Myopericarditis and COVID-19: a systematic review of cases

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Discussion

We recently published a systematic review on the electrocardiographic (ECG) findings in patients with coronavirus disease-19 (COVID-19) [1]. In the abovementioned study, we observed myopericarditis as one of the possible patterns of cardiac involvement in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Earlier studies show that myopericarditis was most frequently linked to post-viral inflammations

with different viruses, and SARS-CoV-2 might be another virus causing this condition [2]. Therefore, we aimed to closely inspect the published studies (mostly case reports) regarding this pattern.

We systematically searched PubMed (29 results), Embase (26 results), Scopus (25 results), and Cochrane (no results) databases for the following key-terms: "Myopericarditis" and "COVID-19", "SARS-CoV-2", "SARS-CoV2", "2019-nCoV" or "Novel coronavirus." We included the original studies investigating myopericarditis in patients with COVID-19. Articles without a retrievable full-text were excluded, including abstracts and conference abstracts.

We found a total of 24 cases in 20 studies (19 case reports and a case series). Among the 19 patients with available age, gender, and comorbidity data, 10 (52.6%) were female. The mean age was 50.6 ± 8.9 , with one of the cases being a pediatric patient [3]. Seven (36.8%) had no known previous comorbidities. Two patients had a history of previous myopericarditis [4,5]. Of these 19 patients, eight (42.1%) and 10 (52.6%) presented with chest pain and dyspnea respectively.

Ten of 21 patients (47.6%) with ECG data had typical or mostly-typical findings of pericarditis: diffuse ST elevations with PR depressions in nonaVR leads and reverse changes in the aVR. In 14 cases with reports of left ventricular (LV) function on echocardiography, a decreased LV ejection fraction (LVEF) (LVEF <50% (6, 7)) was observed in 7/14 (50%). Five of 24 (20.8%) patients developed cardiac tamponade, and 4/24 (16.7%) died. Table 1 presents patient characteristics, symptoms, physical examinations,

Table 1: Summary of the findings in the included studies

Study (Ref)	Patient characteristics and comorbidities	Symptoms on admission	Physical examin- ation	1) ECG* and 2) cardiac biomarkers at presentation	Echocardiographic findings	Complication	Management
3		Persistent fever,	1) Vital signs: HR: 120 bpm, RR: 26, SpO ₂ : 92%, T: 38.6 °C	1) N/A	Normal cardiac chambers size,		
	1-year-10- month-old girl with no previous cardiovascular history	conjunctivitis, generalized rash, edema in eyelids, hands, and feet, general discomfort, occasional cough, and light arthralgia.	2) Heart: normal sounds and rhythm, no murmurs.	2) Troponin T: 29.1 pg/ml	normal diameter of coronary arteries, and	Pericardial thickening, minor effusion without signs of tamponade; survived	Antibiotics (azithromycin, ampicillin/ sulbactam), paracetamol, and intravenous hydration
			3) Lungs: preserved vesicular murmur.	CK-MB; 18.1 ng/ml	light pericardial effusion more evident in right chambers, without signs of cardiac tamponade		
	47-year-old woman with previous myopericarditis	old with us rrditis	1) Vital signs:	1) Sinus tachycardia and concave infero- lateral ST elevation	Initial echocardiogram: normal LV function and a global pericardial effusion with a	Cardiac tamponade; survived	Pericardiocentesis, IV fluid resuscitation, transferred to the ITU for vasopressor support.
			BP. 80/50, HR: 110, T: 36.9 ℃	2) Troponin T levels were 225 and 253 ng/L.	maximum depth of 1.1 cm and no tamponade, Repeat		
					echocardiogram: further accumulation of		
					pericardial effusion to a maximal depth of 2 cm, with evidence of cardiac tamponade		

