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.

Heart, Lung and Circulation (2021) **30**, 1425–1429
1443-9506/21/$36.00
https://doi.org/10.1016/j.hlc.2021.07.011

EDITORIAL

Myocarditis, Pericarditis and Cardiomyopathy After COVID-19 Vaccination☆

Salvatore Pepe, PhD, FAHA, FCSANZ [a,b,1],
Ann T. Gregory, MBBS, GradCertPopHealth [a,2],
A. Robert Denniss, MD, MSc, FCSANZ [a,c,d,3,*]

[a]*Heart, Lung and Circulation*, Sydney, NSW, Australia
[b]Murdoch Children's Research Institute, Heart Research and Department of Paediatrics, University of Melbourne, Royal Children's Hospital Melbourne, Melbourne, Vic, Australia
[c]Department of Cardiology, Westmead Hospital, and University of Sydney, Sydney, NSW, Australia
[d]Department of Cardiology, Blacktown Hospital, and Western Sydney University, Sydney, NSW, Australia

Keywords mRNA vaccine • COVID-19 • Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) • Myocarditis • Pericarditis • Cardiomyopathy • Cardiovascular disease • Australia • CSANZ • ANZSCTS

The impact of the global health crisis due to the virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)—the causative pathogen of the coronavirus disease 2019 (COVID-19)—has begun to alter with the timely development, approval and administration of vaccines [1]. Although SARS-CoV-2 infection primarily targets the respiratory system [2–6], it is now recognised that the infection and its clinical manifestations are systemic [7–12], and also affecting the cardiovascular system of adults and children [13–20]. Cardiac complications of variable severity with acute and long-term sequelae are now known to include acute myocardial injury, arrhythmias, vasculitis and endothelial dysfunction, thrombosis, myocardial fibrosis, and myocarditis [13–23]. The cardiovascular and cellular pathophysiology of COVID-19, and the clinical management of previously healthy subjects and patients with existing cardiovascular or other disease conditions remain under intense investigation particularly as early in the pandemic, myocarditis was identified as a risk factor for increased mortality in COVID-19 patients [23–25].

Viral infections are a common cause of acute myocarditis, which usually presents with the hallmark of inflammatory infiltrate and myocardial cell injury unrelated to ischaemia, and in the absence of overt vascular disease [26,27]. In healthy subjects, anti-viral vaccine-associated immune eosinophilic myocarditis is rare but has previously been reported in healthy adults for the smallpox vaccine and the seasonal influenza vaccine [28–31].

Not surprisingly, highly publicised adverse events following immunisation with COVID-19 vaccine have been of great concern to the public and to health authorities world-wide, particularly when associated with the death of 'previously healthy' individuals. There has been considerable focus on the rare occurrence of Thrombosis with

*Corresponding author at: Department of Cardiology, Westmead Hospital and University of Sydney, PO Box 3, Westmead NSW 2145, Australia; Email: journal@csanz.edu.au; Twitter: @heartlungcirc

☆*Heart, Lung and Circulation*'s Digital Collection of publications relating to COVID-19 is available at (www.heartlungcirc.org). The *COVID-19 Vaccination-Guidance on Myocarditis and Pericarditis After mRNA COVID-19 Vaccines* can be assessed at: https://www.health.gov.au/sites/default/files/documents/2021/08/covid-19-vaccination-guidance-on-myocarditis-and-pericarditis-after-mrna-covid-19-vaccines_1.pdf. The guidance was jointly developed by the Australian Technical Advisory Group on Immunisation (ATAGI) and the Cardiac Society of Australia and New Zealand (CSANZ).

[1]Basic Cardiovascular Science Editor, *Heart, Lung and Circulation*.

[2]Commissioning Editor, *Heart, Lung and Circulation*.

[3]Editor-in-Chief, *Heart, Lung and Circulation*.

Thrombocytopenia Syndrome (TTS), Guillain-Barré Syndrome and Capillary Leak Syndrome reported after receipt of the adenoviral vector vaccine made by AstraZeneca (Covishield/Vaxzevria), even though a causal relationship with each respective vaccination incident has not been consistently established and these events are not exclusive to the AstraZeneca vaccine. However, in the past few months there has been a growing international list of reports of the rare incidence of myocarditis and/or pericarditis within one week after receiving the second dose of mRNA COVID-19 vaccines (Pfizer-BioNTech BNT162b2/Comirnaty and Moderna mRNA-1273), more often in males, mostly in adolescents and young adults [32–38].

