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Archives of Cardiovascular Disease 114 (2021) 434—438

Available online at ScienceDirect www.sciencedirect.com

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EXPERT CONSENSUS

Coronavirus disease vaccination in heart failure: No time to waste

Vaccination contre le coronavirus dans l'insuffisance cardiaque : pas de temps à perdre

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Available online 24 May 2021

Abbreviations: CHF, Chronic Heart Failure; COVID-19, Coronavirus Disease 2019; HF, Heart Failure; mRNA, messenger Ribonucleic Acid; RNA, Ribonucleic Acid; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

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https://doi.org/10.1016/j.acvd.2021.04.004

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Received 26 January 2021; received in revised form 5 April 2021; accepted 12 April 2021
Available online 24 May 2021

KEYWORDS
COVID-19;
Heart failure;
Vaccination

MOTS CLÉS
COVID-19 ;
Insuffisance cardiaque ;
Vaccination

Background

Viral diseases are well-established factors responsible for acute decompensation in chronic heart failure (CHF) (Fig. 1). The underlying pathophysiology includes increased myocardial work and an infection-related inflammatory response, which further contribute to the increase in diastolic and/or systolic dysfunction. Direct myocardial viral involvement may also lead to myocarditis, which can worsen pre-existing ventricular dysfunction. Thus, viruses are expected to increase cardiovascular mortality in heart failure (HF), and influenza vaccination might be considered as an effective treatment strategy to improve survival in HF [1].

Impact of coronavirus disease 2019 on cardiovascular disease

In the context of the coronavirus disease 2019 (COVID-19) pandemic, the risk of cardiac complications (including worsening CHF) reported in the international CAPACITY-COVID registry appeared to be relatively low, with the notable exception of pulmonary embolisms, even in patients

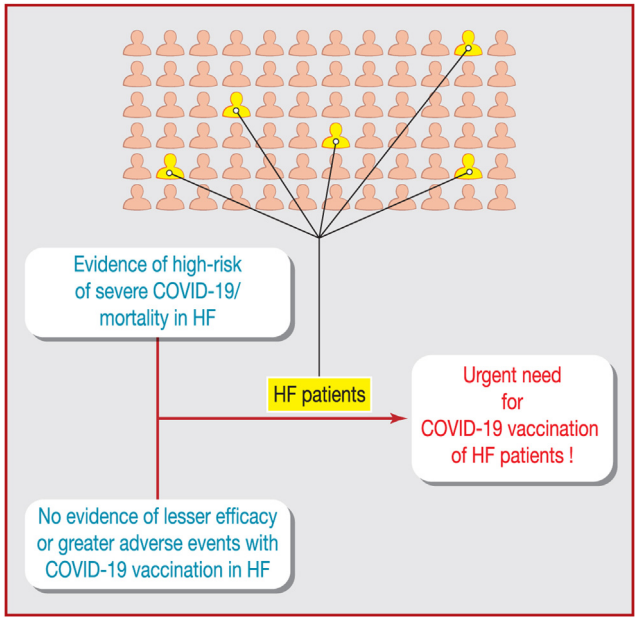

Figure 1. Central illustration. Among the general population (blue faces), the prognosis of patients with heart failure (HF) (yellow faces) is greatly jeopardized in case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which largely supports the urgent need for vaccination against coronavirus disease 2019 (COVID-19).

with a history of cardiovascular disease [2]. Indeed, in 3011 patients hospitalized for pulmonary involvement related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (mean age, 67 years; 31% with cardiovascular history), cardiac complications occurred in 11.6% of patients, with atrial fibrillation (4.7%) being the most common, followed by HF (1.8%), acute coronary syndrome (0.5%) and ventricular arrhythmia (0.5%). Myocarditis occurred in only 0.1% of patients, whereas pulmonary embolism was diagnosed in 6.6% [2]. COVID-19-related myocarditis

is currently under investigation in the large multicentre MYOCOVID French registry (ClinicalTrials.gov identifier: NCT04375748).

