

Older, critically ill patients with COVID-19 may have increased risk of bradycardia with lopinavir and ritonavir

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Older, critically ill patients with COVID-19 who received a combination of the antiretroviral medications lopinavir and ritonavir experienced bradycardia, a slow heart rate, more often, according to new research published today in *Circulation: Arrhythmia and Electrophysiology*, an American Heart Association journal.

The combination of antiretroviral medications lopinavir (LPV) and ritonavir (RTV) have been previously used to treat patients with SARS-Cov-1 and MERS-Cov, as well for HIV-1 patients. Among HIV-1 patients, a risk of bradycardia was also reported.

In this small, preliminary, prospective study, researchers recorded the risk of bradycardia in critically ill COVID-19 patients treated with this combination of medications. Bradycardia is classified as a [heart rate](#) below 60 beats per minute for a period of more than 24 hours. Bradycardia can cause problems if the slow [heart](#)

rate leads to a decrease in [blood flow](#) to the body. This can lead to heart failure, fainting, chest pain and [low blood pressure](#). In some people, bradycardia does not cause any symptoms.

The study included 41 patients with COVID-19 admitted to the [intensive care unit](#) at Amiens University Hospital, in Amiens, France, who were treated with 200 mg LPV and 50 mg RTV twice daily for 10 days. All patients received continuous electrocardiogram (ECG) monitoring.

Among the patients who received the LPV/RTV treatment:

- 22% experienced bradycardia for more than 24 hours;
- bradycardia occurred at least 48 hours after initiation of treatment, indicating that the medications may have caused bradycardia;
- a [blood test](#) measuring the concentration of ritonavir (RTV plasma concentration) at 72 hours after receiving the treatment showed higher concentrations of RTV in the patients who had bradycardia;
- no correlation was found between RTV plasma concentration, LPV plasma concentration and mean heart rate at 3-days after LPV/RTV treatment began;
- patients experiencing bradycardia were on average older than patients receiving the treatment who did not experience bradycardia (ages 62-80 vs. 54-68, respectively); and,
- bradycardia resolved after LPV/RTV were discontinued or doses were reduced.

Researchers noted, "[LPV and RTV] have complex pharmacokinetic characteristics [how the body processes a [medication](#)] ... Bradycardia could be a sign of severe cardiological or neurological

impairment since it is associated with lymphopenia [lower than normal number of white blood cells] that seems to reflect the severity of COVID-19 infection. Intensivists should be aware of this potential side effect in order to closely monitor LPV/RTV plasma levels, notably in elderly patients."

More information: Christophe Beyls et al. Lopinavir-ritonavir Treatment for COVID-19 Infection in Intensive Care Unit: Risk of Bradycardia, *Circulation: Arrhythmia and Electrophysiology* (2020). DOI: [10.1161/CIRCEP.120.008798](https://doi.org/10.1161/CIRCEP.120.008798)

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