In Australia, to 11 July 2021, the Department of Health Therapeutic Goods Administration (TGA) has received 50 reports of suspected myocarditis and/or pericarditis out of 288 total adverse event reports after 3.7 million doses of Pfizer mRNA COVID-19 vaccine [32]. These reported cases of temporally associated possible myocarditis/pericarditis and their clinical course are being evaluated and may be an overestimate of the incidence; however, if all these events are confirmed as likely vaccination complications, this represents an incidence of 13.5 per million doses administered. After long delays in vaccine administration in Australia, as vaccine availability and the mRNA vaccination rate finally begin to ramp up over the next few months, TGA monitoring and clinician vigilance will be very important, as is consideration of the experience in North America and Europe with large populations where vaccine administration is most advanced.

International Monitoring of Post-COVID-19 Vaccine Myocarditis

Below, we draw attention to brief summaries of post-COVID-19 vaccine myocarditis accounts from Israel, the UK, Europe, Canada, and the USA. At the time of writing this report, event monitoring, clinical confirmation, patient outcomes and exploring a causal relationship with the vaccines remain in progress between respective governing health agencies and COVID-19 vaccine manufacturers. However, adjustment of product safety information risk statements is already being recommended and communicated to health care professionals.

One of the earliest reports was from Israel where from April 2021, the Ministry of Health detailed, by early June, over 62 cases of myocarditis out of 5 million vaccinated exclusively with the Pfizer mRNA vaccine (an incidence of 12.4 per million patients). Notably, the cases were predominantly younger than 30 years of age, mainly male, and had received their second dose of vaccine within the preceding 3 days. Importantly, all were previously well and although 60 had recovered within less than a week, there were 2 deaths (one male aged 35 years and one female aged 22 years [33]. Against a background of current considerations over whether to vaccinate children (<12 years) against COVID-19, adverse events and dosing regimen are being closely studied.

In the UK to 7 July 2021, 19.7 million first doses and about 11.6 million second doses of the Pfizer/BioNTech vaccine plus about 1.1 million first doses of the COVID-19 Vaccine Moderna have been administered [34]. As part of their open 'Yellow Card' reporting, the UK Medicines and Healthcare Products Regulatory Agency (Department of Health and Social Care) have listed the incidence of suspected myocarditis and pericarditis after receiving the Pfizer/BioNTech vaccine (81 myocarditis, 63 pericarditis), and Moderna (9 myocarditis, 9 pericarditis, 1 endocarditis), with an incidence of 5.0 per million doses. Of interest is that, after administration of the AstraZeneca COVID-19 vaccine (adenoviral vector; not an mRNA vaccine), there were also reports of myocarditis (69) and pericarditis (107), after 24.7 million first doses and 22.3 million second doses (an incidence of 3.7 per million doses).

The European Medicines Agency, as of the end of May 2021, cited vaccination with approximately 160 million COVID-19 vaccine doses for Pfizer, 19 million doses for Moderna, 40 million for AstraZeneca and 2 million for Janssen [35]. EudraVigilance adverse event data for these dose exposures reported myocarditis following vaccination with Pfizer (122 cases), Moderna (16 cases), and AstraZeneca (38 cases). Post-vaccine pericarditis was also reported for Pfizer (126 cases), Moderna (18), AstraZeneca (47) and the Janssen COVID-19 viral vector vaccine (1). This represented a very low incidence of reported myocarditis/pericarditis of 2.0 per million doses for viral vector vaccines and 1.6 per million doses for mRNA vaccines.

