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REVIEW ARTICLE

COVID-19 review shows that benefits of vaccinating children and adolescents appear to outweigh risks of post-vaccination myopericarditis

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Abstract

Aim: Myopericarditis after COVID-19 vaccination were the most serious adverse events reported in children over 5 years of age. We want to summarise these cases, describing their incidence, clinical features, diagnostic pathways, therapeutic strategies and outcome.

Methods: A systematic review of the literature was conducted until 20 March 2022 by bibliographic electronic databases. We included all reports of post-vaccination myopericarditis in children aged between 5 and 18 years.

Results: All reported cases had elevated serum Troponin levels, associated with electrocardiogram changes, but often with normal echocardiogram. Cardiac magnetic resonance images always showed typical alterations. The pathogenetic mechanism is still unknown. Myocarditis following post-COVID vaccination is more frequent in boys with an average age of about 15 years. Treatment involves the usage of non-steroidal anti-inflammatory drugs, and the average hospitalisation is about 3 days. The long-term consequences are not yet known, so these patients should be studied in a cardiological follow-up and abstention from physical activity should be recommended.

Conclusion: The benefits of COVID-19 vaccination in children and adolescents appear to outweigh the risk of developing post-vaccination myopericarditis. We can also speculate a possible approval of vaccination in children under 5 years for the coming winter.

KEYWORDS
adolescents, children, COVID-19 vaccination, myopericarditis, SARS-CoV-2 vaccination

Abbreviations: cardiac MRI, Cardiac magnetic resonance imaging; CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus disease 2019; EMA, European Union medicines regulator Agency; FDA, United States Food and Drug Administration; ICSRs, Global individual case safety reports; LV, left ventricular; MISC, multisystem inflammatory syndrome; mRNA, messenger RNA; NSAIDs, non-steroidal anti-inflammatory drugs; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; VAERS, Vaccine adverse event reporting system; WHO, World Health Organisation.

1 | INTRODUCTION

Since the beginning of the COVID-19 global pandemic, researchers have been evaluating the prevalence of this disease among children, its clinical presentation and long-term consequences. Early 2022 saw a dramatic increase in COVID-19 paediatric cases not only due to the spread of the Omicron variant, which presents high infectivity because of extensive mutations in the spike protein, but also due to lower vaccination rates in paediatric patients compared with adults.[1] According to the American Academy of Paediatrics, by 10 February 2022, 12.34 million cases among children in the United States had been reported. These represented 19% of all COVID-19 cases, with a rate of hospitalisations ranging from 0.1% to 1.5%.[2] By December 2020, the U.S. Food and Drug Administration (FDA) issued an emergency use authorisation for the Pfizer-BioNTech COVID-19 messenger RNA (mRNA) vaccine in prevention of COVID-19 for individuals aged ≥16 years.3 By May 2021, first the FDA and then also the European Union medicines regulator Agency (EMA) extended the emergency use authorisation for this vaccine to children aged ≥12 years.[3,4] As reported by preliminary studies, Pfizer-BioNTech vaccine has a 95% efficacy in preventing COVID-19 disease in people 16 years of age or older.[5] By November 2021, EMA extended the authorisation for the COVID-19 vaccination to children aged >5 years.[6] According to Centers for Disease Control and Prevention (CDC) updated reports, by 03 April 2022 in United States, 74% of children aged 12–17 years and 69.7% of children aged 5–11 years were fully vaccinated; instead, 86.7% of children aged 12–17 years and 81.9% of children aged 5–11 years received at least one dose of COVID-19 vaccination.[7] From available data about safety, the most common non-serious adverse events reported after vaccination in paediatric population were injection site pain, swelling and redness, fatigue, malaise, headache, myalgia, arthralgia, fever, lymphadenopathy and chest pain.[3] In addition, the most common emergent serious adverse event detected in post-authorisation safety monitoring was the risk of myopericarditis.[3,8]

