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REVIEW

Risk of Coronavirus Disease 2019 Messenger RNA Vaccination-Associated Myocarditis and Pericarditis – A Systematic Review of Population-Based Data

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Purpose: Early studies showed that the risks of mRNA vaccine-associated myocarditis and pericarditis are low but with substantial variation across studies. Study characteristics, ethnicity, vaccine types, dose intervals, and SARS-CoV-2 infection prevalence may influence the rates of myocarditis and pericarditis after mRNA vaccination in population-based studies.

Methods: We comprehensively searched MEDLINE for relevant articles published before November 30, 2022. We also searched the websites of health authorities in several countries for unpublished surveillance data on myocarditis and pericarditis after mRNA vaccination. The outcome of interest was the incidence of myocarditis and pericarditis developed after mRNA vaccination for COVID-19.

Results: A total of 17 studies form 10 countries were included for review. We noted that considerable heterogeneity in study characteristics, including surveillance method, case definition, and observation period, may partially be responsible for the widely varied reported rates. Studies from countries that adopted active surveillance reported higher rates than those using passive surveillance. Compared to BNT162b2 vaccine, mRNA-1273 may have a higher risk of myocarditis only in young men after the second dose. Our comparison of sex-, age-, vaccine type-, and dose-specific rates of myocarditis across countries did not support the hypothesis that individuals with recent SARS-CoV-2 infection and young Asian males were at higher risk. We also could not find sufficient evidence to conclude whether extending the between-dose interval could reduce myocarditis incidence following mRNA vaccination.

Conclusion: Differences in the study characteristics must be fully considered when comparing the risks of mRNA vaccine-related myocarditis and pericarditis in different countries.

Keywords: COVID-19, mRNA vaccine, myocarditis, population-based study, surveillance data

Introduction

Since the first case of myocarditis following mRNA COVID-19 vaccination was reported, cardiac inflammation has been the most concerning serious adverse event of special interest.[1] Despite a considerable number of case reports or case series of myocarditis following mRNA vaccination,[2–5] only a few population-based studies quantifying the risks of myocarditis have been published.[6] Early studies showed that mRNA vaccine-associated myocarditis and pericarditis are rare, mainly occurring in young male recipients following a second dose, but with huge variations in the magnitude of the risk.[7–13] For example, after the second dose of BNT162b2, an Israeli group reported an incidence rate of 150.7 cases and 108.6 cases per million doses for myocarditis in males aged 16–19 years and 20–24 years, respectively,[7] whereas the

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reported rate in US males aged 16–17 years and 18–24 years was 105.9 cases and 52.4 cases per million doses, respectively.[8] In contrast, a Canadian study found a rate of myocarditis in men aged 18–24 years following the second dose of BNT162b2 of 35.5 cases per million doses, and rates after the second dose of mRNA-1273 vaccine was as high as 299.5 cases per million doses.[9] Variations in the risk across these studies may be related to differences in surveillance methods, case definitions, observation periods after vaccination, ethnicity, vaccine types, interval between two doses, and potential interaction between recent SARS-CoV-2 infection and vaccination. However, to the best of our knowledge, no research has systematically explored the source of the heterogeneity.

A study in Singapore showed that the total incidence of myocarditis and pericarditis after mRNA vaccine in males aged 12–19 years was 48.3 cases per million doses.[10] A Hong Kong study reported an incidence of myocarditis and pericarditis in males aged 12–17 years following the first and second dose of BNT162b2 of 55.7 cases and 373.2 cases per million doses, respectively,[11] several folds higher than the incidence reported in the US. These data raised concerns as to whether young Asian men have a higher risk of mRNA vaccine-associated myocarditis and pericarditis.

Four systematic reviews examining the risk of myocarditis and pericarditis following mRNA vaccination have been published.[13–16] They included population-based studies from Israel, North America, Denmark, and Hong Kong, with limited data from the Asia-Pacific region. As an increasing number of new investigations of the risk of mRNA vaccine-associated myocarditis and pericarditis were reported recently, the purpose of this study was to provide the most updated data. We aimed to compare the study characteristics and rates of myocarditis and pericarditis after mRNA vaccination in population-based studies in several countries to scrutinize the possible explanation of variations in the risk. These data can ensure the safety of the mRNA COVID-19 vaccine, help health authorities improve risk management plans, and provide important information for the public to improve COVID-19 vaccine coverage.

Methods

Identification of Studies

We searched MEDLINE for relevant articles published before November 30, 2022. Medical Subjects Heading (MeSH) terms used for keyword and text word searching included COVID-19 vaccines, myocarditis, and pericarditis. The references of systematic reviews on COVID-19 vaccine-related myocarditis and pericarditis were manually examined to identify additional reports not found in the computerized databases.[13–16] We also searched the medRxiv server and the websites of health authorities of several countries for unpublished surveillance data on myocarditis and pericarditis after mRNA vaccination.

Eligibility Criteria

We included population-based studies that provided sex- and age-specific cumulative incidences of myocarditis or myocarditis and pericarditis in vaccine recipients aged 12 years or above following the first and second doses of BNT162b2 or mRNA-1273 vaccine separately because the incidences of mRNA vaccine-associated myocarditis and pericarditis varied substantially across sex and age strata and following different doses of mRNA vaccine. We excluded case reports, case series, and cohort studies in which the participants were not taken from the general population (eg, including only healthcare workers or military members).

Data Extraction

For the comparison of the risk associated with myocarditis, including cases with and without pericarditis, two physician reviewers (YC Lin, CH Chang) independently evaluated each study and extracted relevant characteristics. Disagreement on specific studies between the two reviewers was resolved through discussion. Extracted information included country, study period, study population, data source, data collection, case definition, ascertainment and criteria, observational period after vaccination, number of study participants, and outcomes. Reported rates of myocarditis at 0–7, 0–21, or 0–28 days after vaccination or without restriction on time of onset after vaccination were extracted if these data were available.

Results

We identified 327 studies on mRNA COVID-19 vaccine-associated myocarditis and pericarditis from the computerized literature databases, systematic review reference lists, and the websites of health authorities in several countries (Supplementary Figure 1). A total of 301 studies were excluded because they were case reports, case series, and cohort studies in which the participants were not taken from the general population. We identified 26 potentially eligible reports or surveillance data. Among them, data from Australia,[17] three Canadian studies,[9,18,19] Denmark and Nordic countries,[12,20,21] France,[22] Hong Kong,[11,23] two Israeli studies,[7,24] two Japanese studies,[25,26] Taiwan,[27] and three studies from the US[8,28,29] met our inclusion criteria. Reports or surveillance data from England or the UK,[30–32] Germany,[33] Italy,[34] Singapore,[10] and South Korea[35–37] did not provide sufficient information and were excluded. The characteristics of the 17 studies from 10 countries are listed in Table 1.