The Public Health Agency of Canada (PHAC), Health Canada, as of 9 July 2021, has administered over 41.5 million COVID-19 vaccine doses and listed 163 cases of 'myocarditis/pericarditis' (median age, 39 years; range, 15–86) [36]. The breakdown is: 111 cases after Pfizer-BioNTech, 40 after Moderna, 11 cases after AstraZeneca; and 1 case with vaccine unspecified. This represents an incidence of 3.9 per million doses. The timing of post-vaccination onset of symptoms ranged from 5 hours to 92 days. There were 52 females (median age, 49 years; range, 15–86) and 59 males (median age, 38 years; range, 15–82). Interestingly, 67 cases occurred after the first dose, 26 cases after the second vaccine dose; and, 18 cases, no dose number specified. Detailed reporting of the cases, their clinical management and outcomes with regard to an association or a causal link between myocarditis/pericarditis and mRNA vaccines are in progress with the growing receipt of data.

The US Centers for Disease Control and Prevention (CDC) by mid-June 2021 had reported 1,226 cases of myocarditis after mRNA vaccination (Pfizer or Moderna, 29 December 2020–11 June 2021) from 296 million doses [37,38], an incidence of 4.1 per million doses. As the median age of these cases was 26 years (range, 12–94 years) and the median onset of first symptom was 3 days (range, 0–179), it is important to

note that more than half the patients were less than 30 years old, more than two-thirds were male, and more than 75% had received the second dose of mRNA vaccine [37,38]. Consequently, CDC physicians and cardiologists evaluated 484 cases of patients aged under 30 years, with 323 individuals that strictly met definitions as per Dallas Criteria and Lake Louise Criteria for acute myocarditis, acute pericarditis or myopericarditis [38]. The median age for these individuals was 19 years (range, 12–29 years) with first symptom onset at a median of 2 days (range, 0–40 days), and 92% with onset within 7 days. Of note is that 96% of these individuals were promptly hospitalised. Most patients were managed through mild clinical courses that resolved, with subsequent hospital discharge; there were no deaths.

The mounting number of case and cohort studies that we have identified to date provide considerable detailed insight into patient demographics, disease at presentation, diagnosis, clinical management, and outcome [39–43]. The report by Montgomery *et al.* [43] is one of the larger retrospective series: 23 male individuals were treated for chest pain and confirmed with myocarditis after mRNA COVID-19 vaccination between January and April 2021 (Pfizer, n=7 cases; Moderna, n=16 cases). All were military staff members with a high level of fitness and health. During this time 2.8 million doses of mRNA COVID-19 vaccine were administered by the US Military Healthcare Service. All patients had markedly elevated cardiac troponin levels, with consistent indications for myocarditis and no evidence of infection, existing autoimmune conditions, or ischaemic disease; however only eight patients were examined with cardiac magnetic resonance imaging (MRI) at the acute phase of illness, thus clinically confirming myocarditis. Notably, managed care was brief, with rapid recovery in all patients.

A common feature of these post-COVID-19 vaccine reports of myocarditis [39–44] is the very low incidence, general similarity of patient demographics, condition, symptom onset and outcomes. These reports also highlight the importance of decision making as to when to include cardiac MRI in evidence not only in confirming each case but also in assisting with excluding confounding abnormalities. Recently published in *Heart Lung & Circulation* [45], Berto *et al.*, from the Universitätsklinik für Kardiologie at Inselspital, Bern, Switzerland, present a case of Takotsubo cardiomyopathy in a previously healthy 63-year-old female within one day of a first dose Moderna (mRNA-1273) COVID-19 vaccination. As far as we are aware, there have been no previously published reports of this association, although Takotsubo cardiomyopathy has been reported after influenza vaccination [46]. In this case, cardiac MRI provided valuable confirmative diagnostic support and reinforces the need to characterise specific cardiomyopathic features and subtype. As a 'stress'-associated cardiomyopathy, Takotsubo and its excess catecholamine-mediated myocardial stunning may provide targets for further investigation following post-COVID-19 vaccination systemic and cardiac inflammation and inform medical management of cardiac dysfunction.