Myocarditis is defined as an inflammatory process involving the myocardium, caused by infections, mainly viral, immune-mediated and toxic etiologies.[9] Clinical presentation of myocarditis includes chest pain, fever, palpitation, tachycardia, shortness of breath, fatigue, nausea, vomiting, abdominal pain and oedema. The laboratory tests used include serum concentrations of inflammatory markers and cardiac biomarkers, electrocardiogram, echocardiogram, cardiac magnetic resonance imaging (MRI), serologic testing to detect any viral infections. The diagnosis is confirmed by endomyocardial biopsy, which should show acute myocyte injury with inflammatory cells infiltration.[10] Instead, pericarditis is an inflammatory process involving the pericardium; it may present clinically as acute or recurrent pericarditis, pericardial effusion without major hemodynamic compromise, cardiac tamponade or constrictive pericarditis. In addition, features of myocarditis and pericarditis may overlap in many patients and present as myopericarditis.[11] Given the alarm caused by the reporting of these adverse events, the aim of our review was to summarise the cases of myopericarditis after COVID-19 vaccination in paediatric patients and describe its incidence, clinical features, diagnostic pathways, therapeutic strategies and outcome.

Key Notes

- Myopericarditis after COVID-19 vaccination were the most severe adverse event reported in children over 5 years old.
- The benefits of COVID-19 vaccination in children and adolescents appear to outweigh the risk of developing post-vaccination myopericarditis.
- Based on ongoing clinical trials, we can assume a possible approval of COVID-19 vaccination in children aged 6 months to 5 years for the coming winter.

2 | METHODS

The literature review was conducted until 20 March 2022 by electronic databases including PubMed, Scopus and EMBASE. The preferred reporting items for systematic reviews and meta-Analysis guided the search.[12] The keywords used to search the electronic databases were as follows: 'myocarditis' OR 'pericarditis' OR 'myopericarditis' AND 'COVID-19 vaccination' OR 'SARS-CoV-2 vaccination'.

The search was limited to English language papers reporting cases of myopericarditis after COVID-19 vaccination in paediatric patients, aged between 5 and 18 years.

We used inclusion and exclusion criteria to choose suitable papers for the review. We included papers with: children aged 5–18 years with a diagnosis of myopericarditis; cases of myopericarditis secondary to vaccination for SARS-CoV-2; cases of myopericarditis for which all other etiologies had been excluded. We excluded the following: non-English language articles, studies in which the results included patients older than 18 years, reviews, meta-analysis, letters to editor, commentaries and not available papers. No restrictions were applied on gender or country.

We selected case series, case reports, observational studies including cross-sectional and retrospective/prospective cohorts. A single author (LM) rigorously applied the inclusion/exclusion criteria mentioned above, assessing the abstracts of the papers, to decide whether a paper was suitable for full review. Subsequently, each paper meeting the inclusion criteria was analysed in full by two authors (RM and AC). Of the selected studies, we collected the epidemiological and clinical data, including age, sex, symptoms and signs, laboratory findings, instrumental exams, treatment and outcome.

3 | RESULTS

3.1 | Study selection

During the screening phase, we found 319 papers. Of these, we excluded the following: 131 concerning patients with age over 18 years, 13 observational studies including both adolescent and adult patients, 64 not relevant, 24 reviews, 2 meta-analyses, 13 editorials, 18 letters to editor, 11 comments, 6 non- English papers, 9

not available and 1 withdrawn. The inclusion criteria were met by twenty-seven papers that were systematically analysed. These comprised 7 paediatric case reports, 6 paediatric case series, 6 mixed case series including both adults and children of which we only analysed cases ≤18 years, 1 prospective study, 1 cross-sectional study, 2 cohort studies and 4 retrospective studies.

The detailed summary of the literature search is showed in Figure 1. The characteristics of all included studies are summarised in Table S1.