Eligible Studies

Of the included studies, Israel and Hong Kong granted emergency authorization only for BNT162b2, whereas other countries approved both BNT162b2 and the mRNA-1273 vaccine. Taiwan recommended a minimum between-dose interval of 4 weeks for adults and 12 weeks for teenagers aged 12–17 years, the other countries adopted 3 to 4-week between-dose intervals for both adults and adolescents. Notably, in Canada, an initial delay in scheduling the second dose because of limited vaccine supply resulted in a longer between-dose interval. We found substantial discrepancies in surveillance methods, case definitions, and observation periods after vaccination across countries. In contrast to the passive surveillance adopted by other countries, the Health Departments of Israel, Hong Kong, and Canada implemented active surveillance for all hospitalized cases. The majority of studies, including Australia, Canada (Ontario), Canada (nationwide), Denmark (Husby et al), France, Hong Kong, Israel, Japan (MHLW), Japan (Yamaguchi et al), Taiwan, the US (VAERS) and the US (VSD), undertook a review of the case history to ascertain whether the diagnostic criteria were met and whether the inclusion criteria were satisfied. Israel included only definite and probable cases of certainty according to the Brighton Collaboration case definition, whereas Canada, Hong Kong, Japan, and Taiwan also enrolled cases classified as possible. The US enrolled patients that were classified as confirmed and probable cases based on Centers for Disease Control and Prevention (CDC) case definitions. Both sets of criteria utilize clinical symptoms, biomarkers, imaging study, and electrocardiogram as diagnostic standards (Supplementary Materials 1–3). In addition, the observation period after vaccination varied in each study. The follow-up period was 7 days in the report from the US and in a nationwide Canadian study enrolling vaccines aged 18–39 years, 14 days in the Hong Kong study, 21 days in the Israeli study, and no restrictions on time were set in the Australian, French, Canadian (Ontario), Japanese, and Taiwanese reports. The follow-up period was set both 7 days and 21 days postvaccination in the Canadian (British Columbia) study. In the two reports from Japan, the follow-up period was 28 days in the study disclosed by Yamaguchi et.al, and there was no restriction on time in the surveillance data provided by the Ministry of Health, Labour and Welfare (MHLW) of Japan.

Heterogeneity in Study Characteristics

Reported rates of myocarditis and pericarditis after mRNA vaccination varied widely across included studies. We explored possible sources of the large variation in cardiac inflammation rates and found considerable heterogeneity in study characteristics, such as surveillance method, case definition, and duration of observation among included studies. Studies from Israel, Hong Kong, and Canada that adopted active surveillance reported higher rates than countries using passive surveillance. Furthermore, we found that duration of observation also had an impact on reported rates (Table 2). Myocarditis and pericarditis cases with onset time 0–7 days following vaccination may account for 61–90% of all cases occurring within the observational period after vaccination. Regarding cases of myocarditis with or without pericarditis, data from Australia and British Columbia, Canada suggested they comprised only 41% and 46% of the total cases, whereas other studies reported that it comprised 61–94% of all myocarditis and/or pericarditis cases combined.

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Table 1 Characteristics of Seventeen Population-Based Studies Included for the Comparison of the Sex- and Age-Specific Incidence of Myocarditis and/or Pericarditis Following mRNA COVID-19 Vaccinations

Study	Study Period	Study Population	Data Source	Number of Individuals Receiving Two Doses of mRNA Vaccination	Data Collection	Myocarditis/ Pericarditis	Case Ascertainment	Criteria	Observational Period After Vaccination	Number of Cases	Stratum with the Highest Incidence (per Million Doses)
Australia[17]	2021/3/1-2022/11/13	Recipients aged 5 years or older received a total of 44.3 million doses of BNT vaccines and 5.4 million doses of Moderna vaccines	Safety reports from Australian Department of Health	NA	Passive surveillance	Myocarditis and pericarditis	Reports were reviewed against an internationally accepted criteria	NA	NA	BNT 706; Moderna 116	Male, 2nd dose, Moderna, age 12–17: 236
Canada, Ontario[9]	2020/12/14- 2021/9/4 (primary analysis on those vaccinated on or after 2021/6/1)	All individuals in Ontario, Canada (population 14.7 million) aged 12 years or older who received at least one dose of COVID-19 mRNA vaccine (total 19.74 million doses)	The Public Health Case and Contact Management Solution and Ontario's electronic reporting system for COVID-19 Adverse Events Following Immunization to identify reports of myocarditis and pericarditis following COVID-19 vaccination submitted to local Public Health Units	BNT 5.83 million; Moderna 3.21 million	Passive surveillance 2020/12-2021/5; Enhanced surveillance 2021/6/1-	Myocarditis and. pericarditis	Case level review of all reports was completed by a group of specialized nurses and physicians on the vaccine safety team	Brighton criteria of definite, probable, and possible cases	No restriction on time to onset	BNT 159; Moderna 138	Male, 2nd dose, Moderna, age 18–24: 299.5
Canada, nationwide[18]	2020/12-2021/10/8	9.20 million individuals aged 18–39 years received at least one dose of mRNA COVID-19 vaccines	Reports of myocarditis and pericarditis submitted to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) by provincial/territorial/federal public health authorities received from their local or regional public health units	BNT 53.24 million; Moderna 28.05 million	Active and passive surveillance	Myocarditis and pericarditis	Cases were reviewed and verified by public health nurses and physicians at public health organizations, and underwent additional medical review after submission to CAEFISS	Brighton criteria of definite, probable, and possible cases	7 days for both vaccine doses	BNT 143; Moderna 229	Male, 2nd dose, Moderna, age 18–29: 139.5