Considerations in Limiting the Age Risk

As fatality rates due to COVID-19 markedly rise in those over 70 years of age, particularly in those with comorbidities, the advantages of vaccination in those with advanced age have been well appreciated during the pandemic. In contrast, as children and younger adolescents have had relatively lower rates of SARS-CoV-2–related symptomatic disease, or severe conditions requiring hospitalisation, intensive care, or death, there has been reticence and limited focus in vaccinations for these age groups. This has been reinforced by a predominance of experience featuring asymptomatic or mainly mild, upper respiratory tract infection that resolves in a few days. Case rates with severe conditions and subsequent fatality in children have been low, though more common in adolescents with pre-existing severe life-threatening conditions [47]. However, a greatly concerning complication in children, within 2-4 weeks of SARS-CoV-2 infection, has been the emergence of a hyper-inflammation condition that has features similar to toxic circulatory shock and Kawasaki disease—Paediatric Multisystem Inflammatory Syndrome (PIMS-TS), or Multisystem Inflammatory Syndrome in Children (MIS-C). Presentation involves fever, elevated markers of inflammation and injury, circulatory shock, acute renal injury, cardiac dysfunction, coronary artery aneurysm, and myocarditis, requiring urgent intensive care support [47]. Given the remaining high prevalence of COVID-19 in the community and the rapid spread of new SARS-CoV-2 variants, North American, European, and other health regulatory authorities have begun to extend use of the Pfizer-BioNTech mRNA COVID-19 vaccine in children aged 12-15 years, particularly with the recent support of new safety trial data. The recent randomised, placebo-controlled, observer-blinded, Phase 3 trial (of a Phase 1–2–3 trial) assessing safety, immunogenicity, and efficacy of the Pfizer-BioNTech BNT162b2 vaccine in 2,260 subjects (aged 12–15 and 16–25 years) demonstrated a highly effective response with 100% efficacy [48]. No vaccine-related serious adverse events were reported in these cohorts. As other trials currently in progress come to completion there will be greater confidence and emphasis on vaccination in children and adolescents, especially when vaccine production levels augment sufficiently to meet the international demand for all age groups.

Conclusions

As greater proportions of populations complete immunisation across the world—and many nations are still at an early phase of this process—there remain many questions regarding the specific molecular aetiology underlying post-COVID-19 vaccination myocarditis or milder conditions that are presently either not investigated or not reported. While definitive evidence for myocarditis diagnoses is important, it is also vital that aetiology is carefully

distinguished between vaccine-related myocarditis, that is rapidly resolvable with managed medical care, versus confounding an associated vaccination with other aetiology, complex co-morbidities and other co-existent medical conditions, and greater cardiovascular risk.

Regardless of aetiology, it remains that post-COVID-19 vaccine-associated cardiac diagnoses require timely and stringent specialist clinical management, as has been highlighted by rare cardiovascular and cardiac-related deaths following COVID-19 vaccination. Thus, informed consent for mRNA COVID-19 vaccines should include information regarding the rare but potential incidence of myocarditis or pericarditis in the week following COVID-19 vaccination, and individuals should be advised of potential symptoms and the need to seek immediate clinical care. Although age (mainly <30 years) and sex (mainly male) may alter general consideration of the rare risk for myocarditis after COVID-19 vaccination, discussion should consider an individual's personal risk, based on their current health status, impact of severe COVID-19 disease and the risk of infection from locally circulating variants of SARS-CoV-2. As a larger proportion of the total population is vaccinated, mounting data regarding safety events, vaccine response and the incidence of COVID-19 infection will rapidly evolve our understanding, thus the reader is referred to the regular updates of the document *COVID-19 Vaccination-Guidance on Myocarditis and Pericarditis After mRNA COVID Vaccines*, jointly developed by the Australian Technical Advisory Group on Immunisation (ATAGI) and the Cardiac Society of Australia and New Zealand (CSANZ); (https://www.health.gov.au/sites/default/files/documents/2021/08/covid-19-vaccination-guidance-on-myocarditis-and-pericarditis-after-mrna-covid-19-vaccines_1.pdf, Version 1.1 August 6th, 2021).

To date, the world-wide safety monitoring data suggests that life-threatening serious adverse events are rare following vaccination for COVID-19 but do require careful clinical vigilance and early detailed investigation and clinical management as they can occur following all COVID-19 vaccine types, at first or second dose. Importantly, analyses of this data and their discussion by North American and European health agencies at this early stage conclude that the benefits of COVID-19 vaccination outweigh the risks in all populations, including the rare risk of myocarditis, for all recommended age groups.

