Srdce a COVID 19

ELIŠKA SOVOVÁ, FNOL A LF UPOL OLOMOUC

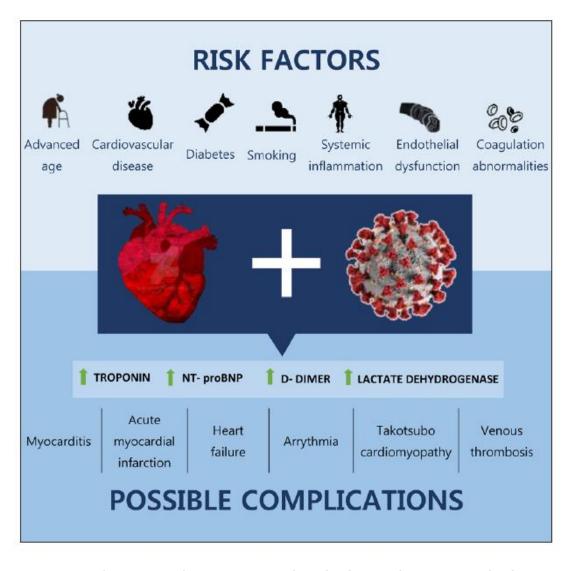
Obsah přednášky

Akutní COVID 19 a postižení srdce

Post COVID 19

Komplikace po vakcinaci proti COVID 19

Akutní COVID 19



AUTHOR	N	(%) WITH ELEVATED TROPONIN	ASSAY USED	PATIENT SETTING
Metkus et al. ²⁰	243	51	Troponin I or T	ICU
Giustino et al. ²¹	305	62	Troponin T	Inpatient
Huang et al. ²²	41	12	Hypersensitive troponin I	Inpatient
Han et al. ²³	273	5.05% (outpatients) 23.33% (inpatients) 20% (ICU)	Hypersensitive troponin I	Outpatient, inpatient, ICU
Richardson et al. ¹²	5,700	22.6	Variety of assays	Inpatient
Petrilli et al. ²⁴	4,103	11.7	Not reported	Outpatient and inpatient
Wang et al.25	138	7.2	Troponin I	Inpatient
Zhou et al. ²⁶	191	17	High-sensitivity troponin I	Inpatient
Guo et al. ¹⁸	187	27.8	Troponin T	Inpatient
Shi et al. ¹⁹	416	19.7	High-sensitivity troponin I	Inpatient

Table 1 Summary of cardiac injury prevalence (defined as troponin elevation) in COVID-19 studies. 12,18-76 ICU: intensive care unit

Myokardiální postižení (pozitivní troponin nebo pozitivní BNP) u 12-62% osob, u těchto osob vyšší mortalita (51% vs 4,5%)

Akutní COVID 19 a myokarditis

Acute Myocarditis

Probable Case

- Presence of ≥ 1 new or worsening of the following clinical symptoms
- · chest pain/ pressure/ discomfort
- · dyspnea/shortness of breath
- · palpitations
- syncope
- AND ≥ 1 new finding of · elevated troponin above upper limit of
- normal · abnormal ECG or rhythm monitoring
- findings consistent with myocarditis'
- · abnormal cardiac function or wall motion abnormalities on echocardiogram
- · cardiac MRI findings consistent with myocarditis †
- · AND no other identifiable cause of the symptoms and findings

Confirmed Case

CDC Working Case Definitions

- Presence of ≥ 1 new or worsening of the following clinical symptoms
- chest pain/ pressure/ discomfort
- · dyspnea/shortness of breath
- palpitations
- syncope
- AND
- · histopathologic confirmation of myocarditis ‡
- OR
- · elevated troponin above upper limit of normal AND cardiac MRI findings consistent with myocarditis[†]
- · AND no other identifiable cause of the symptoms and findings

Acute Pericarditis

Probable Case

- acute chest pain (typically described as pain made worse by lying down, deep inspiration, cough, and relieved by sitting up or leaning forward, although other types of chest pain may occur) 5
- · pericarditis rub on exam
- · new ST-elevation or PRdepression on ECG
- · new or worsening pericardial effusion on echocardiogram or
- pericarditis on basis of meeting histopathologic criteria of the pericardium

 Presence of ≥ 2 new or worsening of the following clinical symptoms

- · Autopsy cases may be classified as

Figure 1. Centers for Disease Control and Prevention working case definitions for acute myocarditis and acute pericarditis. Adapted from Centers for Disease Control and Prevention. Copyright ©2021, Centers for Disease Control and Prevention.

Bolesti, dušnost

EKG

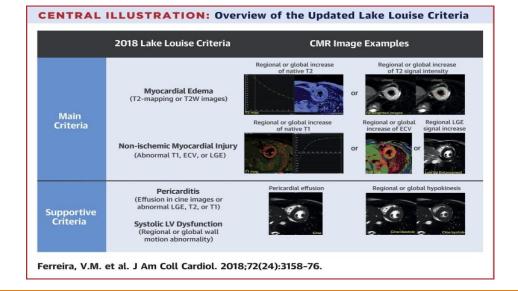
Laboratoř

Echokardiografie

MRI

STATE OF THE ART

Endomyokardiální biopsie



Association Between COVID-19 and Myocarditis Using Hospital-Based Administrative Data — United States, March 2020–January 2021

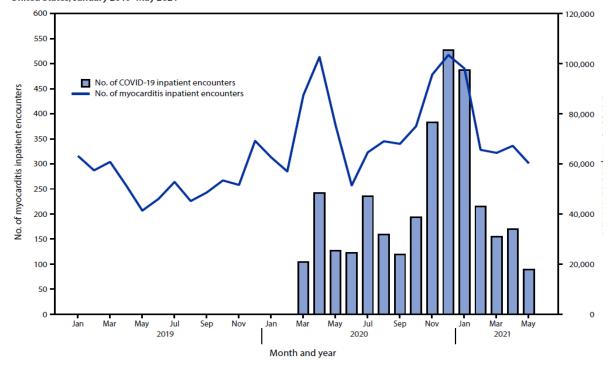
Tegan K. Boehmer, PhD^{1,*}; Lyudmyla Kompaniyets, PhD^{1,*}; Amy M. Lavery, PhD¹; Joy Hsu, MD¹; Jean Y. Ko, PhD¹; Hussain Yusuf, MD¹; Sebastian D. Romano, MPH¹; Adi V. Gundlapalli, MD, PhD¹; Matthew E. Oster, MD^{1,2,3}; Aaron M. Harris, MD¹

TABLE. Frequency of and risk for myocarditis among patients with and without COVID-19 and adjusted* myocarditis risk differences and risk ratios comparing patients with and without COVID-19 — Premier Healthcare Database Special COVID-19 Release, United States, March 2020–January 2021