Canada, British Columbia[19]	2020/12/15- 2022/3/10	3.99 million individuals aged 12 years or older received at least one dose of mRNA COVID-19 vaccines	Population health administrative data from the BC COVID-19 Cohort	NA	Active surveillance	Myocarditis	NA	NA	7 days and 21 days for both vaccine dose	BNT 84; Moderna 57	Male, 2nd dose, Moderna, age 18–29: 229.7 (21 days of observational period)
Denmark, Nygaard et al[20]	2021/5/15 – 2021/8/15	A total of 133,477 male and 127,857 female Danish inhabitants 12–17 years of age who received the first dose of BNT vaccine	A multicenter study including all 18 Danish Pediatric Departments for prospective real-time data collection of vaccine-associated disease from May 15, 2021. Cases of myopericarditis were cross checked with the Danish VAERS	NA	Active surveillance	Myocarditis and pericarditis	NA	NA	No restriction on time to onset	BNT 15	Male, 1st dose, BNT, age 12–17: 97
Denmark, Husby et al[12]	2020/10/1-2021/10/5	4.93 million of residents aged 12 years or older; excluding individuals with prior hospital diagnosis of myocarditis or pericarditis between 2017/1/1-2020/9/30	Danish Vaccination Register, Danish National Patient Register, Register of Laboratory Results for Research	BNT 3.42 million; Moderna 0.48 million	Active surveillance	Myocarditis	Co-occurrence of increased troponin and hospital stay more than 24 hours	NA	28 days for both vaccine doses	BNT 48; Moderna 21	Male, 2nd dose, Moderna, age 12–39: 94
Nordic countries[21]	2020/12/27-2021/10/5	23.1 million residents aged 12 years or older in Denmark, Finland, Norway, and Sweden	Nationwide health registers on SARS-CoV-2 vaccination, myocarditis and pericarditis diagnoses in Denmark, Finland, Norway, and Sweden	BNT 13.32 million; Moderna 1.96 million	Active surveillance	Myocarditis and pericarditis	NA	NA	28 days for both vaccine doses	BNT 220; Moderna 75	Male, 2nd dose, Moderna, age 16–24: 198.1

(*Continued*)

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Table 1 (Continued).

Study	Study Period	Study Population	Data Source	Number of Individuals Receiving Two Doses of mRNA Vaccination	Data Collection	Myocarditis/ Pericarditis	Case Ascertainment	Criteria	Observational Period After Vaccination	Number of Cases	Stratum with the Highest Incidence (per Million Doses)
France[22]	2020/12/27-2021/09/20	44.18 million individuals aged 12 years or older received at least one dose of mRNA COVID-19 vaccines	Reports of myocarditis submitted to the regional pharmacovigilance centers (CRPV) of Bordeaux, Marseille, Toulouse, and Strasbourg	BNT 34.09 million; Moderna 4.77 million	Passive surveillance	Myocarditis	Reviewed and analyzed by the CRPVs	NA	NA	BNT 377; Moderna 106	Male, 2nd dose, Moderna, age 16–24: 138.9
Hong Kong[11]	2021/6/14-2021/9/4	178,163 individuals aged 12–27 years (51.8% of the population) received at least one dose of the BNT vaccine (total 305,406 doses)	Reports of myocarditis/ pericarditis cases admitted to one of the public funded hospitals through the Advanced Incident Reporting System to the Drug Office of the Department of Health Hong Kong	NA	Active surveillance	Myocarditis and pericarditis	Suspected cases were investigated according to the Hong Kong Pediatric Investigation Protocol, which was implemented in all HA hospitals. The study team followed the myocarditis and pericarditis case definitions	Brighton criteria of definite, probable, and possible cases	14 and 28 days for both vaccine doses	BNT 33	Male, 2nd dose, Moderna, age 12–17: 388.8 (28 days of observational period)
Israel[7]	2020/12/20-2021/5/31	9.29 million of residents aged 16 years or older	Data received by the Ministry of Health about all hospitalizations on subjects aged ≥16 years where myocarditis was the primary reason for admission.	BNT 5.13 million	Passive surveillance 2020/12-2021/1; Active surveillance 2021/2-	Myocarditis	Hospital records were reviewed by cardiologist/ rheumatologist	Brighton criteria of definite and probable cases	21 days for both vaccine doses	BNT 136	Male, 2nd dose, BNT, age 16–19: 150.7
Israel, adolescent[24]	2021/6/2-2021/10/20	Adolescents aged 12–15 years	Data received by the Ministry of Health about all hospitalizations on subjects aged 12–15 years where myocarditis was the primary reason for admission	BNT 0.33 million	Active surveillance	Myocarditis	Medical records were reviewed by cardiologist/ rheumatologist	Brighton criteria of definite and probable cases	21 days for both vaccine doses	BNT 13	Male, 2nd dose, BNT, age 12–15: 80.9

Japan, MHLW[25]	2021/2/17-2022/7/10	100.88 million residents aged 10 years or older received at least one dose of mRNA COVID-19 vaccines	Reports of suspected adverse reactions from vaccine marketing authorisation holders to the Pharmaceuticals and Medical Devices Agency under the Ministry of Health, Labour and Welfare (MHLW)	BNT 83.61 million; Moderna 16.10 million	Passive surveillance	Myocarditis and pericarditis	Additional investigations and causality assessments, and reports evaluation were conducted by the Pharmaceuticals and Medical Devices Agency.	NA	No restriction on time to onset	BNT 486; Moderna 332	Male, 2nd dose, Moderna, age 10–14: 154.8
Japan, Yamaguchi et al[26]	2021/2/17-2022/5/15	102.21 million residents aged 12 years or older received at least one dose of mRNA COVID-19 vaccines	Reports of suspected adverse reactions from vaccine marketing authorisation holders to the Pharmaceuticals and Medical Devices Agency under the Ministry of Health, Labour and Welfare	BNT 85.81 million; Moderna 16.40 million	Passive surveillance	Myocarditis	Additional investigations and causality assessments, and reports evaluation were conducted by the Pharmaceuticals and Medical Devices Agency	NA	28 days for both vaccine doses	BNT 394; Moderna 251	Male, 2nd dose, Moderna, age 15–19: 129.6
Taiwan[27]	2021/3/22-2022/2/9	19.8 million of individuals aged 12 years or above who received at least one dose of COVID-19 mRNA vaccines	Reports of myocarditis to the Vaccine Adverse Event Reporting System in Taiwan	BNT 5.50 million; Moderna 3.57 million	Passive surveillance	Myocarditis and. pericarditis	Hospital records were reviewed by clinical pharmacists	Brighton criteria of definite, probable, and possible cases	No restriction on time to onset	BNT 160; Moderna 44	Male, 2nd dose, BNT, age 12–17: 122.9
United States, VAERS[8]	2020/12/14-2021/8/31	192.41 million individuals aged 12 years or older received at least one dose of mRNA COVID-19 vaccines	Reports of myocarditis to the US Vaccine Adverse Event Reporting System (VAERS)	BNT 95.53 million; Moderna 66.16 million	Passive surveillance	Myocarditis	Reviewed by CDC physicians and public health professionals	US CDC criteria of confirmed and probable cases	No restriction on time to onset	BNT 1136; Moderna 490	Male, 2nd dose, BNT, age 16–17: 105.9 (7 days of observational period)

(*Continued*)

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Table 1 (Continued).