3.2 | Study characteristics and demographics data

Of the 27 studies included in our systematic review, 8 were observational studies while 19 were case reports and case series. In particular, we included the following: 7 paediatric case reports,[13–19] 6 paediatric case series,[20–25] 6 mixed case series, including both adolescent and adult patients in which we collected only cases ≤18 years.[26–31] Analysing all these reports, we summarised cases of hospitalised myocarditis following COVID-19 vaccination among adolescents. We reported fifty-seven cases with age range from 12 to 18 years, of which fifty-five (96.5%) were boys, only two girls. White, Asian and Hispanic patients were described. All patients included were previously healthy except five cases: one with Marfan syndrome, one with history of attention-deficit hyperactivity disorder and mild intermittent asthma, one with Von Willebrand disease, anxiety disorder and Lennox–Gastaut syndrome, one suffering from vitiligo and one with obesity, insulin resistance and dyslipidemia. Fifty-two (91.2%) cases occurred after the second dose of vaccinal cycle, only 5 cases after first dose. About symptoms, all patients reported chest pain—in five cases radiated to the left arm—and 21 (36.8%) patients presented fever; other possible experienced symptoms were palpitation, nausea, vomiting, dyspnoea, coughing, diarrhoea, headache, myalgia, fatigue, abdominal pain and sore throat. Physical examination was often normal, only in two cases was detected tachycardia. Blood pressure and oxygen saturation were normal. Regarding laboratory findings, we observed that in all reports analysed Troponin T serum concentrations was elevated, while NT-proBNP was high only in eight (14%) cases. C-reactive protein were elevated in 14 cases, erythrocyte sedimentation rate in three cases. The most common electrocardiogram alteration was diffuse or left-lead ST segment elevation; other possible pathological described findings were ST segment depression or non-specific ST segment changes, T-wave inversion or T- abnormality, left axial deviation, RSR' pattern in V1, atrioventricular dissociation with junctional escape and intraventricular conduction delay. About radiological findings, chest X-ray performed in 8 cases (14%) was normal. Echocardiography showed small pericardial effusion in only 4 cases and borderline or mild depressed left ventricular systolic function in 15 cases. In only one case, a mitral and aortic valve insufficiency was documented. Coronary computed tomography angiogram, when performed, showed normal coronary origins and no anomalies. It is interesting to note that all cardiac MRIs performed were abnormal and showed myocardial oedema and late gadolinium enhancement