	No. of	No. of	No. of	patien	Myocarditis among patlents with COVID-19		among ts VID-19	Adjusted	Adjusted
Characteristic	patients with COVID-19	patients without COVID-19	patients with myocarditis	No. (% of patients with myocarditis)	Risk, %	No. (% of patients with myocarditis)	myocardit th risk differei		myocarditis risk ratio (95% CI)
Overall	1,452,773	34,552,521	5,069	2,116 (41.7)	0.146	2,953 (58.3)	0.009	0.126 (0.112-0.140)	15.7 (14.1–17.2)
Sex									
Male	680,722	14,339,356	3,008	1,274 (42.4)	0.187	1,734 (57.6)	0.012	0.165 (0.146-0.183)	13.8 (12.3-15.3)
Female	772,051	20,213,165	2,061	842 (40.9)	0.109	1,219 (59.1)	0.006	0.100 (0.087-0.113)	17.8 (15.6-20.0)
Age group, yrs									
<16	64,898	3,670,762	218	86 (39.4)	0.133	132 (60.6)	0.004	0.122 (0.065-0.179)	36.8 (25.0-48.6)
16-24	123,865	3,067,575	511	121 (23.7)	0.098	390 (76.3)	0.013	0.088 (0.061-0.115)	7.4 (5.5-9.2)
25-39	268,549	6,246,568	862	208 (24.1)	0.077	654 (75.9)	0.010	0.067 (0.052-0.081)	6.7 (5.5-8.0)
40-49	198,561	4,147,909	620	213 (34.4)	0.107	407 (65.6)	0.010	0.093 (0.078-0.109)	10.0 (8.1-11.9)
50-64	356,697	7,965,264	1,226	553 (45.1)	0.155	673 (54.9)	0.008	0.137 (0.121-0.154)	17.0 (14.7-19.3)
65-74	214,331	5,318,474	801	398 (49.7)	0.186	403 (50.3)	0.008	0.160 (0.135-0.184)	23.0 (19.4-26.7)
≥75	225,872	4,135,969	831	537 (64.6)	0.238	294 (35.4)	0.007	0.208 (0.179-0.237)	31.6 (25.9-37.2)

Abbreviation: CI = confidence interval.

FIGURE 1. Number of myocarditis and COVID-19 inpatient encounters, by month* — Premier Healthcare Database Special COVID-19 Releas United States, January 2019–May 2021



^{*} Adjusted risk differences and risk ratios for myocarditis during or after COVID-19 (reference group: no COVID-19), obtained from a single logit model with the following covariates: a three-way interaction between presence of COVID-19, sex, and age group, including lower-order interactions and main effects; race/ethnicity; payer type; hospital U.S. Census region; and hospital urbanicity.



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Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations



Marc K. Halushka^{a,*}, Richard S. Vander Heide^b

Méně než 2%

Journal of Cardiac Failure Vol. 27 No. 1 2021

Clinically Suspected Myocarditis in the Course of Severe Acute Respiratory Syndrome Novel Coronavirus-2 Infection: Fact or Fiction?

KRZYSZTOF OZIERANSKI, ¹ AGATA TYMINSKA, ¹ SZYMON JONIK, ¹ RE MARCIN GRABOWSKI, ¹ KRZYSZTOF J. FILIPIAK, ¹ GRZEGORZ

COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis?

Massimo Imazio , ^{1,2} Karin Klingel, ³ Ingrid Kindermann, ⁴ Antonio Brucato, ⁵ Francesco Giuseppe De Rosa, ⁶ Yehuda Adler, ⁷ Gaetano Maria De Ferrari ⁸

Cardiovascular Pathology 54 (2021) 107361



Contents lists available at ScienceDirect

Cardiovascular Pathology





Original article

COVID-19 myocarditis: quantitative analysis of the inflammatory infiltrate and a proposed mechanism *.**



Sharon E. Fox 1,2, Lacey Falgout 1, Richard S. Vander Heide 1,*

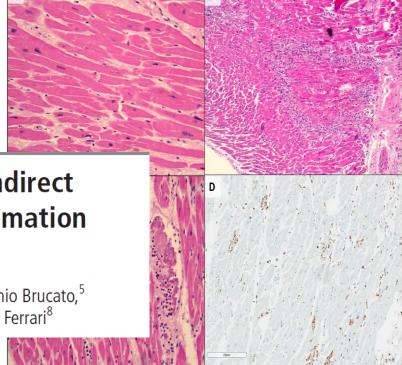


Fig. 1. (A) Cardiac myocytes from control patient (H&E). (B) Myocarditis, characterized by patchy, dense inflammation within the myocardium (H&E). (C) Endotheliitis and diffuse, perivascular distribution of inflammation in COVID-19. (D) CD68 immunostaining highlighting the presence of CD68+ cells in a mild, diffuse intravascular and perivascular distribution in a case of COVID-19.

European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis

The Task Force for the management of COVID-19 of the European Society of Cardiology

Prosinec 2021

While initial studies suggested that myocarditis may occur early during COVID-19, more recent studies have been less convincing in showing an association between myocarditis and SARS-CoV-2 infection. A definitive diagnosis of myocarditis should be based on endomyocardial biopsies or autopsy using established histologic and immunohistochemical criteria. While the presence of virus has

been demonstrated in the heart from patients who died from COVID-19,¹⁰⁹ the endomyocardial biopsy criteria for myocarditis, with the classic type of acute lymphocytic myocarditis or lymphocytic inflammatory cardiomyopathy, have yet to be convincingly demonstrated. Thus, myocarditis seems to be an uncommon complication in the course of SARS-CoV-2 infection.¹¹⁰

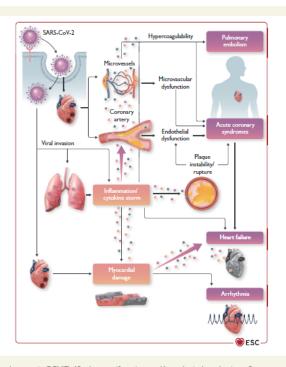


Figure 2 Cardiovascular involvement in COVID-19—key manifestations and hypothetical mechanisms. Severe acute respiratory syndrome cororavirus 2 anchors on transmembrane ACE2 to enter the host cells including type 2 pneumocytes, macrophages, endothelial cells, pericytes, and cardiac myocytes, leading to inflammation and multiorgan failure. In particular, the infection of endothelial cells or pericytes could lead to severe microvascular and macrovascular dysfunction. Furthermore, in conjunction with the immune over-reactivity, it can potentially destabilize atherosclerotic plaques and explain the development of the acute coronary syndrome. Infection of the respiratory tract, particularly of type 2 pneumocytes, by severe acute respiratory syndrome coronavirus 2 is manifested by the progression of systemic inflammation and immune cell overactivation, leading to a 'cytokine storm', which results in an elevated level of cytokines such as IL-6, IL-7, IL-22, and CXCL10. Subsequently, it is possible that activated T cells and macrophages may infiltrate infected myocardium, resulting in the development of fulminant myocarditis and severe cardiac damage. This process could be further intensified by the cytokine storm. Similarly, the viral invasion could cause cardiac myocyte damage directly leading to myocardial dysfunction and contribute to the development of arrhythmia. CXCL10, C-X-C motif chemokine ligand 10, IL-6, interleukin 6; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

ARTICLE IN PRESS

Trends in Cardiovascular Medicine xxx (xxxx) xxx



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[m5G; January 5, 2022; 2:22]

Diagnosing COVID-19 myocarditis in athletes using cMRI

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Published studies with cardiac screening post COVID-19 in athletes,