References

[1] Forchette L, Sebastian W, Liu T. A comprehensive review of COVID-19 virology, vaccines, variants, and therapeutics. *Curr Med Sci*. 2021 Jul 9;1–15. https://doi.org/10.1007/s11596-021-2395-1. Online ahead of print.

[2] Canatan D, Vives Corrons JL, De Sanctis V. The multifacets of COVID-19 in adult patients: a concise clinical review on pulmonary and extrapulmonary manifestations for healthcare physicians. Acta Biomed. 2020;91(4):e2020173.

[3] Triposkiadis F, Starling RC, Xanthopoulos A, Butler J, Boudoulas H. The counter regulatory axis of the lung renin-angiotensin system in severe COVID-19: pathophysiology and clinical implications. Heart Lung Circ. 2021 Jun;30(6):786–94.

[4] Habashi NM, Camporota L, Gatto LA, Nieman G. Functional pathophysiology of SARS-CoV-2-induced acute lung injury and clinical implications. J Appl Physiol (1985). 2021;130(3):877–91.

[5] Ambardar SR, Hightower SL, Huprikar NA, Chung KK, Singhal A, Collen JF. Post-COVID-19 pulmonary fibrosis: novel sequelae of the current pandemic. J Clin Med. 2021;10(11):2452.

[6] Kvietys PR, Fakhoury HMA, Kadan S, Yaqinuddin A, Al-Mutairy E, Al-Kattan K. COVID-19: lung-centric immunothrombosis. Front Cell Infect Microbiol. 2021;11:679878.

[7] Satsangi S, Gupta N, Kodan P. Current and new drugs for COVID-19 treatment and its effects on the liver. J Clin Transl Hepatol. 2021;9(3):436–46.

[8] Ruscitti P, Conforti A, Cipriani P, Giacomelli R, Tasso M, Costa L, et al. Pathogenic implications, incidence, and outcomes of COVID-19 in autoimmune inflammatory joint diseases and autoinflammatory disorders. Adv Rheumatol. 2021;61(1):45.

[9] Zacharias H, Dubey S, Koduri G, D'Cruz D. Rheumatological complications of Covid 19. *Autoimmun Rev*. 2021 Jul 5;20(9):102883. https://doi.org/10.1016/j.autrev.2021.102883. Online ahead of print.

[10] Cao TT, Zhang GQ, Pellegrini E, Zhao Q, Li J, Luo LJ, et al. COVID-19 and its effects on the digestive system. World J Gastroenterol. 2021;27(24):3502–15.

[11] Sepehrinezhad A, Gorji A, Sahab Negah S. SARS-CoV-2 may trigger inflammasome and pyroptosis in the central nervous system: a mechanistic view of neurotropism. Inflammopharmacology. 2021;29(4):1049–59.

[12] Afshar ZM, Babazadeh A, Hasanpour A, Barary M, Sayad B, Janbakhsh A, et al. Dermatological manifestations associated with COVID-19: a comprehensive review of the current knowledge. *J Med Virol*. 2021 Jul 9. https://doi.org/10.1002/jmv.27187. Online ahead of print.

[13] Smadja DM, Mentzer SJ, Fontenay M, Laffan MA, Ackermann M, Helms J, et al. COVID-19 is a systemic vascular hemopathy: insight for mechanistic and clinical aspects. *Angiogenesis*. 2021 Jun 28:1–34. https://doi.org/10.1007/s10456-021-09805-6. Online ahead of print.

[14] Barssoum K, Victor V, Salem A, Kumar A, Mubasher M, Hassib M, et al. Echocardiography, lung ultrasound, and cardiac magnetic resonance findings in COVID-19: a systematic review. *Echocardiography*. 2021 Jul 8. https://doi.org/10.1111/echo.15152. Online ahead of print.

[15] Farshidfar F, Koleini N, Ardehali H. Cardiovascular complications of COVID-19. JCI Insight. 2021;6(13):148980.

[16] Chung MK, Zidar DA, Bristow MR, Cameron SJ, Chan T, Harding III CV, et al. COVID-19 and cardiovascular disease: from bench to bedside. Circ Res. 2021;128(8):1214–36.

[17] Carrizales-Sepúlveda EF, Vera-Pineda R, Flores-Ramírez R, Hernández-Guajardo DA, Pérez-Contreras E, Lozano-Ibarra MM, et al. Echocardiographic manifestations in COVID-19: a review. Heart Lung Circ. 2021;30(8):1117–29.

