



Myocardial injury after COVID-19 infection and vaccination. Two sides of the same coin or different?

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In this issue of the journal, Doeblin et al. [1] report on a comparative cardiac magnetic resonance (CMR) study in patients after COVID-19 infection versus vaccination, presenting with suspected cardiac involvement due to limiting clinical cardiac symptoms in a tertiary cardiac center. The authors investigated several CMR metrics, including left ventricular (LV)-ejection fraction, myocardial fibrosis, and edema by T1 and T2 mapping techniques, respectively, extracellular volumes (ECV) and late gadolinium enhancement (LGE) extent and patterns in 104 patients after COVID-19 infection and 27 individuals after vaccination. In addition, the updated ‘Lake Louise Criteria’ incorporating non-ischemic patterns of myocardial damage and edema by T2 mapping and LGE for the diagnosis of myocarditis [2] were systematically applied in both patient groups. Of note, the presence of other cardiac pathologies, such as myocardial ischemia, pericardial effusion and pericardial LGE, compatible with pericarditis were also evaluated.

In this study, patients with suspected myocardial involvement after COVID-19 infection presented later to the hospital (112 ± 76 versus 44 ± 35 days) and less frequently reported persistent cardiac symptoms at the time of the CMR examination (56% versus 93%) compared with postvaccination patients. Although, post-COVID patients were older (48 ± 14 versus 44 ± 20 yrs.) and more co-morbid than post-vaccination patients, the presence of cardiac involvement after vaccination was higher. Thus, CMR provided a diagnosis in 22(82%) of postvaccination patients, including

4(15%) cases with isolated pericarditis, 9(33%) with acute myocarditis, 6(22%) with possible myocarditis, 1(4%) with isolated pericardial effusion and 3(11%) with inducible myocardial ischemia. In patients after COVID-19 infection on the other hand, a clinically relevant diagnosis was present in only 34(33%), including 10(10%) with isolated pericarditis, 7(7%) with acute myocarditis, 5(5%) with possible myocarditis and 8(8%) with ischemia or old myocardial infarction. After application of the updated ‘Lake Louise Criteria’, myocarditis was present in 2(2%) post-COVID versus 9(33%) postvaccination patients. In addition, patients after COVID-19 infection exhibited a markedly higher number of segments with non-ischemic LGE and regional edema, compared to postvaccination patients (63% versus 14% and 33% versus 5%, $p < 0.001$ for both).

The report of Doeblin et al. [1] is the first study, systematically comparing CMR findings and clinical features of patients referred to CMR due to suspected cardiac involvement related to COVID-19 infection versus vaccination after the administration European Union approved COVID-19 vaccines. The data need to be considered in the context of the decreasing hospitalization and mortality rates of COVID-19 infections versus the increasing numbers of the applied COVID-19 vaccinations during the study period between May 2020 to 2021 [3]. During this time the German COVID-19 vaccination campaign reached its preliminary peak regarding the number of administered doses [3]. This aspect might serve as a potential explanation for the reported ‘positivity rates’ of CMR findings that appear to be very high compared to population based epidemiologic studies, where the true incidence of myocarditis was approximately 100-fold higher in cases of COVID-19 infection than after vaccination [4–7]. It must be critically considered, however, that epidemiological data based on ICD-10 codes in medical records may not necessarily be consistent with CMR based studies [1]. Thus, these discrepancies due to the use of different diagnostic tools and referral biases merit

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further clarification in future studies. Another potential confounder of the present observations may have been a differing disease awareness by the referring physicians, which potentially changed from COVID-19 related myocarditis at the beginning of the pandemic towards to vaccine associated myocarditis after the first case reports have been published by fall 2021 [8–10].

In general, myocardial damage during COVID-19 infection appears to be common and allows for a valuable risk stratification [11], although the detrimental causes appear to be heterogenic and excess rates of heart failure may also be attributed to ischemic events as demonstrated Doeblin et al. and by others [1, 12]. Vaccine-associated myocardial damage on the other hand, appears to be more specifically associated with an inflammatory response either due to the generation of autoantibodies [13] or in terms of a multisystemic inflammatory syndrome [14]. The data by Doeblin [1] should also remind clinicians of the importance of coronary artery disease, which currently remains by far the most common cause of cardiac damage. In this regard, it is remarkable that even in this highly selected group of relatively young patients after COVID-19 vaccination, myocardial ischemia could be detected in 11% of the cases.

Patterns of myocardial injury by CMR were similar in patients after COVID-19 infection and vaccination but different from those seen with classical viral myocarditis, where lesions are more prone to the inferolateral wall of the left ventricle [15, 16], as already established within expert statements [2]. The detection of a potential pericardial involvement, however, remains challenging due to the absence of a true diagnostic gold-standards. In this regard, dedicated imaging studies on the incidence and clinical impact of vaccine-related pericarditis are still missing, whereas epidemiological data may probably underestimate this entity [17]. Current reports on (peri-)myocarditis related to COVID-19 vaccines are still limited to small study cohorts, which accounts to the low incidences of these adverse events. In addition, the long-term prognosis of such patients remains unclear. Hereby, CMR may play a central role not only for the initial diagnosis but also for the estimation of long-term outcomes in such patients [18, 19], where the risks of such relatively rare adverse effects due to vaccination, need to be balanced against the benefits of protection from severe forms and complications due to the COVID-19 disease.

Some limitations need to be considered when interpreting the results of the present study. First, the time intervals between symptoms onset and CMR were relatively long both after COVID-19 infection and after vaccination. Although, this was obviously attributed to infectivity concerns with the first group, the time delay with postvaccination patients is not completely clear. In addition, cardiac biomarkers were not available in most of the patients, whereas CMR follow-up examinations, which would have been helpful to

understand the mid- or long-term prognosis of such patients are also not available.

Despite these limitations, the study by Doeblin et al. [1] provides excellent evidence that both COVID-19 infection and vaccination are potentially associated with myocardial damage, which can be detected by CMR, requiring medical attention and treatment in 33% and 82% of the cases, respectively. Clinicians need to be aware of such adverse effects both during COVID-19 infection and after vaccination and use CMR in conjunction with careful evaluation of clinical symptoms, ECG, echocardiography, and cardiac biomarkers for the prompt diagnosis and treatment of these clinical entities.

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Declarations

Competing interests The authors declare no competing interests.

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