Study	Study Period	Study Population	Data Source	Number of Individuals Receiving Two Doses of mRNA Vaccination	Data Collection	Myocarditis/ Pericarditis	Case Ascertainment	Criteria	Observational Period After Vaccination	Number of Cases	Stratum with the Highest Incidence (per Million Doses)
United States, claims databases[28]	2020/12/18-2021/12/25	15.1 million individuals aged 18–64 years who received at least one dose of a COVID-19 mRNA vaccine in four claims databases in the US	Four administrative claims databases in the US (Optum, HealthCore, Blue Health Intelligence, and CVS Health)	NA	Active surveillance	Myocarditis and pericarditis	NA	NA	No restriction on time to onset	BNT/ Moderna 411	Male, 2nd dose, Moderna, age 18–25: 142.0 (1–7 days after an mRNA vaccination.)
United States, VSD[29]	2020/12/14-2022/1/15	Members aged 18–39 years of eight integrated healthcare organizations within the Vaccine Safety Datalink (VSD) and vaccinated with either mRNA vaccine.	The electronic health records and medical or pharmacy claims data from eight VSD data-contributing sites for capture of vaccination records along with comprehensive data on demographics, comorbidities, and healthcare utilization	BNT 1.41 million; Moderna 0.88 million	Active surveillance	Myocarditis and pericarditis	All identified potential cases underwent medical record review	US CDC criteria of confirmed and probable cases	7 days for both vaccine doses	BNT 41; Moderna 38	NA

Table 2 Number of Cases, Proportion of Myocarditis with or without Pericarditis, Definite or Probable Cases, Cases Occurring 0–7 Days After Vaccination Over Total Cases Among Seventeen Population-Based Studies

Study	Proportion of Myocarditis with or without Pericarditis Over Total Cases	Proportion of Definite or Probable Cases Over Total Cases	Proportion of Cases 0–7 Days After Vaccination Over Total Cases
Australia, aged ≥12 years[17]	40.6%	78.8%	NA
Canada, Ontario, aged ≥12 years[9]	71.4%	96.7%	73.9%
Canada, nationwide, aged 18–39 years[18]	NA	93.2%	60.6%
Canada, British Columbia, aged ≥12 years[19]	45.8%	NA	70.2%
Denmark, Nygaard et al, aged 12–17 years[20]	80.0%	NA	73.3%
Denmark, Husby et al, aged ≥12 years[12]	NA	NA	NA%
Nordic countries, aged ≥12 years[21]	60.9%	NA	NA
France, aged ≥12 years[22]	NA	NA	NA
Hong Kong, aged 12–27 years[11]	93.9%	97.0%	87.9%
Israel, aged ≥16 years[7]	NA	90.1%	74.3%
Israel, adolescent, aged 12–15 years[24]	NA	NA	NA
Japan, MHLW, aged ≥10 years[25]	81.3%	NA	89.7%
Japan, Yamaguchi et al, aged ≥12 years[26]	75.1%	NA	NA
Taiwan, aged ≥12 years[27]	80.4%	NA	69.1%
United States, VAERS, aged ≥12 years[8]	74.4%	81.7%	87.3%
United States, claims databases, aged 18–64 years[28]	NA	NA	NA
United States, VSD, aged 18–39 years[29]	87.3%	83.2%	NA

Comparing the Risk of Myocarditis

To more lucidly compare the incidence of cardiac inflammation associated with mRNA vaccination, we aimed to visualize the difference of the incidences across the studies under a same observation period and focus solely on myocarditis cases. We extracted individual patient data from the Hong Kong, Japanese (MHLW), and Taiwanese reports and re-calculated the rates of myocarditis (including myopericarditis but excluding pericarditis alone) at 0–7, 0–21, or 28 days, and rates without restriction on time after the first and second doses of BNT162b2 and mRNA-1273 vaccine according to sex and age group. Two Danish reports[12,20] were not included due to the selection of a larger study analyzing data from four Nordic countries. The reports from Canada (British Columbia)[19] and Japan (Yamaguchi et.al)[26] were also not included because of the smaller case numbers comparing to their counterparts from Canada (Ontario) and Japan (MHLW). Two reports from the US[28,29] analyzing claims or electronic healthcare data and one nationwide Canadian study[18] enrolling vaccine recipients aged 18–39 years did not provide the incidence of myocarditis alone and were not included in the comparison as well. Finally, a total of 10 studies were included for comparison (Figure 1–3 and Supplementary Figure 2).

There tended to be a higher rate of mRNA vaccine-related myocarditis in younger individuals than in older individuals, in males than in females, and after the second vaccine dose than after the first dose. The highest risk was observed among young male recipients after two doses of mRNA vaccine. However, the age group with the highest risk differed across these studies. Studies from Australia and Taiwan found that male vaccines aged 12–17 years had the highest risk, and the studies from the

