Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

2.485, p = 0.141 for AKR_1; HR 0.701, 95% CI 0.351 to 1.397, p = 0.312 for AKR_2) but were both associated with an improvement of renal function at 12 months. A central illustration is provided in Figure 1.

This report strengthens the argument that a validated definition of AKR after TAVI is still lacking. Indeed, conflicting results have been provided on AKR predictors and clinical implications. AKR after TAVI was first defined by Azarbal et al[3] as a 25% improvement in estimated GFR at 48 hours after TAVI. Based on a population of 366 patients, the lack of chronic β-blocker use, male gender, and CKD were identified as predictors of AKR. The previously mentioned authors on a 1502 TAVI population from the Northern New England registry reported AKR to occur in 25% of the procedures and to be predicted by CKD, chronic obstructive pulmonary disease, and previous aortic valve surgery, whereas diabetes mellitus, anemia, and a high Society of Thoracic Surgeons score (>6.1) were less likely linked with AKR. In the previously mentioned report, AKR was defined as an increase of GFR >25% at the hospital discharge compared with the admission value, such as AKR_1 in our manuscript.[3] Nijenhuis et al,[6] on a 639 TAVI population, using a different definition criterion of AKR (after to before transcatheter aortic valve replacement ratio within 48 hours ≤0.80), reported a potential protective effect on the 2-year mortality rate (HR 0.53, 95% CI 0.30 to 0.93) compared with a stable kidney function. In the previously mentioned study, the predictors of AKR were also conflicting with previous reports: indeed, independent predictors were female gender, preserved kidney function, hemoglobin level, and absence of atrial fibrillation.[6] A recent analysis using AKR_2 definition showed that AKR might also increase cardiovascular mortality after TAVI, compared with unchanged renal function.[5]

In conclusion, to date, a validated and shared definition of AKR is lacking. As a consequence, different and often conflicting predictors of such a phenomenon have been proposed, preventing the identification of a clear interaction with the clinical outcomes at long-term follow-up. Thus, a collective and integrated effort is warranted to provide a valid definition for AKR, supported by a clear pathogenetic foundation to investigate its real impact on cardiac and noncardiac clinical outcomes, as previously required for the AKI phenomenon.[7,8]

Disclosures

The authors have no conflicts of interest to declare.

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Meta-Analysis of Risk of Myocarditis After Messenger RNA COVID-19 Vaccine

The Novel COVID-19, caused by SARS-CoV-2, broke out in 2019. It also occurred in various countries around the world. Since then, countries have been working to prevent the spread of COVID-19, whereas efforts to develop vaccines against COVID-19 have simultaneously achieved great success. However, reports of vaccine-related adverse events cannot be ignored.

Since June 2021, cases of myocarditis after the BNT162b2 vaccine (Pfizer/BioNTech) have been reported, mainly in young men after the second dose of the vaccine.[1] A report from Israel stated that during a nationwide vaccination campaign involving >5 million residents, conducted from December 2020 to May 2021, the Israeli Ministry of Health recorded 136 definite or probable cases of myocarditis that were timed to coincide with the receipt of the 2 doses of the BNT162b2 messenger RNA (mRNA) vaccine.[2] Recently, an increasing number of cases of myocarditis after the mRNA COVID-19 vaccine have been reported, not only with the BNT162b2 vaccine (Pfizer/BioNTech) but also after vaccination with the mRNA-1273 vaccine (Moderna).[3–5] Of the 2,000,287 subjects who received at least 1 dose of a COVID-19 vaccine, 20 were reported with a diagnosis of myocarditis, and 11 of which occurred after receiving the mRNA-1273 vaccine, whereas the other 9 received the BNT162b2 vaccine.[4]

Myocarditis is a heterogeneous disease with different clinical patterns, etiologies, and treatment responses, reflecting the inflammatory damage of myocardial tissue in the absence of ischemia.[3] Common clinical manifestations of COVID-19 vaccination-related myocarditis include chest pain, fever, palpitations, shortness of breath, fatigue, nausea, vomiting, abdominal

Table 1
Basic information of included studies

Study	mRNA vaccine	Events of myocarditis	Total number of vaccinations
Hause 2021[1]	Pfizer-BioNTech	37	8900000
Mevorach 2021[2]	Pfizer-BioNTech	136	5442696
Montgomery 2021[3]	Pfizer-BioNTech/ Moderna	20	1065000
Diaz 2021[4]	Pfizer-BioNTech/ Moderna	20	1934277
Kim 2021[5]	Pfizer-BioNTech/ Moderna	4	556146