Study	Clark et al [12]	Rajpal et al [13]	Starekova Et al [14]	Brito et al [15]	Malek et al [16]	Martinez et al [17]	Moulson et al [20]	Hendrickson et al [18]	Daniels et al [19]
Design Study size (cMRI performed)	Retro Obs 59 (59)	Prosp Obs 26 (26)	Retro Obs 145 (145)	Cross Obs 160 (48)	Retro Obs 26 (26)	Cross Obs 789 (30)	Prosp Obs 3018 (317)	NA 137 (5)	Retro Obs 1597 (1597)
Control group	60 military personal & athletes (h); 27 Healthy controls (i)	no	no	20 Athletes (cMRI not performed)	no	no	no	no	no
Blind read	no	no	no	no	no	no	no	no	no
Mean Age	20 (19-22)b	19.5 (1.5)a	19,6 (1,3)a	19 (18-21)b	24 (21-27)b	25 (3)a	20 (1)a	20 (18-27)c	NC
Mean Time to cMRI (SD or Median IQR)	21,5 (13-37)b	26 (10)a	15 (11-194)c	27 (22-33)c	32 (22-62)b	19 (17)a	33 (18-63)b	22 (11)a	22 (10-77)c
T1 Elevation No√total No. tested (%)	23/59 (39%), 8/60 (13%) (h), 2/27 (8%) (i)D	none	2/145 (1,3%)	9 (19%)	none	none	3/317 (0.9%)	NA	5/1597 (0,31%)
T2 Elevation, No./total No. tested (%)		4/26 (15,3%)	2/145 (1,35%)	0/48	4/26 (15%)	1/30 (3,3%)	7/317(2.2%)	0/5	31/1597 (1,9%)
LGE, No./total No. tested (%)	16/22 (27%) 10/27 (24%)(h)	12/26 (46,1%)	42/145 (28,9%)	1/48 (2%)	1/26 (4%)	2/30 (6,6%) with LGE	13/317 (4,1%)	0/5	36/1597 (2,2%)
Pericardial enhancement (x) No./total No. tested (%)	1/22 (4.5%)	2/4 (7.7%)	1/145 (0,6%)	19/48(39,5%)	1 (3.8%)	2/30 (6,6%)	10/317 (3,1%)	NA	1/1597 (0,06%)
Elevated troponin No./total No. tested (%)	none	none	5/145 (3.4%)	1/48 (2%)	4/26 (15%)e	12/789 (1,52%)	24/2719 (0.9%)	4/137 (2,9%)	6/1597 (0,37%)
Outcome in full cohort No/total No. tested (%)	2/59 (3,3%) myocarditis 1/59 (1,6%) pericarditis	4/26 (15,4%) myocarditis	2/145 (1,38%) myocarditis	0	No myocarditis	3/789 (0,38%) myocarditis; 2/789 (0,25%) pericarditis	15/3018 myocarditis (0.5%)f	No myocarditis	37/2461 myocarditis (1,5%)g

Akutní COVID 19 a akutní koronární syndrom



European Heart Journal - Quality of Care and Clinical Outcomes (2020) **0**, 1–7 ORIGINAL ARTICLE European Society doi:10.1093/ehjqcco/qcaa046

Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: a survey by the European Society of Cardiology

Guilherme Pessoa-Amorim (1) 1,2, Christian F. Camm (1) 1,3, Parag Gajendragadkar (1) 1,3,4, Giovanni Luigi De Maria (1) 2,5, Celine Arsac⁶, Cecile Laroche⁶, José Luis Zamorano (1) 7, Franz Weidinger (1) 8, Stephan Achenbach⁹, Aldo P. Maggioni (1) 6,10, Chris P. Gale (1) 11,12,13, Athena Poppas (1) 14, and Barbara Casadei (1) 2,3,4*

3101 responses were received from 141 countries across 6 continents. 88.3% responded that their country was in "total lockdown" and 7.1% in partial lockdown. 78.8% responded that the number of patients presenting with STEMI was reduced since the coronavirus outbreak and 65.2% indicated that the reduction in STEMI presentations was >40%. Approximately 60% of all respondents reported that STEMI patients presented later than usual and 58.5% that >40% of STEMI patients admitted to hospital presented beyond the optimal window for primary percutaneous intervention (PCI) or thrombolysis. Independent predictors of the reported higher rate of delayed STEMI presentation were a country in total lockdown, >100 COVID-19 cases admitted locally, and the complete restructuring of the local cardiology service.

<u>Circulation</u>

RESEARCH LETTER

Acute COVID-19 and the Incidence of Ischemic Stroke and Acute Myocardial Infarction

oke After COVID-19 Diagnosis

	Ischemic stroke (44 patients)		AMI (17 patients)	
	Incidence ratio (95% CI)	P value	Incidence ratio (95% CI)	P value
Primary analysis, risk interval days 1 through 14	12.9 (7.1–23.5)	<0.001	5.9 (1.9–18.2)	0.002
Sensitivity analyses				
Risk interval days 1 through 21	10.1 (5.6–18.2)	<0.001	3.9 (1.3–11.8)	0.018
Risk interval 1 month (days 1 through 31)	6.6 (3.6–11.9)	<0.001	3.4 (1.2–9.7)	0.021
Controlled for calendar month*	8.7 (4.7–16.2)	<0.001	4.7 (1.5–15.4)	0.010
Preexposure period (7 days)†	14.2 (7.7–26.3)	<0.001	6.3 (2.0–19.4)	0.001
Preexposure period (14 days)†	14.4 (7.7–26.9)	<0.001	6.7 (2.1–20.9)	0.001
Control interval limited to 3 months before exposure	10.0 (5.3–18.6)	<0.001	4.7 (1.5–14.7)	0.008
Control interval limited to 6 weeks before exposure	7.9 (4.2–14.9)	<0.001	4.9 (1.5–16.2)	0.010
Control interval limited to postexposure time	13.3 (5.7–30.7)	<0.001	15.1 (2.8–82.4)	0.002
Control interval limited to preexposure time	12.8 (6.7–24.6)	<0.001	4.6 (1.5–14.6)	0.008
Control interval starting on February 27, 2020‡ (date of first confirmed COVID-19 case in Denmark)	8.1 (4.3–15.3)	<0.001	5.1 (1.5–17.6)	0.009

CONTEMPORARY REVIEW

Akutní COVID 19 a arytmie

Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management @

Bhurint Siripanthong, BA(Cantab),* Saman Nazarian, MD, PhD, FHRS,[†] Daniele Muser, MD,[†] Rajat Deo, MD, MTR,[†] Pasquale Santangeli, MD, PhD,[†] Mohammed Y. Khanji, MBBCh, MRCP, PhD,^{‡§} Leslie T. Cooper Jr., MD,[#] C. Anwar A. Chahal, MBChB, MRCP, PhD^{†¶||}

(Heart Rhythm 2020;17:1463–1471)

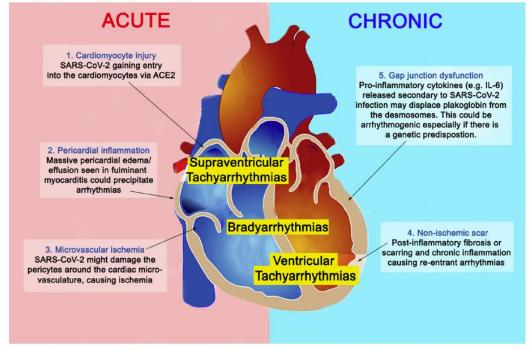


Figure 2 Arrhythmogenesis in SARS-CoV-2-related myocarditis. Possible mechanisms responsible for arrhythmias in SARS-CoV-2-related myocarditis are shown. Mechanisms 1, 2, and 3 could occur in the acute setting, whereas mechanisms 4 and 5 occur in chronic/healed myocarditis. Abbreviations as in Figure 1.