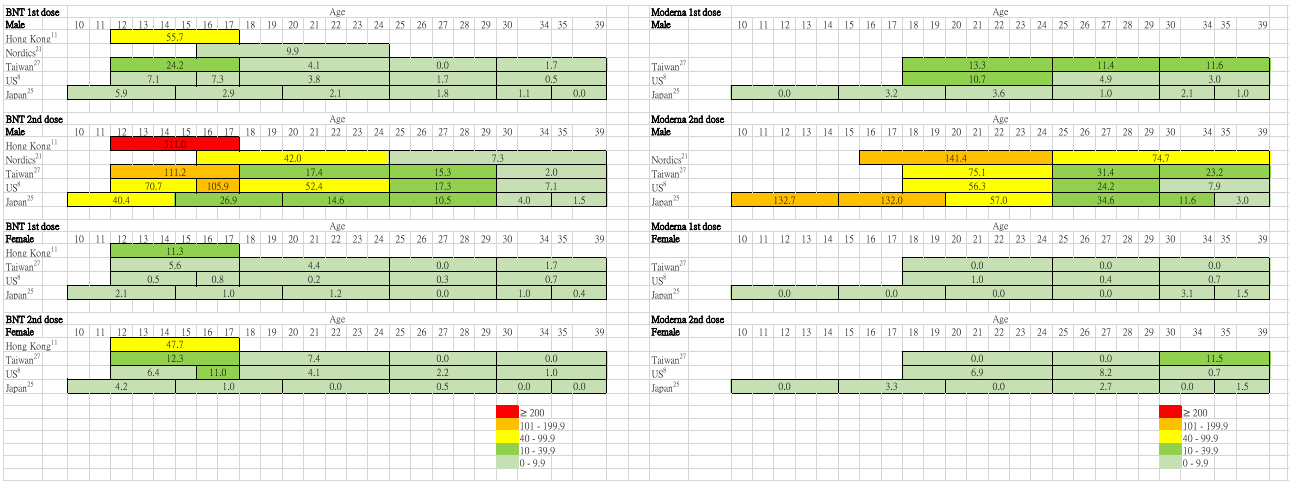

Figure 1 Reported rates of myocarditis (per million persons) at 0–7 days after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine according to sex and age group.

Notes: Studies from Hong Kong, Nordics, Taiwan, the US, and Japan reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) at 0–7 days after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Each risk stratum was marked with a corresponding color.

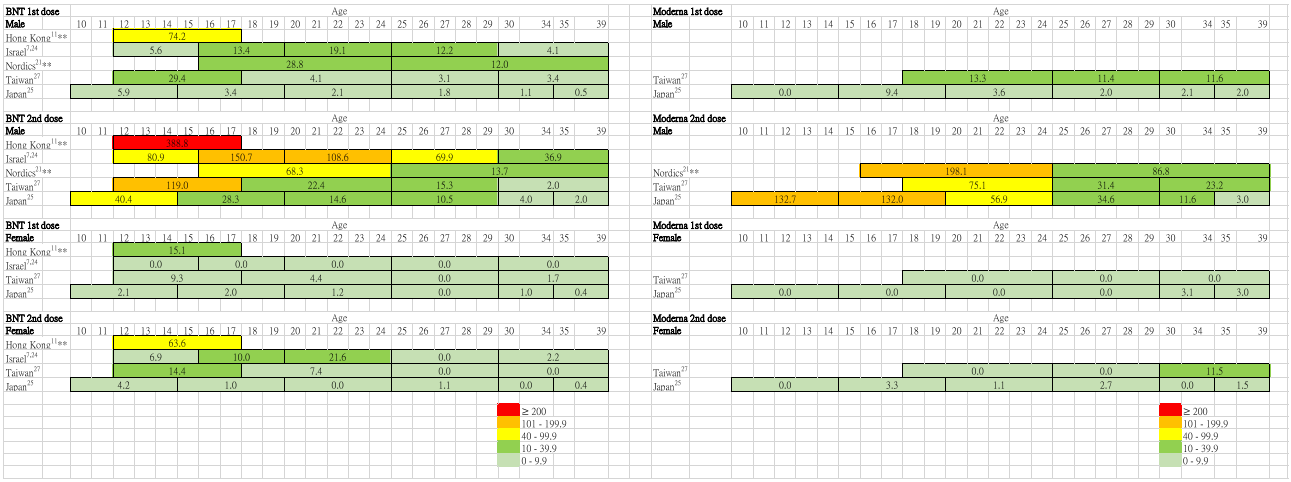

Figure 2 Reported rates of myocarditis (per million persons) at 0–21 or 28 days after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine according to sex and age group.

Notes: Studies from Israel, Taiwan, and Japan reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) at 0–21 days after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Studies form Hong Kong and Nordics reported the risk at 0–28 days. Each risk stratum was marked with a corresponding color. **The observation period after vaccination was 28 days.

US and Israel suggested that 16–17 years and 16–19 years were the age groups with the highest risk, respectively. In contrast, surveillance data from France reported that male vaccine recipients aged 18–24 years had the highest risk.

Between-Dose Interval, Recent SARS-CoV-2 Infection, and Young Asian Males

We further examined whether a shorter between-dose interval, recent SARS-CoV-2 infection, and young Asian males were associated with higher risks of mRNA COVID-19 vaccine-associated cardiac inflammation. Results of a Canadian study indicated that, for males aged 18–24 years receiving two doses of the same mRNA vaccine, the rate of myocarditis and pericarditis was lower in recipients with an interval of more than 56 days compared to less than 30 days.[9] In contrast, a Taiwanese study showed no inverse relationship between a longer between-dose interval and the rate of myocarditis and pericarditis among young males who received two doses of BNT162b2 or the mRNA-1273 vaccine.[27] Based on our comparison, the rate of myocarditis in males aged 12–17 years after the second dose of BNT162b2 in Taiwan was not

Figure 3 Reported rates of myocarditis (per million persons) without restriction on time after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine according to sex and age group.

Notes: Studies from Ontario Canada, Australia, Taiwan, Japan, and France reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) without restriction on time after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Each risk stratum was marked with a corresponding color.

lower with a 12-week interval. In addition, the reported rates of myocarditis after mRNA vaccine among adolescents in Hong Kong and Taiwan were not lower than in other countries with higher prevalence of COVID-19 infections. Meanwhile, despite that Hong Kong reported a significantly higher myocarditis risk, data from Japan and Taiwan did not support that young Asian males were particularly vulnerable to mRNA COVID-19 vaccine-associated myocarditis.

The Risk of Myocarditis Associated with Different Types of mRNA COVID-19 Vaccines

We found that the comparative safety of different types of mRNA COVID-19 vaccines depended on sex, age, and vaccine dosage. For the rate of myocarditis in young men after the first dose of mRNA-1273 vaccine versus BNT162b2, studies from Taiwan, France, and the US reported a slightly higher incidence after the first dose of mRNA-1273 vaccine, whereas the study from Canada showed a higher incidence after the first dose of BNT162b2. In regard to young women, the incidence of myocarditis after the first dose of mRNA-1273 vaccine was similar to the incidence after the first dose of BNT162b2. When we compared the rates of myocarditis after the second dose of different mRNA vaccines, for men, reports from Japan (10–29 years), Taiwan (18–39 years), Nordic countries (16–24 years), Australia (12–39 years), and France (18–29 years), but not the US, showed that the incidences of myocarditis after the second dose of mRNA-1273 vaccine were higher than the incidences after the second dose of BNT162b2. However, for women, the findings became more inconsistent. Women in Taiwan (30–39 years), Australia (12–29 years), France and Canada (18–24 years) had higher rates of myocarditis after the second dose of mRNA-1273 vaccine than after BNT162b2 vaccine. In contrast, reports from Japan and the US found that women had similar rates of myocarditis after the second dose of mRNA-1273 vaccine and BNT162b2.