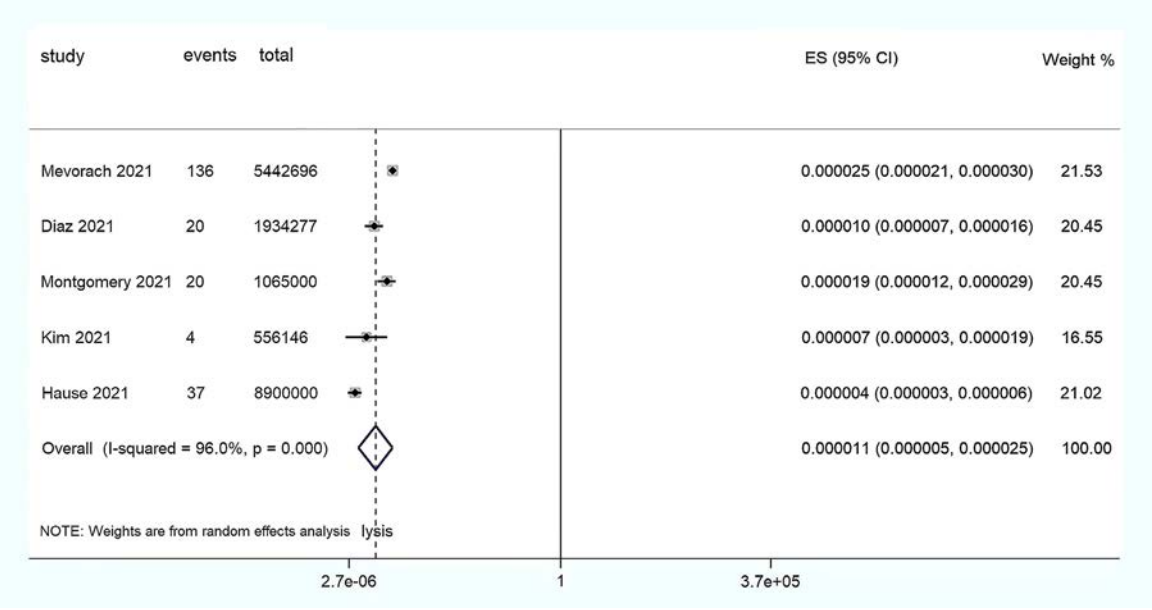

Figure 1. Forest map: mRNA vaccine associated with myocarditis. CI = confidence interval; ES = Effect size.

pain, or abnormal symptoms such as a strong or pounding heartbeat.[6] Recent reports of myocarditis after mRNA vaccination may suggest that myocarditis is a rare potential adverse event associated with mRNA vaccination for COVID-19. However, Diaz et al[4] noted that while the short time interval between vaccination and the onset of myocarditis and the increased incidence of myocarditis and pericarditis in the study hospitals supported a possible relation, the temporal correlation did not prove causation. Therefore, we conducted this meta-analysis to further investigate the correlation between the mRNA vaccine and myocarditis.

By October 9, 2021, a systematic database search was performed in PubMed, Web of Science, and the Cochrane Library using search terms such as "mRNA COVID-19 vaccine," "myocarditis," "adverse event," "BNT162b2 vaccine," and "mRNA-1273 vaccine." A total of 267 publications were preliminarily found, and 5 were finally included in this study (Table 1), with a total of 217 cases of myocarditis.[1–5]

We then used STATA/MP Statistical Software: Release 14 (StataCorp LLC, College Station, Texas) to perform a random-effect meta-analysis for morbidity. Finally, our study found that the incidence of myocarditis was 0.000011 (95% confidence interval 0.000005 to 0.000025) in subjects vaccinated with the mRNA COVID-19 vaccine, which implies an average of 11 cases of myocarditis per 1 million subjects vaccinated with the mRNA COVID-19 vaccine (Figure 1). This very low incidence not only indicates the rarity of myocarditis but also suggests a risk of myocarditis after mRNA vaccination.

