ACADÉMIE NATIONALE DE MÉDECINE

Covid-19 and cardiovascular diseases: dangerous links

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The management of cardiovascular diseases, the leading cause of death in the world, has been delayed or neglected during the Covid-19 pandemic. However, these two conditions have multiple interactions that are being studied extensively. SARS-CoV2 enters the cell via the membrane ACE2 receptor (angiotensin converting enzyme 2). This receptor is an enzyme whose structure and substrates are different from those of ACE1(Converting enzyme of angiotensin 1), which explains that ACE1 inhibitors and receptor antagonists of angiotensin 1, widely used in cardiology, particularly to treat arterial hypertension or the aftermath of myocardial infection, have no effects on ACE2.

It soon became apparent that patients with cardiovascular diseases, as well as patients at high cardiovascular risk, were highly susceptible to developing a severe form of Covid-19. Complications during the immuno-inflammatory phase of Covid-19, dominated by pulmonary involvement, often affect the cardiovascular system in the form of thromboembolic events, but also heart failure (related to myocarditis or other causes) and arrhythmias.

In contrast, the use of ACE inhibitors and ARB-IIs in patients with Covid-19 does not appear to be associated with an increased mortality, hospitalization, or the need for 2 assisted ventilation, confirming that these drugs should not be discontinued in the event of SARS-CoV-2 infection [2].

Vaccination against SARS-CoV-2 may also be the cause of inflammatory damage to the pericardium or myocardium, particularly in adolescent and young adult males [3], but much less frequently than after Covid-19 [4].

In children, myocarditis can occur during the very rare but potentially serious 'pediatric multisystemic inflammatory syndrome' (PIMS), which occurs a few weeks after infection with SARS-CoV-2.

Until now, cardiovascular sequelae occurring after the acute phase of Covid-19 (long Covids) were reported only in hospitalized patients, in small series and with a short follow-up period [5].

However, a US study showed signs of pericardial damage in 39.5% of college student athletes recovering from Covid-19 [6]. More recently, a large study carried out among US veterans reports that late cardiovascular complications after Covid-19 can occur in all patients, with or without a story of cardiovascular risk factors, having been hospitalized or not. This controlled study compared 153,700 subjects (89% male, mean age 61.4 years) one month after Covid-19 infection with two cohorts of 5 million control subjects. The increased risk of cardiovascular diseases (ischemic and non-ischemic heart diseases, dysrhythmias and others) persisted over

one year of follow-up in all patients, even in those who were not hospitalized [6]. These results need to be confirmed in younger subject cohorts with a balanced sex ratio, considering both Delta and Omicron variants, over longer follow-up periods. They lead to predict a significant increase in cardiovascular diseases worldwide.

While the pathogenic mechanisms linking cardiovascular diseases to Covid-19 remain to be clarified, **the French National Academy of Medicine recalls:**

1. that a complete vaccination is the most effective way to avoid the occurrence of cardiovascular complications after Covid-19;

2. that patients treated with ACE inhibitors or ARA-IIs should not interrupt their treatment;

3. that, pending the results of further studies (basic research, epidemiological and clinical), clinical cardiovascular surveillance is required in all subjects with a Covid-19 infection, even a mild one, especially in patients at high cardiovascular risk, with reinforced preventive measures against reinfection by SARS-CoV2.

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