Discussion

In this systematic review, we comprehensively searched for population-based studies and surveillance data from the Asia-Pacific and Western countries and found that the incidence of mRNA COVID-19 vaccine-associated myocarditis and pericarditis was low. A comparison of 10 studies revealed that reported rates of myocarditis were higher in males than in females, in younger age groups than in older age groups, and after the second dose than after the first dose of vaccine. Most studies observed that male recipients aged 12–17 years after the second dose had the highest reported rate of myocarditis. This study had the following new findings. First, considerable heterogeneity in study characteristics, including surveillance method, case definition, and observation period, may partially be responsible for the widely varied reported rates across

studies. Second, there was an interaction between reported rate and sex, age, vaccine type, and dose. The comparative safety of the two types of mRNA vaccines may depend on different age and sex groups. Third, we could not find sufficient evidence to conclude whether extending the between-dose interval could reduce the incidence of cardiac inflammation following mRNA vaccination. We emphasize that differences in the study characteristics must be fully considered when comparing the rates of mRNA vaccine-related myocarditis and/or pericarditis among different countries.

Surveillance Method and the Reporting Rates of mRNA Vaccine-Associated Myocarditis and Pericarditis

We examined possible sources of the huge variation in the reported rates of myocarditis and pericarditis and found surveillance method was probably the most important influential factor for the magnitude of the reported rate. Studies from Israel, Hong Kong, and Canada that adopted active surveillance reported higher rates than countries using passive surveillance. Indeed, the incidence rates of myocarditis and pericarditis 0–7 days following the second dose of BNT162b2 vaccine among males aged 12–17 years estimated from the active surveillance by the Vaccine Safety Datalink (VSD)[29] was 2- to 3-fold higher than the reporting rates of myocarditis obtained from the US VAERS passive surveillance data.[38] In contrast to the lower rates observed in the study examining data from the US VAERS, an active surveillance study analyzing four large healthcare claims databases in the US[28] found incidence rates very close to those observed in the Israeli active surveillance study.

Between-Dose Interval and Risk of Myocarditis

The shorter between-dose interval of mRNA vaccination could possibly augment a greater immune response against cardiac tissue. A study analyzing nationwide registry data in Denmark[12] reported that the risk of myocarditis for male recipients aged 12–39 years within 28 days after a second dose of BNT162b2 was 18 cases per million doses, lower than that reported in Israel and the US. The authors suggested that it could be due to the longer median time interval between first and second doses in Denmark (median interval 5 weeks for BNT162b2). Taiwan launched a nationwide vaccination campaign for adolescents later than other countries. Considering an increased number of cardiac inflammation cases in the younger populations in other countries after a mass immunization program began and the epidemic was under control at that time, the Taiwan Advisory Committee on Immunization Practices revised the recommended two-dose interval for teenagers to 12 weeks.[27] However, compared to reports from other countries, the rate of myocarditis in males aged 12–17 years after the second dose of BNT162b2 in Taiwan was not lower with a 12-week interval. It is possible that a higher myocarditis and pericarditis reporting rate associated with a shorter between-dose interval observed in the Canadian study during the period of acceleration in second-dose administration due to increased vaccine supply may coincide with an increased vigilance from healthcare professionals and vaccine recipients and also with the change from passive vaccine-safety surveillance to enhanced surveillance system.[9] We suggest that more data are needed for the relationship between risk of myocarditis and interdose interval.

Recent Infection with SARS-CoV-2 Virus and the Risk of mRNA Vaccine-Associated Myocarditis

Husby et al proposed another possible explanation for the lower incidence of myocarditis in Denmark.[12] They suggested that it may be due to fewer Danish residents having tested positive for SARS-CoV-2 than residents in other countries, which may have led to less intense immune reactions against the cardiac tissue by preexisting immunity against SARS-CoV-2. This hypothesis was supported by a French study showing that vaccine recipients who had vaccine-associated myocarditis and pericarditis had a higher rate of previous infection with the SARS-CoV-2 virus than those who did not develop myocarditis and pericarditis after mRNA vaccination.[39] Our study comparing reported rates of myocarditis among several countries provided data against this hypothesis. There were no major outbreaks in Hong Kong and Taiwan before or during their massive immunization program for the young population. However, the reported rates of myocarditis after the first and second doses of mRNA vaccine in adolescents aged 12–17 years were not lower than in other countries.

Risk of mRNA Vaccine-Associated Myocarditis in Young Asian Men and Male Teenagers

Much higher rates of myocarditis after the first and second doses of BNT162b2 in vaccines aged 12–17 years were reported in Hong Kong than in Israel, though both studies monitored vaccine adverse events by active surveillance. And yet, notably, only confirmed and probable cases of myocarditis following BNT162b2 vaccination were included in the Israeli study, whereas possible cases were also included in the Hong Kong study. The extremely high reported rate in Hong Kong may also be partially due to the increased vigilance of mRNA vaccine-associated cardiac inflammation among health authorities, healthcare professionals, and the public, and to the highly efficient healthcare and reporting system in Hong Kong as well. Our systemic review showed that, in general, the incidence of myocarditis after mRNA vaccination among young man and teenage boys in Japan and Taiwan was not higher than the incidence in the US, Canada, and Australia. Apart from the higher incidence reported in Hong Kong, there is currently insufficient data to suggest that young Asian men and teenage boys are at higher risk of myocarditis following mRNA vaccination.