Akutní COVID 19 a arytmie

COVID-19 and cardiac arrhythmias

Anjali Bhatla, BA,* Michael M. Mayer, BS,* Srinath Adusumalli, MD, MSc,* Matthew C. Hyman, MD, PhD,* Eric Oh, MS,† Ann Tierney, MS,† Juwann Moss, BS,* Anwar A. Chahal, MD, PhD,* George Anesi, MD, MSCE, MBE,† Srinivas Denduluri, PhD,* Christopher M. Domenico, PharmD,* Jeffrey Arkles, MD,* Benjamin S. Abella, MD, MPhil, John R. Bullinga, MD,* David J. Callans, MD, FHRS,* Sanjay Dixit, MD, FHRS,* Andrew E. Epstein, MD, FHRS,* David S. Frankel, MD, FHRS,* Fermin C. Garcia, MD,* Ramanan Kumareswaram, MD,* Saman Nazarian, MD, PhD, FHRS,* Michael P. Riley, MD, PhD,* Pasquale Santangeli, MD, PhD,* Robert D. Schaller, DO, FHRS,* Gregory E. Supple, MD, FHRS,* David Lin, MD, FHRS,* Francis Marchlinski, MD, FHRS,* Rajat Deo, MD, MTR*

(Heart Rhythm 2020;17:1439–1444)

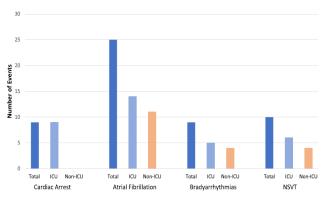


Figure 1 Arrhythmic events by intensive care unit (ICU) status. The number of cardiac arrests and arrhythmias are depicted in the entire cohort of patients with coronavirus disease 2019 (dark blue), those admitted to the ICU (light blue), and those admitted to a non-ICU ward (orange). NSVT = nonsustained ventricular tachycardia.

700 pacientů s COVID 19-9 srdečních zástav, 25 FS, 9 bradykardie, 10 NSKT Závislé na přidružené základní nemoci

Table 2 Characteristics of cardiac arrests in patients with COVID-19

Patient no.	Cardiac arrest on hospital day no.	Cardiac arrest rhythm	Background/etiology	Outcome
1	1	Asystole	85 yo nursing home resident presenting with respiratory distress.	ROSC; eventually WOC
2	5	PEA	59 yo with a h/o systemic scleroderma and recent hospitalization for ILD presented with pneumonia and hypoxia.	ROSC; remains hospitalized
3	2	PEA	35 yo who underwent elective C-section and was diagnosed with COVID-19 per routine screening. Suspected amniotic fluid embolism.	ROSC; discharged with baby
4	18	PEA	41 yo with a h/o obesity, CHD, and diabetes presented with respiratory distress.	ROSC; remains hospitalized
5	5	PEA	55 yo with mitral valve endocarditis and developed acute stroke. Recovering from mechanical thrombectomy and became nonresponsive.	Deceased
6	5	PEA	50 yo with a h/o scleroderma after double lung transplantation 2.5 y ago presented with respiratory failure.	Deceased
7	45	Asystole	74 yo presented with respiratory failure. Complicated hospitalization including multiorgan dysfunction.	Deceased
8	1	TdP	42 yo presented with respiratory failure. Complicated hospitalization including left ventricular dysfunction and ECMO.	ROSC; remains hospitalized
9	1	PEA	43 yo with a h/o morbid obesity presented with fever and respiratory distress.	ROSC; discharged

CHD = coronary heart disease; COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; h/o = history of; ILD = interstitial lung disease; PEA = pulseless electrical activity; ROSC = return of spontaneous circulation; TdP = torsades de pointes; WOC = withdrawal of care; yo = years old.

Akutní COVID 19 a arytmie



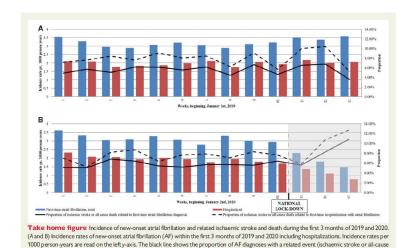
FASTTRACK CLINICAL RESEARCH

Atrial fibrillation

Pokles o 47%

New-onset atrial fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of 5.6 million people

Anders Holt ¹*, Gunnar H. Gislason^{1,2}, Morten Schou ¹, Bochra Zareini¹, Tor Biering-Sørensen¹, Matthew Phelps ², Kristian Kragholm ^{3,4}, Charlotte Andersson ⁵, Emil L. Fosbøl⁶, Morten Lock Hansen¹, Thomas A. Gerds ^{2,7}, Lars Køber^{6,8}, Christian Torp-Pedersen ⁹, and Morten Lamberts ¹



death within 7 days of AF diagnosis); the dotted line shows the proportion among hospitalized patients with new-onset AF. Proportions in % are read

