|---|---|
| CKD | 5.28 (3.19-8.72) | 50/95 (53%) | 348/1463 (24%) | 0% | 6% | 9 |
| CVD | 4.72 (2.92-7.64) | 248/1526 (16%) | 818/9925 (8%) | 64.6% | 13% | 13 |
| CeVD | 3.89 (1.84-8.25) | 28/52 (54%) | 274/1176 (23%) | 31.8% | 4% | 7 |
| COPD | 3.67 (2.65-5.08) | 108/396 (27%) | 983/11239 (9%) | 9.9% | 3% | 14 |
| HT | 2.73 (1.71-4.35) | 392/2953 (13%) | 674/8019 (8%) | 83.8% | 27% | 13 |
| MALI | 2.58 (1.53-4.34) | 34/87 (39%) | 498/2411 (21%) | 0% | 3% | 11 |
| DM | 2.45 (1.68-3.56) | 225/1558 (14%) | 841/9414 (9%) | 61.2% | 14% | 13 |
| ID | 1.61 (1.04-2.5) | 23/253 (9%) | 638/9133 (7%) | 0% | 3% | 2 |
| HepB | 1.2 (0.36-4.02) | 5/11 (45%) | 108/263 (41%) | - | 4% | 1 |
| CLD | 1.14 (0.27-4.81) | 3/9 (33%) | 101/298 (34%) | 0% | 31% | 3 |

**Fig. 1** Summary figure for odds ratios (OR) with 95% confidence interval (95% CI) of mortality for different comorbidities. Forest plots with pooled ORs can be found in Suppl.File 2, Figs. 4–13. 95% CI confidence interval, *CKD* chronic kidney disease, *CVD* cardiovascular disease, *CeVD* cerebrovascular disease, *COPD* chronic obstructive pulmonary disease, *HT* hypertension, *MALI* malignancy, *DM* diabetes mellitus, *ID* immunodeficiency, *HepB* Hepatitis B, *CLD* chronic liver disease, *I2* heterogeneity, *n* number of articles included, *OR* odds ratio

been identified for COVID-19 yet, these results should be considered when applying prevention and therapy.

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### Compliance with ethical standards

### Conflict of interest

The authors declare no conflict interests.

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