Regarding the impact of COVID-19 on patient outcomes, an observational single-centre study [3], including 283 patients referred, on the basis of typical symptoms of acute HF (raised B-type natriuretic protein and echocardiogram), to a district hospital in Bristol (England, UK) over two 8-week periods preceding and following the first reported case of COVID-19-related death, showed a sizeable, albeit not statistically significant, drop of 27% in the number of patients seen between the two periods (164 vs. 119 patients). In the absence of vaccination, this decrease was most likely related to the fear of social contact during the lockdown, and the subsequent reluctance of patients to go to the hospital and/or of primary care physicians to refer their patients during this period. However, the 30-day mortality rate was twice as high in the period following the first COVID-19-related death (21% vs. 11%), which represents an increase of 90% in the relative risk. A sensitivity analysis indicated that the increase in mortality was driven by COVID-19 positive status, which reinforces the expected beneficial role of vaccination in patients with HF.

Impact of cardiovascular disease on COVID-19-related outcome

Patients with CHF are often elderly, and usually present with several co-morbidities, including hypertension, obesity, type 2 diabetes, coronary artery disease, renal failure and chronic obstructive pulmonary disease, so they are likely to be infected with SARS-CoV-2 and also to develop severe forms of COVID-19 pneumonia. Indeed, the underlying heart disease is expected to worsen the consequences of lung infection [4,5]. Thus, patients with pre-existing cardiovascular diseases have paid a significant price during this pandemic, as was immediately highlighted by the first data from China, showing that approximately 50% of patients hospitalized for a COVID-19 infection had a history of chronic disease, which corresponded to a cardiovascular history in 80% of cases. Whereas COVID-19-associated mortality was initially reported to be 2.3%, it was soon described as being much higher in people with diabetes (7.3%) and in patients with pre-existing cardiovascular disease (10.5%). A meta-analysis of six studies, including 1527 subjects with COVID-19 in China, confirmed that cardiovascular history and metabolic co-morbidities increased the risk of severe forms of COVID-19. Patients with a cardiovascular history had a 3-fold increase in the risk of intensive care hospitalization, and a 2-fold increase was reported in patients with hypertension or diabetes [6]. These results were confirmed by Italian data from 1591 patients admitted to intensive care units for COVID-19 infection, with 68% of these severe patients presenting with hypertension [7].

The special relationship between HF and COVID-19

Patients with HF are paying a heavy price to the COVID-19 pandemic by developing severe and potentially fatal pulmonary diseases, whereas congestive flare-ups occurring in the course of the viral attack are uncommon [2,8]. The deleterious impact of CHF on the prognosis of patients hospitalized for COVID-19 was confirmed by data from the Mount Sinai Healthcare System Hospitals (New York, USA). In 6439 patients admitted for COVID-19 (mean age, 64 years), a history of CHF was associated with a 3.6-fold increase in the risk of requiring assisted ventilation, and a 1.9-fold increase in the risk of death, regardless of left ventricular ejection fraction [9]. Another recent study suggested that a decreased left ventricular ejection fraction (< 55%) was associated with an even poorer prognosis [10]. In a large database in North Carolina, USA, the rate of in-hospital mortality of patients with HF hospitalized with COVID-19 was 24.2%, compared with 2.6% and 4.6% in patients hospitalized during the same time frame for acute HF or other reasons, respectively [11]. Of particular concern, patients with a history of CHF are prone to HF worsening while being affected by COVID-19 [12], which further increases the risk of adverse events within the course of the disease.

The mechanisms underlying the susceptibility of patients with HF to develop severe forms of COVID-19 infection remain a matter of debate [13]. Direct myocardial damage caused by the virus binding to a membrane protein is suspected. However, indirect mechanisms are likely to predominate, in relation to hypoxaemia induced by pulmonary involvement, catecholaminergic flooding, microthrombi and, above all, an excessive immune response causing intense inflammation, with a significant release of cytokines (interleukin-6 and interleukin-17), which may, in turn, have a toxic myocardial effect. Moreover, there is no evidence regarding any difference between HF with reduced and preserved ejection fraction.