Akutní COVID 19 a srdeční selhání

Heart Failure Reviews https://doi.org/10.1007/s10741-020-10008-2

Heart failure and COVID-19

Feras Bader 1,2 • Yosef Manla 3 • Bassam Atallah 4 • Randall C Starling 5

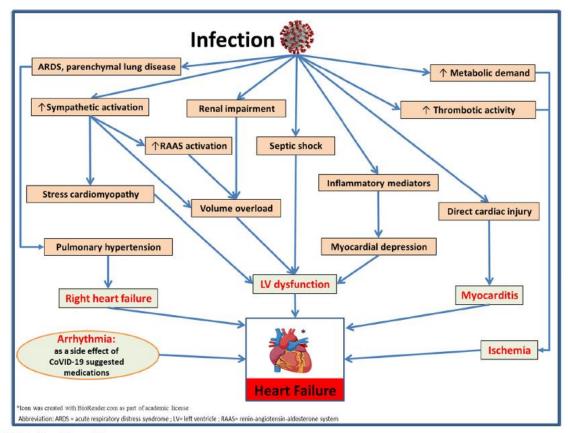


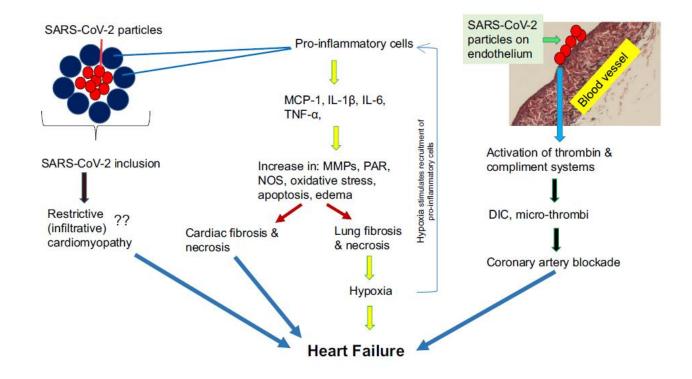
Fig. 1 COVID-19 and heart failure

Akutní COVID 19 a srdeční selhání

Heart Failure Reviews https://doi.org/10.1007/s10741-020-10037-x

Mechanisms of COVID-19-induced heart failure: a short review

Ernest A. Adeghate¹ · Nabil Eid¹ · Jaipaul Singh²



Post COVID



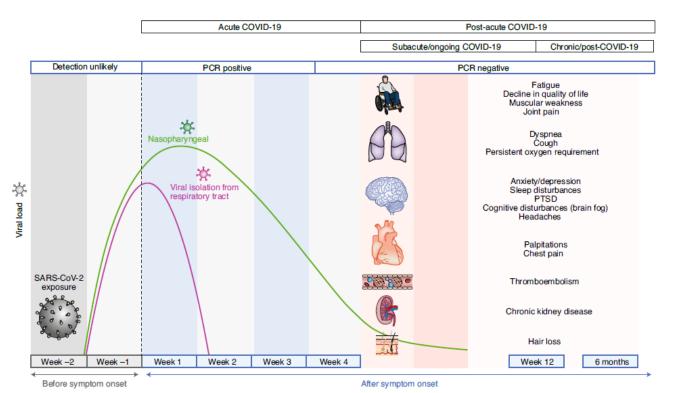
FOCUS | **REVIEW ARTICLE**

https://doi.org/10.1038/s41591-021-01283-z



Post-acute COVID-19 syndrome

Ani Nalbandian 1,24, Kartik Sehgal 2,3,4,24, Aakriti Gupta 1,5,6, Mahesh V. Madhavan 1,5,



Box 1 | Summary of post-acute COVID-19 by organ system

Pulmonar

- Dyspnea, decreased exercise capacity and hypoxia are commonly persistent symptoms and signs
- Reduced diffusion capacity, restrictive pulmonary physiology, and ground-glass opacities and fibrotic changes on imaging have been noted at follow-up of COVID-19 survivors
- Assessment of progression or recovery of pulmonary disease and function may include home pulse oximetry, 6MWTs, PFTs, high-resolution computed tomography of the chest and computed tomography pulmonary angiogram as clinically appropriate

Hematologic

- Thromboembolic events have been noted to be <5% in post-acute COVID-19 in retrospective studies
- The duration of the hyperinflammatory state induced by infection with SARS-CoV-2 is unknown
- Direct oral anticoagulants and low-molecular-weight heparin may be considered for extended thromboprophylaxis after risk-benefit discussion in patients with predisposing risk factors for immobility, persistently elevated D-dimer levels (greater than twice the upper limit of normal) and other high-risk comorbidities such as cancer

Cardiovascular

- Persistent symptoms may include palpitations, dyspnea and chest pain
- Long-term sequelae may include increased cardiometabolic demand, myocardial fibrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction
- Patients with cardiovascular complications during acute infection or those experiencing persistent cardiac symptoms may be monitored with serial clinical, echocardiogram and electrocardiogram follow-up

Neuropsychiatric

- Persistent abnormalities may include fatigue, myalgia, headache, dysautonomia and cognitive impairment (brain fog)
- Anxiety, depression, sleep disturbances and PTSD have been reported in 30-40% of COVID-19 survivors, similar to survivors of other pathogenic coronaviruses
- The pathophysiology of neuropsychiatric complications is mechanistically diverse and entails immune dysregulation,

inflammation, microvascular thrombosis, iatrogenic effects of medications and psychosocial impacts of infection

Renal

- Resolution of AKI during acute COVID-19 occurs in the majority of patients; however, reduced eGFR has been reported at 6 months follow-up
- COVAN may be the predominant pattern of renal injury in individuals of African descent
- COVID-19 survivors with persistent impaired renal function may benefit from early and close follow-up in AKI survivor clinics

Endocrine

- Endocrine sequelae may include new or worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralization
- Patients with newly diagnosed diabetes in the absence of traditional risk factors for type 2 diabetes, suspected hypothalamic-pituitary-adrenal axis suppression or hyperthyroidism should undergo the appropriate laboratory testing and should be referred to endocrinology

Gastrointestinal and hepatobiliary

- Prolonged viral fecal shedding can occur in COVID-19 even after negative nasopharyngeal swab testing
- COVID-19 has the potential to alter the gut microbiome, including enrichment of opportunistic organisms and depletion of beneficial commensals

Dermatologic

 Hair loss is the predominant symptom and has been reported in approximately 20% of COVID-19 survivors

MIS-C

- Diagnostic criteria: <21 years old with fever, elevated inflammatory markers, multiple organ dysfunction, current or recent SARS-CoV-2 infection and exclusion of other plausible diagnoses
- Typically affects children >7 years and disproportionately of African, Afro-Caribbean or Hispanic origin
- Cardiovascular (coronary artery aneurysm) and neurologic (headache, encephalopathy, stroke and seizure) complications can occur

Komplikace vakcinace proti COVID 19

SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study

Anders Husby,^{1,2} Jørgen Vinsløv Hansen,² Emil Fosbøl,³ Emilia Myrup Thiesson,² Morten Madsen,⁴ Reimar W Thomsen,⁴ Henrik T Sørensen,⁴ Morten Andersen,⁵ Jan Wohlfahrt,² Gunnar Gislason,^{6,7,8} Christian Torp-Pedersen,^{9,10,11} Lars Køber,³ Anders Hviid^{2,5}

ABSTRACT

OBJECTIVE

To investigate the association between SARS-CoV-2 vaccination and myocarditis or myopericarditis.

DESIGN

Population based cohort study.

SETTING

Denmark.

PARTICIPANTS

4931775 individuals aged 12 years or older, followed from 1 October 2020 to 5 October 2021.

MAIN OUTCOME MEASURES

The primary outcome, myocarditis or myopericarditis, was defined as a combination of a hospital diagnosis of myocarditis or pericarditis, increased troponin levels, and a hospital stay lasting more than 24 hours. Follow-up time before vaccination was compared with follow-up time 0-28 days from the day of vaccination for both first and second doses, using Cox proportional hazards regression with age as an underlying timescale to estimate hazard ratios adjusted for sex, comorbidities, and other potential confounders.

RESULTS

During follow-up, 269 participants developed myocarditis or myopericarditis, of whom 108 (40%) were 12-39 years old and 196 (73%) were male. Of 3 482 295 individuals vaccinated with BNT162b2

(Pfizer-BioNTech), 48 developed myocarditis or myopericarditis within 28 days from the vaccination date compared with unvaccinated individuals (adjusted hazard ratio 1.34 (95% confidence interval 0.90 to 2.00); absolute rate 1.4 per 100 000 vaccinated individuals within 28 days of vaccination (95% confidence interval 1.0 to 1.8)). Adjusted hazard ratios among female participants only and male participants only were 3.73 (1.82 to 7.65) and 0.82 (0.50 to 1.34), respectively, with corresponding absolute rates of 1.3 (0.8 to 1.9) and 1.5 (1.0 to 2.2) per 100 000 vaccinated individuals within 28 days of vaccination, respectively. The adjusted hazard ratio among 12-39 year olds was 1.48 (0.74 to 2.98) and the absolute rate was 1.6 (1.0 to 2.6) per 100 000 vaccinated individuals within 28 days of vaccination. Among 498814 individuals vaccinated with mRNA-1273 (Moderna), 21 developed myocarditis or myopericarditis within 28 days from vaccination date (adjusted hazard ratio 3.92 (2.30 to 6.68); absolute rate 4.2 per 100 000 vaccinated individuals within 28 days of vaccination (2.6 to 6.4)). Adjusted hazard ratios among women only and men only were 6.33 (2.11 to 18.96) and 3.22 (1.75 to 5.93), respectively, with corresponding absolute rates of 2.0 (0.7 to 4.8) and 6.3 (3.6 to 10.2) per 100 000 vaccinated individuals within 28 days of vaccination, respectively. The adjusted hazard ratio among 12-39 year olds was 5.24 (2.47 to 11.12) and the absolute rate was 5.7 (3.3 to 9.3) per 100 000 vaccinated individuals within 28 days of vaccination.