[18] Kawakami R, Sakamoto A, Kawai K, Gianatti A, Pellegrini D, Nasr A, et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis: JACC Review Topic of the Week. J Am Coll Cardiol. 2021;77(3):314–25.

[19] Sperotto F, Friedman KG, Son MBF, VanderPluym CJ, Newburger JW, Dionne A. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. Eur J Pediatr. 2021;180(2):307–22.

[20] Parato VM, Notaristefani C, D'Agostino S, D'Emilio V, Colella S, Kadiyala M, et al. COVID-19-related pericarditis with pericardial clotting as a hallmark: two cases and a review. J Cardiovasc Echogr. 2021;31(1):1–5.

[21] Bajaj R, Sinclair HC, Patel K, Low B, Pericao A, Manisty C, et al. Delayed-onset myocarditis following COVID-19. Lancet Respir Med. 2021;9(4):e32–4.

[22] Volis I, Livneh I, Hussein K, Raz-Pasteur A. COVID-19-associated suspected myocarditis as the etiology for recurrent and protracted fever in an otherwise healthy adult. Am J Med Sci. 2021;361(4):522–5.

[23] Paterson I, Ramanathan K, Aurora R, Bewick D, Chow C-M, Clarke B, et al. Long COVID-19: a primer for cardiovascular health professionals, on behalf of the CCS Rapid Response Team. *Can J Cardiol*. 2021 Jun 6. https://doi.org/10.1016/j.cjca.2021.05.011. Online ahead of print.

[24] Silva Andrade B, Siqueira S, de Assis Soares WR, de Souza Rangel F, Santos NO, Dos Santos Freitas A, et al. Long-COVID and post-COVID health complications: an up-to-date review on clinical conditions and their possible molecular mechanisms. Viruses. 2021;13(4):700.