Risk of Myocarditis Associated with mRNA-1273 Vaccine versus BNT162b2 Vaccine

A Canadian study analyzing nationwide data from COVID-19 vaccine recipients aged 18–39 years found that the risk of myocarditis and pericarditis after the second dose of mRNA-1273 vaccine were significantly higher than after the second dose of BNT162b2. Among all age and sex groups, men aged 18–29 years had the highest risk after mRNA-1273 vaccination, with a hazard ratio of 4.72 (95% CI: 3.09–7.39).[18] A study analyzing data from eight VSD sites in the US found risk after the second dose of mRNA-1273 vs BNT162b2 was higher in men aged 18–29 years (hazard ratio 1.31; 95% CI: 0.73–2.31) but not in women (hazard ratio 0.53; 95% CI: 0.02–5.81).[29] In contrast, a study analyzing data from veterans in the US found a significantly higher risk of myocarditis and pericarditis after receiving BNT162b2 compared to mRNA-1273 vaccine.[40] In another study analyzing four large healthcare claims databases in the US, no significant difference in the risk between the two mRNA vaccines was found in men aged 18–25 years.[28] Our study suggested that the relative safety of two types of mRNA vaccine may vary by different age and sex groups and by dose. Compared to mRNA-1273 vaccine, BNT162b2 may have a lower risk of myocarditis only in young men after the second dose. Due to the low incidence of mRNA vaccine-associated myocarditis, the number of myocarditis cases in the subgroup analysis stratified by age and sex in individual studies was insufficient for the comparative safety evaluation. We underline that conclusive evidence about the safety of mRNA vaccines in regard to myocarditis can only be provided by experiences from several countries with sufficient sample size and high-quality real-world data.

Strengths and Limitations

The strengths of this study included an extensive search of the published and unpublished population-based data, providing the most updated surveillance results from countries in Asia, Europe, and North America. We examined study characteristics in detail and presented the reported rates of myocarditis and pericarditis according to sex, age, vaccine type, and dose separately. After understanding the differences in study design, we re-calculated the reported rates according to similar definitions, trying to answer several questions that may partially explain the variations by comparing the risks observed across these studies. Our study also had several limitations. First, we focused on the absolute risk because it was the most commonly reported outcome in the population-based studies and also provided important information on the impact on public health. In addition, relative measures had an inherent limitation that they could not be compared directly across studies using different comparator groups. Second, due to inconsistencies in the age cut-offs across countries and some countries not providing the total numbers of vaccinated persons in each sex and age group, we could not conduct a formal meta-analysis and meta-regression to obtain a pooled estimate with a narrower confidence interval. Data synthesis may not be appropriate in the presence of marked heterogeneity in data collection, computation, and reporting methods. Third, our assessment of the comparative safety between BNT162b2 and the mRNA-1273 vaccine and evaluation of the relationship of the between-dose interval and the incidence of myocarditis were based on an inter-country comparison. Although we attempted to reduce the between-country variation in reporting, our findings were still strongly affected by the different surveillance systems and myocarditis definitions used in the various countries.

In conclusion, myocarditis and pericarditis following mRNA COVID-19 vaccination are rare adverse event in Asian Pacific and Western countries. Substantial variations in the reported rates among countries are partly due to different surveillance approaches, case definitions, and length of follow-up. Future international collaborative research under the same framework is needed to continuously monitor and reduce the risk of mRNA vaccine-associated myocarditis, especially in younger populations.

Data Sharing Statement

The data supporting the findings of this study are available within the article and its supplementary materials.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Bozkurt B, Kamat I, Hotez PJ. Myocarditis With COVID-19 mRNA Vaccines. *Circulation*. 2021;144(6):471–484. doi:10.1161/CIRCULATIONAHA.121.056135.
2. Kim HW, Jenista ER, Wendell DC, et al. Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination. *JAMA Cardiol*. 2021;6(10):1196–1201. doi:10.1001/jamacardio.2021.2828
3. 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(12):1446–1450. doi:10.1001/jamacardio.2021.3471
4. Truong DT, Dionne A, Muniz JC, et al. Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults: suspected Myocarditis After COVID-19 Vaccination. *Circulation*. 2022;145(5):345–356. doi:10.1161/CIRCULATIONAHA.121.056583
5. Woo W, Kim AY, Yon DK, et al. Clinical characteristics and prognostic factors of myocarditis associated with the mRNA COVID-19 vaccine. *J Med Virol*. 2022;94(4):1566–1580. doi:10.1002/jmv.27501
6. Krug A, Stevenson J, Hoeg TB. BNT162b2 Vaccine-Associated Myo/Pericarditis in Adolescents: a Stratified Risk-Benefit Analysis. *Eur J Clin Invest*. 2022;52(5):e13759. doi:10.1111/eci.13759.
7. Mevorach D, Anis E, Cedar N, et al. Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel. *N Engl J Med*. 2021;385(23):2140–2149. doi:10.1056/NEJMoa2109730
8. Oster ME, Shay DK, Su JR, et al. Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021. *JAMA*. 2022;327(4):331–340. doi:10.1001/jama.2021.24110
9. Buchan SA, Chi Yon Seo CY, Johnson C, et al. Epidemiology of Myocarditis and Pericarditis Following mRNA Vaccination by Vaccine Product, Schedule, and Interdose Interval Among Adolescents and Adults in Ontario, Canada. *JAMA Netw Open*. 2022;5(6):e2218505. doi:10.1001/jamanetworkopen.2022.18505
10. Yap J, Tham MY, Poh J, et al. Pericarditis and myocarditis after COVID-19 mRNA vaccination in a nationwide setting. *Ann Acad Med Singap*. 2022;51(2):96–100. doi:10.47102/annals-acadmedsg.2021425
11. Chua GT, Kwan MYW, Chui CSL, et al. Epidemiology of Acute Myocarditis/Pericarditis in Hong Kong Adolescents Following Comirnaty Vaccination. *Clin Infect Dis*. 2022;75(4):673–681. doi:10.1093/cid/ciab989
12. Husby A, Hansen JV, Fosbol E, et al. SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study. *BMJ*. 2021;375:e068665. doi:10.1136/bmj-2021-068665
13. Lane S, Yeomans A, Shakir S. Reports of myocarditis and pericarditis following mRNA COVID-19 vaccination: a systematic review of spontaneously reported data from the UK, Europe and the USA and of the scientific literature. *BMJ Open*. 2022;12(5):e059223. doi:10.1136/bmjopen-2021-059223.
14. Pillay J, Gaudet L, Wingert A, et al. Incidence, risk factors, natural history, and hypothesised mechanisms of myocarditis and pericarditis following covid-19 vaccination: living evidence syntheses and review. *BMJ*. 2022;378:e069445. doi:10.1136/bmj-2021-069445
15. Ling RR, Ramanathan K, Tan FL, et al. Myopericarditis following COVID-19 vaccination and non-COVID-19 vaccination: a systematic review and meta-analysis. *Lancet Respir Med*. 2022;10(7):679–688. doi:10.1016/S2213-2600(22)00059-5
16. Liu Q, Qin C, Liu M, Liu J. Effectiveness and safety of SARS-CoV-2 vaccine in real-world studies: a systematic review and meta-analysis. *Infect Dis Poverty*. 2021;10(1):132. doi:10.1186/s40249-021-00915-3.