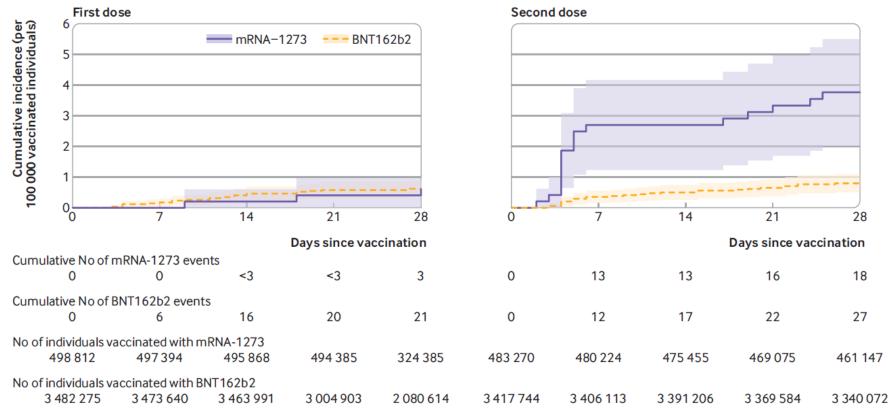


Fig 3 | Cumulative incidence of myocarditis or myopericarditis events after vaccination, by vaccine type and dose number

Myocarditis after Covid-19 Vaccination in a Large Health Care Organization

Guy Witberg, M.D., Noam Barda, M.D., Ph.D., Sara Hoss, M.D., Ilan Richter, M.D., M.P.H., Maya Wiessman, M.D., Yaron Aviv, M.D., Tzlil Grinberg, M.D., Oren Auster, M.Sc., Noa Dagan, M.D., Ph.D., M.P.H., Ran D. Balicer, M.D., Ph.D., M.P.H., and Ran Kornowski, M.D.

RESULTS NEJM 2021

Among more than 2.5 million vaccinated HCO members who were 16 years of age or older, 54 cases met the criteria for myocarditis. The estimated incidence per 100,000 persons who had received at least one dose of vaccine was 2.13 cases (95% confidence interval [CI], 1.56 to 2.70). The highest incidence of myocarditis (10.69 cases per 100,000 persons; 95% CI, 6.93 to 14.46) was reported in male patients between the ages of 16 and 29 years. A total of 76% of cases of myocarditis were described as mild and 22% as intermediate; 1 case was associated with cardiogenic shock. After a median follow-up of 83 days after the onset of myocarditis, 1 patient had been readmitted to the hospital, and 1 had died of an unknown cause after discharge. Of 14 patients who had left ventricular dysfunction on echocardiography during admission, 10 still had such dysfunction at the time of hospital discharge. Of these patients, 5 underwent subsequent testing that revealed normal heart function.

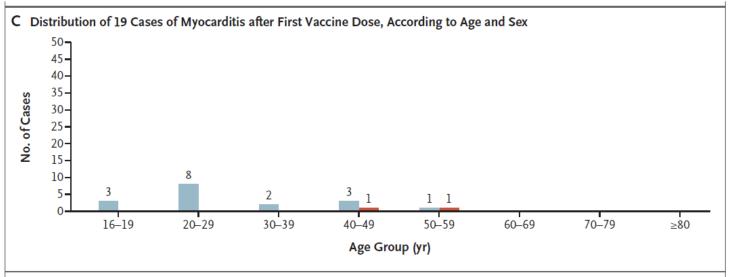
ORIGINAL ARTICLE

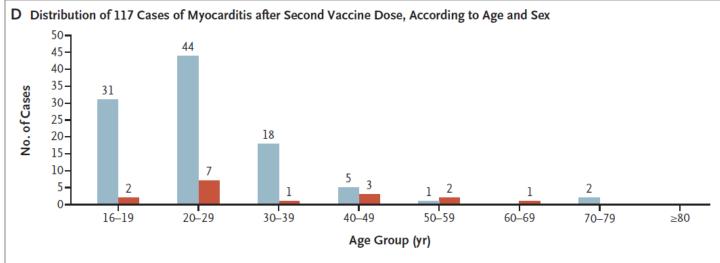
Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

D. Mevorach, E. Anis, N. Cedar, M. Bromberg, E.J. Haas, E. Nadir, S. Olsha-Castell,
D. Arad, T. Hasin, N. Levi, R. Asleh, O. Amir, K. Meir, D. Cohen, R. Dichtiar,
D. Novick, Y. Hershkovitz, R. Dagan, I. Leitersdorf, R. Ben-Ami, I. Miskin,
W. Saliba, K. Muhsen, Y. Levi, M.S. Green, L. Keinan-Boker, and S. Alroy-Preis

RESULTS

Among 304 persons with symptoms of myocarditis, 21 had received an alternative diagnosis. Of the remaining 283 cases, 142 occurred after receipt of the BNT162b2 vaccine; of these cases, 136 diagnoses were definitive or probable. The clinical presentation was judged to be mild in 129 recipients (95%); one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46). As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.





Age and Sex		First Dose			Second Dose	
	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)
	nu	ımber		nur	nber	
All recipients†	25	17.55	1.42 (0.92–2.10)	126	23.43	5.34 (4.48–6.40
16–19 yr						
Male	3	1.86	1.62 (0.32-4.72)	32	2.35	13.60 (9.30–19.2
Female	0	0.23	0	2	0.30	6.74 (0.76–24.3
20–24 yr						
Male	5	2.33	2.14 (0.69–5.00)	26	3.05	8.53 (5.57–12.50
Female	1	0.42	2.37 (0.03-13.20)	6	0.56	10.76 (3.93–23.4
25–29 yr						
Male	3	2.17	1.39 (0.28-4.05)	20	2.87	6.96 (4.25–10.7
Female	0	0.30	0	1	0.39	2.54 (0.03–14.1
≥30 yr						
Male	10	8.13	1.23 (0.59–2.26)	32	11.04	2.90 (1.98–4.09
Female	3	2.11	1.42 (0.29-4.15)	7	2.87	2.44 (0.98–4.09

Table 5. Rate Ratios for a Diagnosis of Myocarditis within 30 Days after the Second Dose of Vaccine, as Compared with Unvaccinated Persons (January 11 to May 31, 2021).