There were no reports of rare myocarditis after non-mRNA vaccination (such as Vaxzevria or Janssen). In contrast, an increasing number of reports cited myocarditis after mRNA vaccination. Why does myocarditis only occur after mRNA vaccination? Several hypotheses have been proposed for this phenomenon. It is speculated from the data reported in preliminary trials of mRNA vaccines in adults that mRNA vaccines may produce very high antibody responses in a small number of young subjects, triggering similar responses in children with multisystem inflammatory syndrome associated with the SARS-CoV-2 infection.[6] The COVID-19 mRNA vaccines contain nucleoside-modified mRNA, and it is believed that, in certain genetically predisposed subjects, the immune response to mRNA may not be inhibited and may drive the activation of abnormal innate and acquired immune responses.[7,8] The immune system may detect genes in the vaccine as antigens, thereby activating proinflammatory cascades and immune pathways that may play a role in the development of myocarditis and become part of the systemic response in some subjects.[8] Other hypothesized mechanisms include inducing cytokine expression mediated

by anti-idiotypic cross-reactive antibodies in the myocardium and abnormal induction of apoptosis leading to myocardial and pericardium inflammation.[6] Although many hypotheses have been proposed in current studies, there is no clear evidence for a specific mechanism of myocarditis after mRNA vaccination, and further studies are needed to prove it.

On June 23, 2021, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices reviewed the available data and concluded that the benefits of COVID-19 vaccination for subjects and the population outweighed the risks of myocarditis and recommended its continued use in subjects aged 12 years and over.[1] Considering the risk of myocarditis in humans, the incidence of myocarditis after vaccination still needs to be monitored intensively. In the context of the current pandemic, vigilance regarding rare adverse events, including myocarditis, after COVID-19 vaccination is warranted, but should not reduce overall confidence in vaccination during the current pandemic.[3] Moreover, the Centers for Disease Control and Prevention needs to continue monitoring for adverse events after vaccination, especially myocarditis, to better guide the efficacy and safety assessment of the mRNA COVID-19 vaccine.

This study is a cross-sectional investigation, and we have conducted the Egger test but found no significant publication bias. However, because of the small number of cases of myocarditis, there may be some limitations in the analysis. In addition, because of the high heterogeneity of this study, we adopted the random-effect model. It should also be noted that we failed to conduct subgroup analysis because of the few publications that could be included in the study and the lack of specific age, gender, and other grouping information in some studies. Accordingly, the influence of confounding factors such as age and gender on the results cannot be excluded. If given the opportunity, it is necessary to expand the study to demonstrate a causal relation between the mRNA vaccine and the incidence of myocarditis.

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Trends and Outcomes of Transcatheter Versus Surgical Aortic Valve Implantation in Patients on Chronic Steroids

Transcatheter aortic valve implantation (TAVI) is a safe and effective alternative to surgical aortic valve replacement (SAVR) in high, intermediate, and low-risk patients with severe, symptomatic aortic stenosis.[1] Corticosteroids are among the most widely prescribed drug classes worldwide, with an estimated prevalence of 1.2% in the United States.[2] Chronic steroid use is a well-known independent risk factor for perioperative complications. The potential for increased risk of infection, vascular fragility, and delayed wound healing after surgery may increase the risk of complications and adversely impact procedural outcomes.[3] However, the anti-inflammatory properties of glucocorticoids have some potential protective benefits. The effect of preprocedural steroid therapy on the comparative outcomes of TAVI and SAVR patients has not been established. The purpose of this study was to compare the safety and outcomes between TAVI and SAVR in patients exposed to steroid therapy.

Data from the National Inpatient Sample database were used to identify hospitalizations with procedural codes for TAVI and SAVR in patients on maintenance chronic steroid therapy from the year 2012 to 2019. Propensity matching was performed in R Statistical Software (The R Foundation for Statistical Computing, Vienna, Austria) with a 1:1 ratio global distance measure.[4] Matching was performed with the caliper set at 0.01, and cases were matched with controls without replacement and with common support. The final model was adjusted on 30 variables of baseline patient characteristics, comorbidities, and hospital characteristics. We have used a similar methodology in the past.[1]

We identified 11,380 hospitalizations: 6,525 (57.3%) for TAVI and 4,855 for SAVR that were on chronic maintenance steroid therapy. There was a marked increase in the number of TAVI procedures from 160 in 2012 to 1,470 in 2019 (p_{trend} <0.01), with a