The vital importance of SARS-CoV-2 vaccination in patients with HF

For all the aforementioned reasons, our expert panel from the Heart Failure Group of the French Society of Cardiology strongly advocates for vaccination against COVID-19 to be offered to patients with CHF as soon as possible, as they represent a particularly vulnerable population (central illustration). HF is a clear established risk factor for poor outcomes, and patients who are decompensated and/or those with poor functional status should be considered at the highest risk of COVID-19 infection, and thus have to be considered for benefit from COVID-19 vaccination [14].

More than four types of COVID-19 vaccines are currently or soon will be available worldwide, which include nucleic acid-based vaccines using genetic material (either ribonucleic acid [RNA] or deoxyribonucleic acid [DNA]), protein subunit vaccines containing specific isolated and harmless SARS-CoV-2-derived proteins, viral vector vaccines containing a weakened version of a live virus and live-virus vaccines, usually corresponding to a weakened version of the virus [15]. Nucleic acid-based vaccines contain no recognizable virus, but only its genetic material, which then migrates into human cells to make them synthesize the virus's identity card. The first available RNA vaccines need to be stored at ultra-cold temperatures (−70 °C or below), which requires

specialized cold storage equipment, but the other RNA-based vaccines to come will only have to be stored at low temperatures, which will simplify the process. All types of COVID-19 vaccines are expected to be as safe for patients with CHF as for people without CHF, and no alert related to COVID vaccination in these patients has been reported so far. Although there has been no warning signal about possible adverse events of vaccination in patients with HF, no published data are yet available on COVID-19 vaccination in this population. However, influenza and pneumococcus vaccinations are recommended in these patients, without any tolerance issues, which also suggests a benefit in this population.

Results from monitoring efforts after COVID-19 vaccination are reassuring. Fortunately, some people have no side effects after COVID-19 vaccination. Others have reported common side effects after COVID-19 vaccination, such as swelling, redness and pain at the injection site, fever, headache, tiredness, muscle pain, chills and nausea. These reactions are common and transient, resolving within a couple of days after onset. A small number of people have had an anaphylaxis reaction after vaccination, but this is extremely rare; this is why, after receiving a COVID-19 vaccine, you are asked to stay for 15—30 minutes for observation, in case you have a severe allergic reaction and need treatment. Overall, more than 145 million doses of COVID-19 vaccines were administered in the USA from 14 December 2020 to 29 March 2021. During this time, the Vaccine Adverse Event Reporting System (VAERS) received 2509 reports of death (0.0017%) among people who received a COVID-19 vaccine. A review by Centers for Disease Control and Prevention and Food and Drug Administration physicians of available clinical information, including death certificates and autopsy and medical records, revealed no evidence that vaccination contributed to patient deaths [16].

The incidence of serious adverse events was similar in the messenger RNA (mRNA) COVID-19 vaccines and placebo groups, without evidence of cardiovascular complications [17,18]. However, although more data are needed to understand the extent and mechanism of hypertension after mRNA-based vaccination, a few data indicate that in elderly patients with a history of hypertension and/or significant previous cardiovascular co-morbidities, control of blood pressure before vaccination and monitoring after vaccination, including symptom screening, may be warranted [19]. Moreover, based on the review of clinical and non-clinical data, there is currently no evidence to suggest an association between thrombotic events and the use of the AstraZeneca COVID-19 vaccine [20]. Finally, data from Israel's largest health care organization, a study performed in a nationwide mass vaccination setting, suggest that the mRNA vaccine is effective for a wide range of COVID-19-related outcomes, a finding that is consistent with that of a randomized trial without evidence of any adverse events related to the vaccination [21].

Conclusions

In conclusion, the prognosis of patients with CHF is greatly jeopardized in case of SARS-CoV-2 infection, as a result of the poor outcomes associated with co-morbidities, which largely supports the prioritization of vaccination against COVID-19. Our group of experts therefore does believe that patients with HF should receive vaccination as soon as possible, and that there is no time to waste!

Funding

None.

Disclosure of interest

The authors declare that they have no competing interest.

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