Association of ACE inhibitors and AT1R blockers and prognosis in hospitalized COVID-19 patients: a cohort study in Italy

Angiotensin-converting enzymes are components of the renin-angiotensin system. ACE2 is an homologue of Angiotensin-Converting Enzyme (ACE) but they have opposite physiological functions. While ACE2 converts angiotensin II to angiotensin 1–7, a peptide with vasodilator activity, ACE cleaves angiotensin I to generate angiotensin II, which, upon binding to Angiotensin II Receptor 1 (AT1R), exerts vasoconstriction, thereby elevating blood pressure. As modulators of the angiotensin pathway, ACE inhibitors and AT1R blockers are widely used drugs among patients with cardiovascular diseases, such as refractory hypertension, coronary artery disease, heart failure, and post-myocardial infarction status. They are also employed for the treatment of diabetes and renal insufficiency. The aim of this study is to verify if the use of ACE inhibitors and/or AT1R blockers before COVID-19 outbreak may modify the clinical course of infection and prognosis of hospitalized SARS-CoV-2 infected patients in Italy.

Methods

Study design

A cohort study will be conducted in several Italian regions and local health units (LHU). All patients aged 18 years and older who are hospitalized for a COVID-19 confirmed diagnosis will be included.

Data source

Italian National Health System claims databases available at the regional level will be linked to regional COVID-19 registries.

Exposure definition

Patients included in the cohort will be identified as ACE inhibitors or AT1R blocker users.

Outcomes

The outcomes of this study will be: death, intensive care unit (ICU) admission, and length of ICU stay.

Statistical analysis

Data will be described using frequencies, percentage, mean with standard deviations (or median with interquartile range, where appropriate). The association between ACE inhibitors and/or AT1R blockers and the study outcomes will be analyzed.

Data protection

Data linkage between the various databases used in the study will be conducted using anonymised patient-level identifiers by data programmers in the individual regions. It will therefore not be possible to trace back patient identity either directly or indirectly for any person included in the study (Art.3, D.lgs. 196/2003). The results of the study will be presented only as aggregate data. Data use will be conducted in strict compliance to EU GDPR regulations (UE 2016/79).

As the study is observational and retrospective, based on the secondary use of administrative data, it is not possible to ask patients for their informed consent to the use of their data for research purposes. Furthermore, the identification of patients meeting inclusion criteria, which occurs at a centralised level (i.e. without any contact with hospitalised patients) and the complete anonymization of data as soon as it is extracted, do not allow the researchers to ask for informed consent.