[25] Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846–8.
[26] Piccirillo F, Watanabe M, Di Sciascio G. Diagnosis, treatment and predictors of prognosis of myocarditis. a narrative review. *Cardiovasc Pathol*. 2021 Jun 27:107362, https://doi.org/10.1016/j.carpath.2021.107362. Online ahead of print.
[27] Law YM, Lal AK, Chen S, Čiháková D, Cooper LT Jr, Deshpande S, et al. American Heart Association Pediatric Heart Failure and Transplantation Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young and Stroke Council. Diagnosis and management of myocarditis in children: a Scientific Statement from the American Heart Association. *Circulation*. 2021 Jul 7:CIR0000000000001001. https://doi.org/10.1161/CIR.0000000000001001. Online ahead of print.
[28] Eckart RE, Love SS, Atwood JE, Arness MK, Cassimatis DC, Campbell CL, et al. Department of Defense Smallpox Vaccination Clinical Evaluation Team. Incidence and follow-up of inflammatory cardiac complications after smallpox vaccination. J Am Coll Cardiol. 2004;44(1):201–5.
[29] Kuntz J, Crane B, Weinmann S, Naleway AL, Vaccine Safety Datalink Investigator Team. Myocarditis and pericarditis are rare following live viral vaccinations in adults. Vaccine. 2018;36(12):1524–7.
[30] Cheng MP, Kozoriz MG, Ahmadi AA, Kelsall J, Paquette K, Onrot JM. Post-vaccination myositis and myocarditis in a previously healthy male. Allergy Asthma Clin Immunol. 2016;12:6. https://doi.org/10.1186/s13223-016-0114-4.
[31] Kim YJ, Bae JI, Ryoo SM, Kim WY. Acute fulminant myocarditis following influenza vaccination requiring extracorporeal membrane oxygenation. Acute Crit Care. 2019;34(2):165–9.
[32] Australian Federal Government, Department of Health, Therapeutic Goods Administration COVID-19 vaccine weekly safety report - 15-07-2021 [cited July 15, 2021]. https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-15-07-2021.
[33] Government of Israel, Ministry of Health, June 02, 2021. Surveillance of Myocarditis (Inflammation of the Heart Muscle) Cases Between December 2020 and May 2021 (Including) [cited June 2, 2021]. https://www.gov.il/en/departments/news/01062021-03.
[34] Medicines and Healthcare Products Regulatory Agency (MHRA). Coronavirus vaccine- weekly summary of Yellow Card reporting [Internet]. London (United Kingdom): Department of Health and Social Care; 2021 July 16 [cited July 20, 2021]. https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adversereactions/coronavirus-vaccine-summary-of-yellow-card-reporting.
[35] European Medicines Agency Pharmacovigilance Risk Assessment Committee Summary June 7-10, 2021 [Cited July 20, 2021]. https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-7-10-june-2021.
[36] Public Health Agency of Canada. COVID-19 daily epidemiology update. Ottawa (ON): Government of Canada; 2021 May 12 [cited May 13, 2021]. https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html AND weekly updated events https://health-infobase.canada.ca/covid-19/vaccine-safety/ [cited July 20, 2021].
[37] Center for Disease Control. United States of America Department of Health and Human Services. COVID-19 Vaccine Safety Technical (VaST) Work Group Report, June 28, 2021 [Cited July 13, 2021]. https://www.cdc.gov/vaccines/acip/work-groups-vast/report-2021-06-28.html.
[38] Gargano JW, Wallace M, Hadler SC, Langley G, Su JR, Oster ME, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: Update from the advisory Committee on Immunization Practices - United States, June 2021. MMWR Morb Mortal Wkly Rep. 2021;70(27):977–82.
[39] Kim HW, Jenista ER, Wendell DC, Azevedo CF, Campbell MJ, Darty SN, et al. Patients with acute myocarditis following mRNA COVID-19 vaccination. *JAMA Cardiol*. 2021 Jun 29. https://doi.org/10.1001/jamacardio.2021.2828. Online ahead of print.
[40] 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*. 2021 Jun 28:1–4. https://doi.org/10.1017/S1047951121002547. Online ahead of print.
[41] Muthukumar A, Narasimhan M, Li QZ, Mahimainathan L, Hitto I, Fuda F, et al. In depth evaluation of a case of presumed myocarditis following the second dose of COVID-19 mRNA vaccine. *Circulation*. 2021 Jun 16. https://doi.org/10.1161/CIRCULATIONAHA.121.056038. Online ahead of print.
[42] D'Angelo T, Cattafi A, Carerj ML, Booz C, Ascenti G, Cicero G, et al. Myocarditis after SARS-CoV-2 vaccination: a vaccine-induced reaction? *Can J Cardiol*. 2021 Jun 9;S0828–282X(21)00286-5. https://doi.org/10.1016/j.cjca.2021.05.010. Online ahead of print.
[43] Montgomery J, Ryan M, Engler R, Hoffman D, McClenathan B, Collins L, et al. Myocarditis following immunization with mRNA COVID-19 vaccines in members of the US Military. *JAMA Cardiol*. 2021 Jun 29;e212833. https://doi.org/10.1001/jamacardio.2021.2833. Online ahead of print.
[44] Schauer J, Buddhe S, Colyer J, Sagiv E, Law Y, Chikkabyrappa SM, et al. Myopericarditis after the Pfizer mRNA COVID-19 vaccine in adolescents. *J Pediatr*. 2021 Jul 3:S0022–3476(21)00665-X. https://doi.org/10.1016/j.jpeds.2021.06.083. Online ahead of print.
[45] Berto MB, Spano G, Wagner B, Bernhard B, Häner J, Huber AT, et al. Takotsubo cardiomyopathy after mRNA Covid-19 vaccination. *Heart Lung Circ*. 2021. Jul 14. https://doi.org/10.1016/j.hlc.2021.06.521. Online ahead of print.
[46] Singh K, Marinelli T, Horowitz JD. Takotsubo cardiomyopathy after anti-influenza vaccination: catecholaminergic effects of immune system. Am J Emerg Med. 2013;31(11):1627.e1–4.
[47] Tsabouri S, Makis A, Kosmeri C, Siomou E. Risk factors for severity in children with Coronavirus Disease 2019: a comprehensive literature review. Pediatr Clin North Am. 2021;68(1):321–38.
[48] Frenck RW Jr, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. C4591001 Clinical Trial Group. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med. 2021;385(3):239–50.