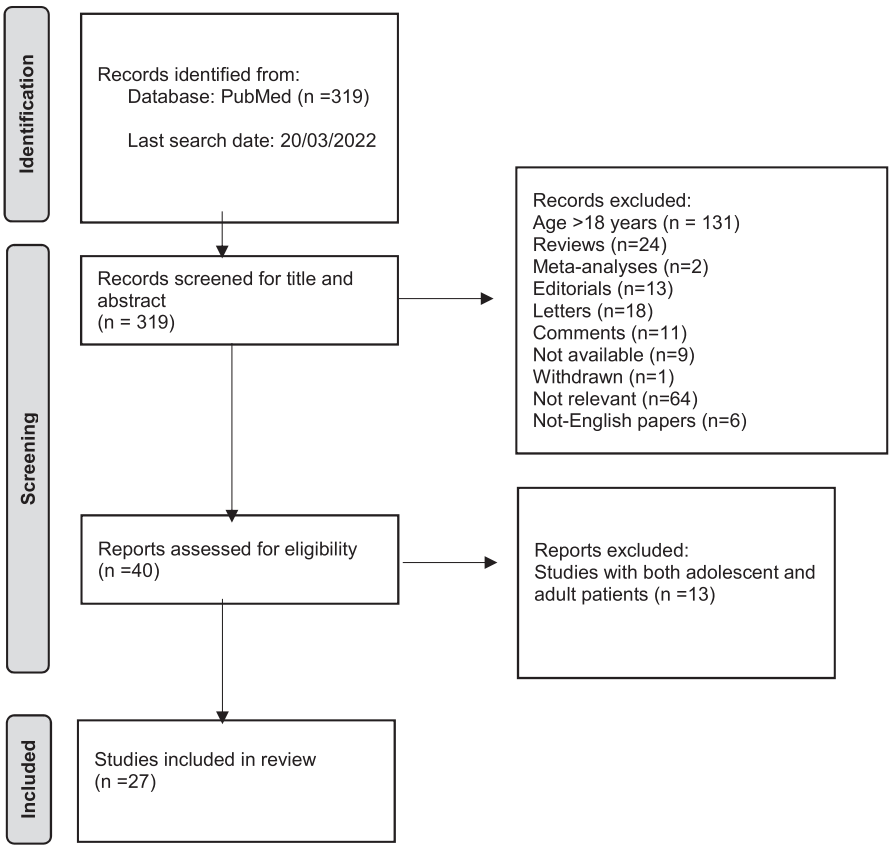

FIGURE 1 Flow diagram of this study selection[12]

compatible with myocarditis. Endomyocardial biopsy has never been performed. The following anomalies were detected on telemetry: occasional isolated premature ventricular contractions, episode of monomorphic ventricular tachycardia, runs of irregular polymorphic ventricular tachycardia and sinus bradycardia during sleep. About therapy, the most used pharmacologic treatments were non-steroidal anti-inflammatory drugs (NSAIDs), followed by intravenous immunoglobulins and steroids. One patient, due to suspected ST segment elevation myocardial infarction, was treated with aspirin, sublingual nitroglycerin and intravenous diltiazem.[13] One patient, after brief episodes of non-sustained ventricular tachycardia, received metoprolol succinate and colchicine.[30] One left heart failure case was treated with ACE-inhibitor and β-blocker.[27] Furosemide was only used in one case.[22] However, most cases were self-limited and the duration of hospitalisation ranged from 3 to 7 days. All patients were discharged with cardiological follow-up and abstention from physical activity.

In addition to the previous clinical case report/series described, prospective, retrospective, cohort and cross-sectional studies on Sars-Cov-2 vaccination myopericarditis in children and adolescents were also available in the literature. Two studies analysed myopericarditis cases in adolescents through the vaccine adverse event reporting system of the United States (US).[32,33] This is a passive vaccine safety surveillance system co-managed by CDC and FDA that monitors adverse events after vaccinations. From 14 December 2020 to 16 July 2021, myocarditis was listed among 4.3% (397) of all vaccine adverse event reports. It was more common in boys and after the second dose. The hospitalisation rate among boys between 12 and 17 years was 87%.[32] The resulting risk–benefit assessment supported paediatric vaccination strategies for protection against COVID-19 disease, continuing to recommend the Pfizer-BioNTech COVID-19 vaccine for all people aged over 12 years.[32] Subsequently, a prospective multicenter study, conducted between May and September 2021, including 18 Danish Paediatric Departments, showed 15 cases of patients between 12 and 17 years of age hospitalised for myopericarditis after COVID-19 mRNA vaccination. Among them, 13 (86.7%) were boys, 8 patients were hospitalised after the first dose and 7 after the second dose. The incidence of myopericarditis among Danish adolescents was 97 and 16 per million, equaling 1 of 10,000 boys and 1 in 63,000 girls, respectively.[34]

Also, Das et al in a U.S. cross-sectional study identified 25 adolescents aged 12–18 years old, with probable myopericarditis after COVID-19 vaccination. Among them, twenty-two (88%) were boys, and in 22 (88%), myopericarditis occurred after the second dose of the mRNA COVID-19 vaccine. Approximately two-thirds of patients underwent cardiac MRI, which revealed evidence of myocardial inflammation despite a lack of echocardiographic abnormalities. All cases of myopericarditis after the mRNA COVID-19 vaccination tend to be mild and transient and improved after NSAIDs therapy.[35]

