High blood pressure linked to increased risk of dying from COVID-19

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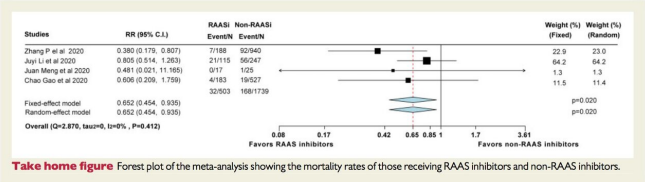

Take home figure Forest plot of the meta-analysis showing the mortality rates of those receiving RAAS inhibitors and non-RAAS inhibitors.

Death rates for COVID-19 patients receiving RAAS inhibitors and non-RAAS inhibitors. Credit: *European Heart Journal*

Patients with raised blood pressure have a two-fold increased risk of dying from the coronavirus COVID-19 compared to patients without high blood pressure, according to new research published in the *European Heart Journal* today.

In addition, the study found that patients with high blood pressure who were not taking medication to control the condition were at even greater risk of dying from COVID-19.

Researchers in China and Ireland analysed data from 2866 patients with COVID-19 who were admitted to Huo Shen Shan hospital in Wuhan, China, between 5 February and 15 March 2020. The hospital was opened on 5 February exclusively to treat coronavirus patients. Of these patients, 29.5% (850) had a medical history of high blood pressure (hypertension).

The researchers, led by Professors Fei Li and Ling Tao from Xijing Hospital, found that 34 out of 850 hypertensive patients (4%) with coronavirus died compared to 22 out of 2027 patients without hypertension (1.1%) - a 2.12-fold increased risk after adjustment for factors that could affect the results, such as age, sex and other medical conditions.

Among the patients with hypertension who were not taking medication for the condition, 11 out 140 (7.9%) died from coronavirus compared to 23 out of 710 (3.2%) of those who were taking medication—2.17-fold increased risk after adjusting for confounding factors.

In a meta-analysis, the researchers pooled the data from the Huo Shen Wan patients with data from nearly 2,300 patients in three other studies to investigate the death rates in patients being treated with drugs to control blood pressure levels by targeting the renin-angiotensin-aldosterone system (RAAS). These drugs include angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). Other, non-RAAS inhibiting drugs used for treating high blood pressure include beta blockers, calcium channel blockers (CCBs) or diuretics.

They found a lower risk of death among the 183 patients treated with RAAS inhibitors than in 527 patients treated with other drugs. However, the researchers say this result should be treated with caution as the number of patients in this analysis was small and so it could be due to chance.

Prof. Li said: "It is important that patients with high blood pressure realise that they are at increased risk of dying from COVID-19. They should take good care of themselves during this pandemic and they need more attention if they are infected with the coronavirus.

"In addition, there were 140 patients admitted to hospital with COVID-19 who had discontinued their anti-hypertensive treatment due to various reasons. We found that this was associated with a greater risk of dying from the coronavirus.

"In contrast to our initial hypothesis, we found that RAAS inhibitors, such as ACE inhibitors or angiotensin receptor blockers, were not linked to an increased risk of dying from COVID-19 and, in fact,

may be protective. Therefore, we suggest that patients should not discontinue or change their usual antihypertensive treatment unless instructed by a physician."

Prof. Ling Tao said: "Soon after we started to treat COVID-19 patients in early February in Wuhan, we noticed that nearly half of the patients who died had high blood pressure, which was a much higher percentage compared to those with only mild COVID-19 symptoms. At the same time, some researchers were raising concerns that RAAS inhibitors might be facilitating the entry of the coronavirus into cells and making people more susceptible to the disease.

"We were quite surprised that these results did not support our initial hypothesis; in fact, the results were in the opposite direction, with a trend in favour of ACE inhibitors and ARBs. We think this is exactly why practice based on clinical evidence is more vital than ever."

As this was a study that looked at data from observations in the hospital, the researchers say it is too early to make clinical recommendations based on these results, and that results from randomised controlled clinical trials are needed to look, in particular, at the role played by RAAS inhibitors.

"These data should be interpreted cautiously. However, they support recommendations for the European Society of Cardiology that patients should not discontinue or change their normal, antihypertensive treatment," said Prof. Tao.

As fewer cases of COVID-19 are being diagnosed now in China, a randomised clinical trial is to be run at the National University of Ireland Galway by Professors J. William McEvoy and Patrick Serruys, who are co-authors of the EHJ paper.

Prof. Serruys said: "There are three remaining questions, and we hope our clinical trial in Ireland will answer the first two: what kind of medication should be given to COVID-19 patients with hypertension—RAAS inhibitors or non-RAAS inhibitors—and could these medications mitigate the risk of dying in these patients?

"As for the last question, a recent population-based study in the *New England Journal of Medicine* has suggested that antihypertensive medications, such as ACE inhibitors and ARBs are not associated with an increased risk of testing positive for COVID-19."

As this is a retrospective, observational study, it cannot show a causal relationship between RAAS inhibitors and the risk of dying from COVID-19. Other limitations include the inability to include all relevant confounding factors; some data, such as electrocardiograms (ECGs) were not recorded in detail; and the impact of antihypertensive medications can only be assessed in the short-term, with prospective studies needed to see longer-term effects.

An editorial about this paper is published in the *EHJ* at the same time.

More information: "Association of hypertension and antihypertensive treatment with COVID-19 mortality: a retrospective observational study", by Chao Gao et al. *European Heart Journal* (2020). DOI: 10.1093/eurheartj/ehaa433

Giuseppe Mancia et al. Renin–Angiotensin–Aldosterone System Blockers and the Risk of Covid-19, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa2006923