Age and Sex	Vaccinated Group		Unvaccina	Rate Ratio (95% CI)	
	Person-Days of Follow-up	Cases	Person-Days of Follow-up	Cases	
		n	umber		
All recipients*	149,786,065	117	296,377,727	98	2.35 (1.10-5.02)
16–19 yr					
Male	6,018,541	31	19,135,706	11	8.96 (4.50–17.83)
Female	6,033,192	2	17,768,696	2	2.95 (0.42-20.91)
20–24 yr					
Male	7,088,335	27	20,926,320	13	6.13 (3.16-11.88)
Female	6,889,399	5	20,832,407	2	7.56 (1.47–38.96)
25–29 yr					
Male	6,590,263	18	20,944,595	16	3.58 (1.82–7.01)
Female	6,417,564	1	20,943,920	0	0
≥30 yr					
Male	53,577,403	26	82,419,957	40	1.00 (0.61-1.64)
Female	57,171,368	7	93,406,126	14	0.82 (0.33–2.02)

^{*} Data for all vaccine recipients have been weighted according to age and sex.

Journal Pre-proof

TEMPORARY REMOVAL: A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products

Jessica Rose PhD, MSc, BSc, Peter A. McCullough MD, MPH

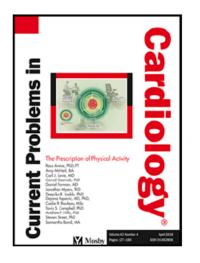
PII: S0146-2806(21)00226-7

DOI: https://doi.org/10.1016/j.cpcardiol.2021.101011

Reference: YMCD 101011

To appear in: Current Problems in Cardiology

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Výskyt myokarditidy je vyšší u mladší populace 13 až 23 let (p<0.0001) 80% u mužů.

U skupiny 12-15 let, byl výskyt myokarditidy po očkování 19x vyšší než je výskyt v této věkové skupině.

Výskyt po 2. dávce byl 5x vyšší.

67% výskytu bylo po BNT162b2 (Pfizer BioNTech)

Z celkového výskytu myokarditidy 6 osob umřelo (1.1%), dva ve věku pod 20 let.

Circulation

PRIMER



Myocarditis With COVID-19 mRNA Vaccines

Biykem Bozkurt[®], MD, PhD; Ishan Kamat, MD; Peter J. Hotez, MD, PhD

ABSTRACT: Myocarditis has been recognized as a rare complication of coronavirus disease 2019 (COVID-19) mRNA vaccinations, especially in young adult and adolescent males. According to the US Centers for Disease Control and Prevention, myocarditis/pericarditis rates are ≈12.6 cases per million doses of second-dose mRNA vaccine among individuals 12 to 39 years of age. In reported cases, patients with myocarditis invariably presented with chest pain, usually 2 to 3 days after a second dose of mRNA vaccination, and had elevated cardiac troponin levels. ECG was abnormal with ST elevations in most, and cardiac MRI was suggestive of myocarditis in all tested patients. There was no evidence of acute COVID-19 or other viral infections. In 1 case, a cardiomyopathy gene panel was negative, but autoantibody levels against certain selfantigens and frequency of natural killer cells were increased. Although the mechanisms for development of myocarditis are not clear, molecular mimicry between the spike protein of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and self-antigens, trigger of preexisting dysregulated immune pathways in certain individuals, immune response to mRNA, and activation of immunologic pathways, and dysregulated cytokine expression have been proposed. The reasons for male predominance in myocarditis cases are unknown, but possible explanations relate to sex hormone differences in immune response and myocarditis, and also underdiagnosis of cardiac disease in women. Almost all patients had resolution of symptoms and signs and improvement in diagnostic markers and imaging with or without treatment. Despite rare cases of myocarditis, the benefit-risk assessment for COVID-19 vaccination shows a favorable balance for all age and sex groups; therefore, COVID-19 vaccination is recommended for everyone ≥12 years of age.

Table 1. Expected Versus Observed Number of Myocarditis/Pericarditis Cases in 7-Day Risk Window After Dose 2 of mRNA Covid-19 Vaccination*

Females			Males			
Age groups	Doses administered	Expected*,†	Observed*	Doses administered	Expected*,†	Observed*
12-17 y	2 189 726	0-2	19	2039871	0-4	128
18-24 y	5 237 262	1-6	23	4337287	1-8	219
25-29 y	4151975	0-5	7	3 625 574	1-7	59
30-39 y	9356296	2-18	11	8311301	2-16	61
40-49 y	9 927 773	2-19	18	8577766	2-16	34
50-64 y	18696450	4-36	18	16255927	3-31	18
65+ y	21708975	4-42	10	18041547	3-35	11

COVID-19 indicates coronavirus disease 2019.

*Preliminary myocarditis/pericarditis reports to US Vaccine Adverse Event Reporting System after dose-2 mRNA vaccination, expected vs observed number of cases using 7-day risk window with data through June 11, 2021. Includes total preliminary reports identified by Centers for Disease Control and Prevention Advisory Committee on Immunization Practices through Vaccine Adverse Event Reporting System database searches for reports with myocarditis/pericarditis codes and prescreened Vaccine Adverse Event Reporting System reports with signs and symptoms consistent with myocarditis/pericarditis. Observed cases may include probable and confirmed cases by Centers for Disease Control and Prevention. Adapted from Centers for Disease Control and Prevention⁵ with permission. Copyright ©2021, Centers for Disease Control and Prevention.

+Based on US population-based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines and expected counts among females 12 to 29 years of age adjusted for lower prevalence relative to males by factor of 1.73.6 Adapted from Centers for Disease Control and Prevention⁵ with permission. Copyright ©2021, Centers for Disease Control and Prevention.

Table 2. Crude Reporting Rates of Myocarditis/Pericarditis Cases per Million Doses After mRNA COVID-19 Vaccination

	Female rates	per million do	ses	Male rates p	Male rates per million doses			
Age groups	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2		
12-17 y	4.2	1.1	9.1	32.4	9.8	66.7		
18-24 y	3.6	1.5	5.5	30.7	8.7	56.3		
25-29 y	2.0	0.8	2.6	12.2	4.5	20.4		
30-39 y	1.8	1.4	1.8	6.9	2.0	10.0		
40-49 y	2.0	0.9	2.8	3.5	1.0	5.1		
50-64 y	1.6	1.0	1.8	1.9	1.0	2.3		
65+ y	1.1	0.6	1.2	1.2	0.7	1.4		

Preliminary myocarditis/pericarditis crude reporting rates per million mRNA vaccine doses administered by sex and dose number to US Vaccine Adverse Event Reporting System following mRNA COVID-19 vaccination with no restrictions on post-vaccination observation time, data through June 11, 2021. Adapted from Centers for Disease Control and Prevention⁵ with permission. Copyright ©2021, Centers for Disease Control and Prevention. COVID-19 indicates coronavirus disease 2019.