A Chinese study including all vaccinated adolescents aged between 12 and 17 years found 33 patients who developed acute myopericarditis. Among them, 29 (87.88%) were boys, with a median age of 15.3 years, and 27 patients (81.82%) developed myopericarditis after receiving the second dose vaccination. All reported cases were mild and required only conservative management.[36] An interesting pharmacovigilance analysis reviewing all reports with mRNA COVID-19 vaccines recorded Vigibase and the World Health Organisation (WHO) global individual case safety reports (ICSRs) database showed that among 4942 report analysed, 49 were pericarditis, 191 myocarditis and 2 myopericarditis.[37] Compared with the first dose of mRNA COVID-19 vaccines, the second dose was associated with an increased risk of myopericarditis. In addition, the risk of myopericarditis was 10 times higher in boys than in girls, but no differences were found comparing different age groups (12–15 vs. 16–17 years). Reports of myopericarditis came mostly from Germany (24%), followed by France (17%) and Italy (10%). Besides, Schauer et al[38] in their retrospective study, analysed all patients aged under 18 years presenting with severe chest pain and signs of myopericarditis within 1 week after the second dose of COVID-19 vaccine. The authors identified 13 patients with myopericarditis, with a median age of 15.1 years (range 12–17 years). Most patients were boys ($n = 12$; 92%), and non-Hispanic ($n = 10$; 76.9%). The median time to presentation from the second dose of the COVID-19 mRNA vaccine was 3 days. All patients had an elevated serum Troponin level. Nine patients had an abnormal electrocardiogram, with ST segment elevation. All patients underwent echocardiography on admission, showing a normal left ventricular (LV) systolic function in 11 patients; only 2 demonstrated mildly reduced LV systolic function and regional LV wall motion abnormalities. No patients had significant pericardial effusion. All cardiac MRIs performed were abnormal, showing late gadolinium enhancement evidence of myocardial inflammation and oedema and met the Lake Louise criteria for myocarditis. The treatment included the use of NSAIDs in all patients; however, two also received corticosteroids and 3 intravenous immunoglobulins. The median hospital length of stay was 2 days (range, 1–4 days) with no intensive care unit admission, significant morbidity, or mortality.[38]

Again, Choe et al[39] in their retrospective study of surveillance within the Korean education system to determine the effectiveness of BNT162b2 mRNA COVID-19 vaccine in adolescents, reported a rate for myopericarditis of 1.8 per 100,000 (95% CI 0.8–3.5) among first-dose recipients and 4.3 per 100,000 (95% CI 2.6–6.7) in second-dose recipients.[39]

4 | DISCUSSION

Myopericarditis as adverse event has already been described following the usage of other vaccines. For example, vaccine-associated myopericarditis following smallpox vaccination presented an incidence of 0.01%.[40] Other vaccines associated with myopericarditis were Haemophilus influenzae type B and hepatitis B.[41] As emerged from our research, it is difficult to establish exactly the prevalence of this adverse event after COVID-19 vaccination in paediatric population. However, this systematic review of scientific literature showed that COVID-19 vaccine-associated myopericarditis is a rare and

mild adverse event, which resolves clinically within a few days. As reported by all the analysed studies, the mean age of myopericarditis presentation was 15 years, it was most common in boys than in girls, and after the second dose of vaccinal cycle, with a mean time between the injection and the clinical manifestations of about 3 days. The main symptom reported was chest pain, sometimes irradiated to the left arm. Objective examination was often normal, but serum concentration of Troponin T was always elevated. Electrocardiographic changes were frequent; the most common pathological findings were ST segment alterations. Echocardiogram was normal, so a negative examination was not enough to exclude a diagnosis of myopericarditis. The available literature showed that cardiac MRI appeared very sensitive in detecting vaccine-associated cardiac injury. Regarding therapies, most of patients fully recover after a treatment with NSAIDs. The role of corticosteroids and intravenous immunoglobulin remains unclear, but these agents could decrease the immune response triggered by the vaccine and may have a role in NSAID-unresponsive patients.[35]