17. COVID-19 vaccine weekly safety report - 17-11-2022. Available from: https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-17-11-2022. Accessed December 5, 2022.
18. Abraham N, Spruin S, Rossi T, et al. Myocarditis and/or pericarditis risk after mRNA COVID-19 vaccination: a Canadian head to head comparison of BNT162b2 and mRNA-1273 vaccines. *Vaccine*. 2022;40(32):4663–4671. doi:10.1016/j.vaccine.2022.05.048
19. Zaeema N, Julia L, Michelle S, et al. Observed versus expected rates of myocarditis after SARS-CoV-2 vaccination: a population-based cohort study. *CMAJ*. 2022;194(45):E1529–E1536. doi:10.1503/cmaj.220676
20. 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(1):e25–e28. doi:10.1097/INF.0000000000003389
21. Karlstad O, Hovi P, Husby A, et al. SARS-CoV-2 Vaccination and Myocarditis in a Nordic Cohort Study of 23 Million Residents. *JAMA Cardiol*. 2022;7(6):600–612. doi:10.1001/jamacardio.2022.0583
22. Pfizer Vaccine Pharmacovigilance Investigation - BioNTech Comirnaty: monthly Focus #1 specific situations until September 30, 2021. Available from: https://ansm.sante.fr/actualites/point-de-situation-sur-la-surveillance-des-vaccins-contre-la-covid-19-periode-du-01-10-2021-au-14-10-2021. Accessed December 5, 2022.
23. Li X, Lai FTT, Chua GT, et al. Myocarditis Following COVID-19 BNT162b2 Vaccination Among Adolescents in Hong Kong. *JAMA Pediatr*. 2022;176(6):612–614. doi:10.1001/jamapediatrics.2022.0101
24. Mevorach D, Anis E, Cedar N, et al. Myocarditis after BNT162b2 Vaccination in Israeli Adolescents. *N Engl J Med*. 2022;386(10):998–999. doi:10.1056/NEJMc2116999
25. The 82nd Adverse Reaction Study Council of the Subcommittee on Immunization and Vaccine of the Ministry of Health and Welfare of Japan, the 8th Safety Measures Study Committee of the Subcommittee on Pharmaceutical Safety Measures of the Pharmaceutical Affairs and Food Sanitation Council in 2022. Available from: https://www.mhlw.go.jp/stf/shingi2/0000208910_00046.html. Accessed December 5, 2022.
26. Yamaguchi T, Iwagami M, Ishiguro C, et al. Updated report of COVID-19 vaccine safety monitoring in Japan: booster shots and paediatric vaccinations. *Lancet Reg Health West Pac*. 2022;27:100600. doi:10.1016/j.lanwpc.2022.100600
27. Su WJ, Liu YL, Chang CH, et al. Risk of myocarditis and pericarditis following Coronavirus Disease 2019 messenger RNA vaccination - A nationwide study. *medRxiv*. 2022. doi:10.1016/j.jmii.2023.01.016
28. Wong HL, Hu M, Zhou CK, et al. Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases. *Lancet*. 2022;399(10342):2191–2199. doi:10.1016/S0140-6736(22)00791-7
29. Goddard K, Lewis N, Fireman B, et al. Risk of myocarditis and pericarditis following BNT162b2 and mRNA-1273 COVID-19 vaccination. *Vaccine*. 2022;40(35):5153–5159. doi:10.1016/j.vaccine.2022.07.007
30. Patone M, Mei XW, Handunnetthi L, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. *Nat Med*. 2022;28(2):410–422. doi:10.1038/s41591-021-01630-0
31. Patone M, Mei XW, Handunnetthi L, et al. Risk of Myocarditis After Sequential Doses of COVID-19 Vaccine and SARS-CoV-2 Infection by Age and Sex. *Circulation*. 2022;146(10):743–754. doi:10.1161/CIRCULATIONAHA.122.059970
32. Coronavirus vaccine – summary of Yellow Card reporting. Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting. Accessed December 5, 2022.
33. The Paul Ehrlich Institute, the Germany Federal Ministry of Health. Safety Report: suspected cases of adverse events and vaccine-related complications following vaccination against COVID-19 from 27 December 2020 (start of vaccination campaign) to 31 December 2021. Available from: https://www.pei.de/EN/newsroom/dossier/coronavirus/medicine-safety.html. Accessed December 5, 2022.
34. Massari M, Alegiani SS, Morciano C, et al. Postmarketing active surveillance of myocarditis and pericarditis following vaccination with COVID-19 mRNA vaccines in persons aged 12 to 39 years in Italy: a multi-database, self-controlled case series study. *PLoS Med*. 2022;19(7):e1004056. doi:10.1371/journal.pmed.1004056
35. Lee DS, Kim JW, Lee KL, et al. Adverse events following COVID-19 vaccination in South Korea between February 28 and August 21, 2021: a nationwide observational study. *Int J Infect Dis*. 2022;118:173–182. doi:10.1016/j.ijid.2022.03.007
36. Kim S, Hwang I, Ko M, Kwon Y, Lee YK. Safety monitoring of COVID-19 vaccination among adolescents aged 12 to 17 years old in the Republic of Korea. *Osong Public Health Res Perspect*. 2022;13(3):230–237. doi:10.24171/j.phrp.2022.0122.
37. Korea Disease Control and Prevention Agency, the South Korean Ministry of Welfare and Health. Weekly analysis of adverse reactions after COVID-19 vaccination (week 90); 2022. Available from: https://ncv.kdca.go.kr/board.es?mid=a12609010000&bid=0032#content. Accessed December 5, 2022.
38. Centers for Disease Prevention and Control. Update on myocarditis following mRNA COVID-19 vaccination. Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-06-22-23/03-covid-shimabukuro-508.pdf. Accessed December 5, 2022.
39. Le Vu S, Bertrand M, Jabagi MJ, et al. Age and sex-specific risks of myocarditis and pericarditis following Covid-19 messenger RNA vaccines. *Nat Commun*. 2022;13(1):3633. doi:10.1038/s41467-022-31401-5
40. Dickerman BA, Madenci AL, Gerlovin H, et al. Comparative Safety of BNT162b2 and mRNA-1273 Vaccines in a Nationwide Cohort of US Veterans. *JAMA Intern Med*. 2022;182(7):739–746. doi:10.1001/jamainternmed.2022.2109

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