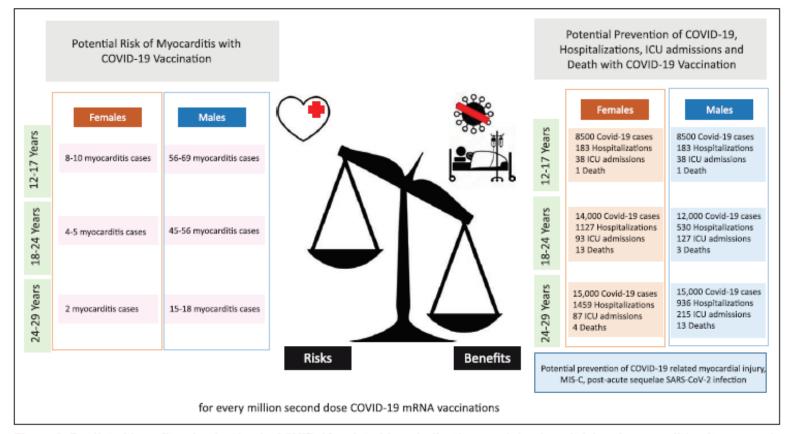


Figure 2. Predicted benefits of reduction in COVID-19-related hospitalizations and death and risks of myocarditis after second dose of mRNA COVID-19 vaccination by age group.

Adapted from Centers for Disease Control and Prevention⁵ with permission. Copyright ©2021, Centers for Disease Control and Prevention (*COVID-19 mRNA vaccines in adolescents and young adults: Benefit-risk presentation"). Predictions for hospitalization and myocarditis rates were calculated for every million doses of mRNA vaccine based on hospitalization rates from Coronavirus Disease 2019 (COVID-19)—Associated Hospitalization Surveillance Network (COVID-NET) as of May 22.⁷¹ Benefit/risk were calculated over 120 days. To meet the ECG or rhythm-monitoring criterion, at least 1 of the following must be included: ST-segment or T-wave abnormalities, paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias, atrioventricular nodal conduction delays or intraventricular conduction defects. COVID-19 indicates coronavirus disease 2019; ICU, intensive care unit; MIS-C, multisystem inflammatory syndrome in children; and SARS-CoV-2, severe acute respiratory syndrome coronavirus-2. †Using either the original or revised Lake Louise criteria.⁷² ‡Using the Dallas criteria.⁷³ §Autopsy cases may be classified as pericarditis on the basis of meeting histopathologic criteria of the pericardium.

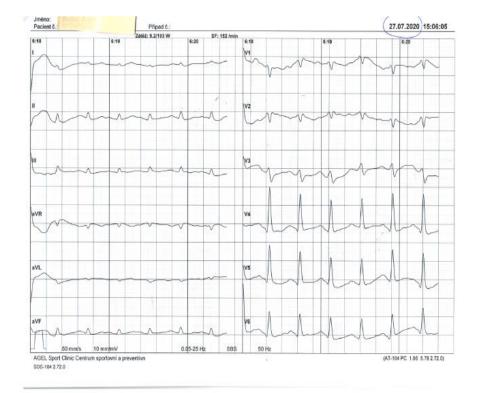
Kazuistika

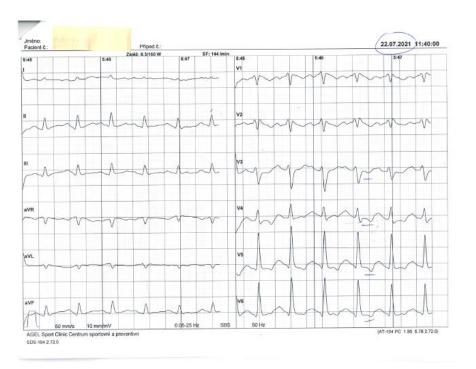
Hokejista XY 20 let, negativní osobní anamnéza (pouze opakované fraktury z hokeje)

RA: sestra AVRT, dědeček aneurysma aorty

Očkovaný proti COVID 19

Odeslán pro neg T vlny, deprese ST úseku, KES, hraniční QTc





2020 2021

Kazuistika

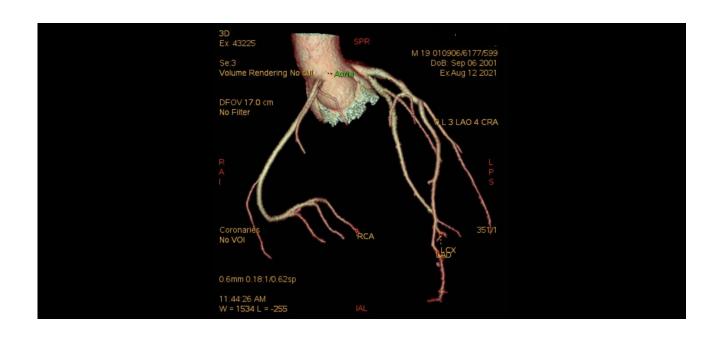
EKG bez patologie

Echokardiografie normální rozměry, bez poruchy diastolické fce, minimální mitrální a trikuspidální regurgitace

Laboratoř: vyšší gamaglobuliny

MRI EF 43%, bez pozdního sycení

CT koronarografie negativní nález



Kazuistika

Kontrola za 3 měsíce

EKG holter ojedinělé SVES

MRI: EF 45%

Spiroergometrie: 4,7 W/kg, VO2 max 5066 ml (138% normy), VO2 max ml/kg/min 50

Doporučení pro... I Guidelines

Doporučené postupy ESC pro sportovní kardiologii a pohybovou aktivitu pacientů s kardiovaskulárním onemocněním, 2020.

Souhrn dokumentu připravený Českou kardiologickou společností

(2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. Summary of the document prepared by the Czech Society of Cardiology)

Vladimír Tuka^a, Otakar Jiravský^{b,c}, Peter Kubuš^d, Eliška Sovová^e

Doporučení pro pohybovou aktivitu a sport u jedinců s myokarditidou						
Doporučení	Třídaª	Úroveň				
Komplexní vyšetření včetně zobrazovacích metod, zátěžového testování a EKG holterovského monitorování je doporučeno po zotavení z akutní myokarditidy k určení rizika NSS spojeného se zátěží.	1	В				

Doporučení pro pohybovou aktivitu a sport u jedinců s myokarditidou (Dokončení)

Doporučení	Třídaª	Úroveň
Návrat ke všem intenzitám zátěže včetně závodního sportu by měl být zvážen po 3–6 měsících u asymptomatických jedinců s normální hodnotou troponinu a biomarkerů zánětu, s normální EF LK při echokardiografii a CMR, s absencí známek pokračujícího zánětu nebo myokardiální fibrózy na CMR, s dobrou funkční kapacitou a s absencí četných a/ nebo komplexních KA při EKG holterovské monitoraci nebo při zátěžovém testu.	lla	c
Ani rekreační, ani závodní sport není doporučen jedincům s pravděpodobnou nebo potvrzenou diagnózou akutní myokarditidy po dobu aktivního zánětu.	III	С
Pohybová aktivita se střední až vysokou intenzitou zátěže není doporučena v období 3–6 měsíců po akutní myokarditidě.	Ш	В
Ani rekreační, ani závodní sport s vysokou intenzitou zátěže není doporučen u jedinců s reziduální myokardiální fibrózou a přetrvávající dysfunkcí LK.	Ш	С

CMR – magnetická rezonance srdce; EF LK – ejekční frakce levé komory; KA – komorová arytmie; NSS – náhlá srdeční smrt. ^a Třída doporučení. ^b Úroveň důkazů.

Děkuji za pozornost