The underlying relationship between mRNA COVID-19 vaccination and myopericarditis has not been identified yet, and no risk factors have been reported in the studies we analysed. However, Park et al hypothesised that this pathological process was related to the immune response triggered by the vaccine in a genetically susceptible host.[21] As the host generated antibodies against the viral particle assembled in response to the mRNA vaccine, the antibodies might cross-react with surface antibodies on the cardiomyocytes resulting in an inflammatory reaction with cell damage.[21] This cell damage, manifesting as focal patchy myocarditis, caused the ST segment elevation and chest pain.[21] Marshall et al speculated that myopericarditis could be an additional rare adverse event related to systemic reactogenicity greater in children than in adults.[22] Similarly, Schauer et al assumed that myocarditis could be the consequence of a hyperimmune response to the second dose of the vaccine.[38] In fact, children have demonstrated a more robust immune response to SARS-CoV-2 infections than adults, as observed in multisystem inflammatory syndrome (MISC).[38] Finally, Gill et al after a cardiac autopsy observed that myocardial injury seen in post-vaccine hearts was different from typical myocarditis and had an appearance most closely resembling a catecholamine-mediated stress (toxic) cardiomyopathy.[42] However, despite these speculations currently, no causal association has been established between COVID-19 vaccine and myopericarditis.

From our point of view, it is necessary for healthcare providers to consider myopericarditis in all adolescents complaining about chest pain after COVID-19 vaccination. However, it is mandatory to exclude all other etiologies of myocarditis disease in young patients (viruses and toxins) before considering myocarditis as related to COVID-19 vaccination. The long-term consequences of these adverse events are not yet known, so these patients should be systematically evaluated and studied in a follow-up setting including a cardiological evaluation. In addition, abstention from physical activity should always be recommended until cardiological authorisation.

In conclusion, the adverse events post-COVID-19 vaccination are rare and the cardiac involvement in case of acute SARS-CoV-2 infection and eventually MISC could be much more serious and life-threating. Data from 40 healthcare systems participating in a large network found that the risk of cardiac complications was significantly higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination for both male patients and female patients in all age groups.[43] About public health, as emerged by the data we reported and according to CDC, the benefits coming from vaccination are higher that the risk of developing myopericarditis. Some interesting food for thought concerns how to report adverse events after vaccination. Currently, the most common method is self and voluntary reporting through specific surveillance platforms. Considering the large number of subjects involved in vaccination campaigns, active pharmacovigilance systems seem difficult to apply. About future prospective, clinical trials evaluating the use of vaccines against SARS-CoV-2 in children under 5 years are ongoing. In particular, Moderna® and Pfizer-BioNTech® are conducting studies about safety, tolerability and immunogenicity of COVID-19 vaccine in children 6 months to under 5 years of age.[44,45] Many adverse events were mild or moderate and more frequent after the second dose. Among them, fever greater than 38°C was the most common. No deaths, no myocarditis or pericarditis and no MIS-C were reported. Therefore, we can speculate a possible approval of vaccination in children under 5 years of age for the coming winter.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

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REFERENCES

1. Curatola A, Ferretti S, Gatto A, Chiaretti A. Will cases of multisystem inflammatory syndrome rise with the greater spread of the omicron variant amongst children? Acta Paediatr. 2022;111:1207-1208. apa.16304.
2. Children and COVID-19: State-Level Data Report [Internet]. Accessed July 7, 2021. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/
3. Pfizer-BioNTech Full emergency use authorization (EUA) prescribing information [Internet]. Accessed May 15, 2021. http://labeling.pfizer.com/ShowLabeling.aspx?id=14471&format=pdf&#page=13
4. EMA News 28/05/2021 [Internet]. Accessed May 28, 2021. https://www.ema.europa.eu/en/news/first-covid-19-vaccine-approved-children-aged-12-15-eu

5. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383:2603-2615.
6. Comirnaty COVID-19 vaccine: EMA recommends approval for children aged 5 to 11 [Internet]. Accessed November 25, 2021. https://www.ema.europa.eu/en/news/comirnaty-covid-19-vaccine-ema-recommends-approval-children-aged-5-11
7. COVID-19 Vaccinations in the United States [Internet]. Accessed April 3, 2022. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total
8. Lv M, Luo X, Shen Q, et al. Safety, immunogenicity, and efficacy of COVID-19 vaccines in children and adolescents: a systematic review. Vaccine. 2021;9:1102.
9. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19–related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm. 2020;17:1463-1471.
10. Tschöpe C, Ammirati E, Bozkurt B, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol. 2021;18:169-193.
11. Sexson Tejtel SK, Munoz FM, Al-Ammouri I, et al. Myocarditis and pericarditis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2022;40:1499-1511.
12. Page MJ, McKenzie JE, Bossuyt PM, et al. Statement: an updated guideline for reporting systematic reviews. BMJ. 2020;2021:n71.
13. Azir M, Inman B, Webb J, Tannenbaum L. STEMI mimic: focal myocarditis in an adolescent patient after mRNA COVID-19 vaccine. J Emerg Med. 2021;61:e129-e132.
14. Minocha PK, Better D, Singh RK, Hoque T. Recurrence of acute myocarditis temporally associated with receipt of the mRNA coronavirus disease 2019 (COVID-19) vaccine in a male adolescent. J Pediatr. 2021;238:321-323.
15. Giray D, Epçaçan S. Acute myocarditis following COVID-19 mRNA vaccination: a paediatric case. Cardiol Young. 2022;1-3.
16. Visclosky T, Theyyunni N, Klekowski N, Bradin S. Myocarditis following mRNA COVID-19 vaccine. Pediatr Emer Care. 2021;37:583-584.
17. Türe M, Akın A, Demir M, Akay C. A paediatric case of myopericarditis post-COVID-19 mRNA vaccine. Cardiol Young. 2022;1-4.
18. McLean K, Johnson TJ. Myopericarditis in a previously healthy adolescent male following COVID-19 vaccination: a case report. Acad Emerg Med. 2021;28:918-921.
19. Isaak A, Feisst A, Luetkens JA. Myocarditis following COVID-19 vaccination. Radiology. 2021;301:E378-E379.
20. Tano E, San Martin S, Girgis S, Martinez-Fernandez Y, Sanchez VC. Perimyocarditis in adolescents after Pfizer-BioNTech COVID-19 vaccine. J Pediatr Infec Dis Soc. 2021;10:962-966.
21. Park J, Brekke DR, Bratincsak A. Self-limited myocarditis presenting with chest pain and ST segment elevation in adolescents after vaccination with the BNT162b2 mRNA vaccine. Cardiol Young. 2022;32:146-149.
22. Marshall M, Ferguson ID, Lewis P, et al. Symptomatic acute myocarditis in 7 adolescents after Pfizer-BioNTech COVID-19 vaccination. Pediatrics. 2021;148:e2021052478.
23. Ambati S, Colon M, Mihic M, Sanchez J, Bakar A. Acute Myopericarditis after COVID-19 vaccine in teenagers. Case Rep Cardiol. 2021;2021:1-5. Sciarra L, ed.
24. Dionne A, Sperotto F, Chamberlain S, et al. Association of Myocarditis with BNT162b2 messenger RNA COVID-19 vaccine in a case series of children. JAMA Cardiol. 2021;6:1446.
25. Snapiri O, Rosenberg Danziger C, Shirman N, et al. Transient cardiac injury in adolescents receiving the BNT162b2 mRNA COVID-19 vaccine. Pediatr Infect Dis J. 2021;40:e360-e363.
26. Abu Mouch S, Roguin A, Hellou E, et al. Myocarditis following COVID-19 mRNA vaccination. Vaccine. 2021;39:3790-3793.
27. Istampoulouoglou I, Dimitriou G, Späni S, et al. Myocarditis and pericarditis in association with COVID-19 mRNA-vaccination: cases from a regional pharmacovigilance Centre. Gcsp. 2021;2021:e202188. https://globalcardiologyscienceandpractice.com/index.php/gcsp/article/view/517
