

## The importance of hypertension as a risk factor for severe illness and mortality in COVID-19

The virus responsible for COVID-19 binds to the angiotensin converting enzyme-2 (ACE-2) receptor [1]. Several articles have noted that hypertension is a risk factor for COVID-19 [2-7]. It is currently difficult to distinguish between hypertension as an independent risk factor in COVID-19 from one that co-varies with other patient factors such as age and cardiovascular disease. It is difficult from individual reports to determine whether hypertension is a risk factor for development of symptomatic disease or hospitalisation or for more severe disease. Reviewing the literature that reports rates of hypertension amongst included patients indicates a consistent association with more severe disease and increased mortality.

Wang et al. [2] reported on 138 COVID-19 patients hospitalised in Wuhan, China: 31% had hypertension. Of those requiring ICU admission, 58% had hypertension compared with 22% who did not. Zhou et al. [3] reported on 191 hospitalised patients from Wuhan, all of whom had final outcomes recorded (discharge or death): 30% had hypertension, with 48% of those who died having hypertension compared with 23% of survivors. Guan et al. [4] reported on 1099 COVID-19 cases across China: 15% of all patients had hypertension, including 24% of severe cases and 13% of mild cases. Amongst patients who were admitted to an intensive care unit (ICU), required tracheal intubation or died, 36% had hypertension. Wang et al. [5] reported on 344 patients admitted to ICU in Wuhan, of whom 41% had hypertension. Of those who died, 52% had hypertension and of those who survived 28 days, 34% had hypertension [5]. The Chinese Centre for Disease Control reported on 44,672 confirmed COVID-19 hospitalised patients of whom 13% had hypertension. Of the patients who died, 40% had hypertension. Mortality rate was 2.3% overall and 6% in those with hypertension [6].

Finally, Grasselli et al. [7] reported on 1591 patients admitted to ICU in northern Italy, of whom 49% were hypertensive; this is approximately twice the prevalence in the Italian population. The paper reported a 26% mortality rate, with 63% of those who died having hypertension and 40% in those who were discharged from ICU. However, at the time the paper was reported, 58% of patients were still in ICU. The intensive care mortality at the point of reporting (i.e. deaths in ICU as a proportion of those dying in ICU or surviving to ICU discharge) was 68%. The ICU mortality rate

for different age groups with and without hypertension is shown in Table 1.

The prevalence of hypertension in China is approximately 23% [8] and in Italy, 26% [9]. These reports therefore do not provide robust evidence as to whether hypertension is a risk factor for developing symptomatic COVID-19 requiring hospitalisation. Yang et al. [10] reported that hypertension was not more common in those in China with COVID-19 than the general population. However, in all the above reports, hypertension is notably associated with poor outcome from COVID-19. The current data do not clarify the mechanism of this increased risk, for instance whether it is due to hypertension itself or treatment, nor whether it is associated with the use of ACE inhibitors and angiotensin-2 type-I receptor blockers, though this has been previously suggested [11].

The limitation of this analysis is that in several of the studies, final patient outcomes are uncertain as patients' hospitalisation or ICU stay has not been completed.

Hypertension is included in many reports as a 'risk factor' for COVID-19 but there has been a lack of clarity as to whether this means risk factor for acquiring the disease, the severity of disease or for poor outcomes. It is also easy to dismiss high blood pressure as a risk factor as other factors such as underlying cardiovascular or respiratory disease might initially seem more likely to impact outcome, as they do for other critical illnesses. However, the evidence shown here indicates that hypertension is consistently associated with severe or critical illness, and with death.

There is increasing understanding that severe COVID-19 causes considerable vascular abnormalities including widespread microthrombotic and macrothrombotic events, renal and cardiac failure. The association of hypertension with its potential microvascular disease, with more severe disease and poor outcomes from COVID-19, is therefore an important consideration.

**Table 1** Mortality rate by age group for patients admitted to critical care in northern Italy with COVID-19 disease [7].

Age; y	< 50	51-60	61-70	> 70
With hypertension	31%	48%	77%	78%
Without hypertension	12%	30%	57%	79%

Based on the current evidence, hypertension should be considered as a significant risk factor for poor outcomes amongst those presenting to hospital with COVID-19. This evidence may also have implications when considering which healthcare workers are at increased risk of severe COVID-19 and might therefore be shielded from direct patient care [12].

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No competing interests declared.

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doi:10.1111/anae.15103