28. Starekova J, Bluemke DA, Bradham WS, Grist TM, Schiebler ML, Reeder SB. Myocarditis associated with mRNA COVID-19 vaccination. Radiology. 2021;301:E409-E4011.
29. Shaw KE, Cavalcante JL, Han BK, Gössl M. Possible association between COVID-19 vaccine and myocarditis. JACC Cardiovasc Imaging. 2021;14:1856-1861.
30. Vidula MK, Ambrose M, Glassberg H, et al. Myocarditis and other cardiovascular complications of the mRNA-based COVID-19 vaccines. Cureus. 2021;13:e15576. https://www.cureus.com/articles/61030-myocarditis-and-other-cardiovascular-complications-of-the-mrna-based-covid-19-vaccines
31. Meyer-Szary J, Bazgier M, Lubocka P, Dorniak K, Sabiniewicz R. Cardiac magnetic resonance characteristics of acute myocarditis occurring after mRNA-based COVID-19 vaccines immunization. 3.
32. Krug A, Stevenson J, Høeg TB. BNT162b2 vaccine-associated Myo/pericarditis in adolescents: a stratified risk-benefit analysis. Eur J Clin Invest. 2022;52:e13759. doi:10.1111/eci.13759
33. Hause AM, Gee J, Baggs J, et al. COVID-19 vaccine safety in adolescents aged 12–17 years — United States, December 14, 2020–July 16, 2021. MMWR Morb Mortal Wkly Rep. 2021;70:1053-1058.
34. Nygaard U, Holm M, Bohnstedt C, et al. Population-based incidence of Myopericarditis after COVID-19 vaccination in Danish adolescents. Pediatr Infect Dis J. 2022;41:e25-e28.
35. Das BB, Kohli U, Ramachandran P, et al. Myopericarditis after messenger RNA coronavirus disease 2019 vaccination in adolescents 12 to 18 years of age. J Pediatr. 2021;238:26-32.e1.
36. Chua GT, Kwan MYW, Chui CSL, et al. Epidemiology of acute myocarditis/pericarditis in Hong Kong adolescents following Comirnaty vaccination. Clin Infect Dis. 2021;ciab989.
37. Foltran D, Delmas C, Flumian C, et al. Myocarditis and pericarditis in adolescents after first and second doses of mRNA COVID-19 vaccines. Eur Heart J - Qual Care Clin Outcomes. 2022;8:99-103.
38. Schauer J, Buddhe S, Colyer J, et al. Myopericarditis after the Pfizer messenger ribonucleic acid coronavirus disease vaccine in adolescents. J Pediatr. 2021;238:317-320.
39. June Choe Y, Yi S, Hwang I, et al. Safety and effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents. Vaccine. 2022;40:691-694.
40. Halsell JS. Myopericarditis following smallpox vaccination among vaccinia-naive US military personnel. Jama. 2003;289:3283-3289.
41. Su JR, McNeil MM, Welsh KJ, et al. Myopericarditis after vaccination, vaccine adverse event reporting system (VAERS), 1990–2018. Vaccine. 2021;39:839-845.
42. Gill JR, Tashjian R, Duncanson E. Autopsy histopathologic cardiac findings in two adolescents following the second COVID-19 vaccine dose. Arch Pathol Lab Med. 2022. doi:10.5858/arpa.2021-0435-SA/477788/Autopsy-Histopathologic-Cardiac-Findings-in-Two
43. Block JP, Boehmer TK, Forrest CB, et al. Cardiac complications after SARS-CoV-2 infection and mRNA COVID-19 vaccination — PCORnet, United States, January 2021–January 2022. MMWR Morb Mortal Wkly Rep. 2022;71:517-523.
44. Pfizer and BioNTech provide update on rolling submission for emergency use authorization of their COVID-19 vaccine in children 6 months through 4 years of age [internet]. 2022. Accessed February 11, 2022. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-provide-update-rolling-submission
45. Moderna announces its covid-19 vaccine phase 2/3 study in children 6 months to under 6 years has successfully met its primary endpoint [internet]. 2022. Accessed March 23, 2022. https://investors.modernatx.com/news/news-details/2022/Moderna-Annou

nces-its-COVID-19-Vaccine-Phase-23-Study-in-Children-6-Months-to-Under-6-Years-Has-Successfully-Met-Its-Primary-Endpoint/default.aspx

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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