5	50-year-old woman with a history of hypertension, reactive arthritis, and previous myeopericarditis in 2012	Central chest pain (worse on lying flat and deep inspiration), without dyspnea and cough	 1) Vital signs: BP.116/74 mmHg, HR: 85 bpm, SatO2: 97%, afebrile 2) Heart: normal 3) Lungs: normal Examination findings were normal 	 Poor R-wave progression and small QRS complexes Troponin T: 77 ng/L 	Trivial anterior pericardial effusion with good biventricular function	Myopericarditis, myositis; survived	Colchicine, ibuprofen, and prednisolone
	60-year-old	Severe ongoing	1) Stable hemodynamic parameters, T= 39°C, no need for oxygen therapy.	1) Normal sinus rhythm and flattened T waves in lateral leads		COVID-19	Colchicine,
9	man with no comorbities	a week, and acute anosmia	2) The physical examination was normal	2) High-sensitivity cardiac troponin I peak: 639 ng/L	N/A	myopericarditis, AF; survived	Flecainide.
							maintenance dose of colchicine
		Palpitations and general malaise without dyspnea, chest pain, or respiratory symptoms	1) Vital signs: HR: 137 bpm, BP: 98/54, SpO2: 95%, T: 36.5 °C	1) Diffuse concave ST elevation,	Global LV hypokinesia, severely reduce LV systolic function (LVEF <30%), mild pericardial effusion (2 mm), no valvular disease	Fulminant myocarditis with stage B cardiogenic shock, COVID-19 pneumonia; survived	ICI I admission O
12	38-year-old woman with no comorbidities		2) Heart: Tachycardia without elevated JVP or heart murmurs	PR segment depression, Spodick's sign			supplementaion, methylprednisolone, IVIg, HCQ, azithromycin, lopinavir/ritonavir, norepinephrine, dobutamine, and
			3) Lungs: Bibasal soft inspiratory crackles	2) Troponin I: 1,190 ng/L, BNP: 13,000 pg/ml			levosimendan; Furosmide
			1) Vital signs	1) Sinus tachycardia with ST segment elevation and PR depression in leads I, aVL, and V5-V6, and			
13	25-year-old man with no comorbidities	Acute-onset chest pain, with no orbidities fatigue and fever	BP: 130/80, HR: 140 bpm, SpO2: 98%, T: 37.1 °C	ST depression and PR elevation in aVR	Diffuse LV hypokinesia with EF= 35%, and PAP= 30 mmHg	th Myopericarditis; P= survived	Ampicillin- sulbactam, clarithromycin, oseltamivir, acetylsalicylic acid,
			2) Lungs: coarse crackles in the both lower lungs	2) Troponin: 21.471 ng/m, CK-MB: 37.1 ng/mL, troponin I: 6.499 ng/mL			metoprolol

	60-year-old male with hypertension	fevers, cough, and worsening dyspnea, with	1)Vital signs:	1) Diffuse ST elevation, with QTc interval= 437 ms	Severe segmental	Myopericarditis, acute	
14	and hyperlipidemia	mild abdominal pain and diarrhea, without chest pain, nausea, or vomiting	T: 37.4, HR: 96 bpm, SpO2: 87%,	2) LDH: 588 U/L, High-sensitivity troponin: 582 ng/L, CK-MB: 28.2 ng/ mL, pro-BNP: 15642 pg/mL	LV systolic dysfunction (EF= 15–20%) with hypokinesis of the apex, distal anterior septum, anterior and lateral walls, with a small pericardial effusion. Normal RV size and function.	hypoxemic respiratory failure; survived	IVIg, methylprednisolone, intubation, HCQ, epinephrine
			2) Lungs: clear lungs and tachypnoea				
15	39-year-old man with no comorbidities	Chest pain, dyspnea, without fever or cough	N/A	1) Diffuse ST elevation and PQ depression	Moderate circumferential pericardial effusion, without any sign of	Myopericarditis, rhabdomyolysis, acute liver injury, pleural effusion (exudative), an episode of paroxysmal AF, mild acute	Colchicine, low doses of diuretics, insulin, fluid restricted diet, amiodarone
				2) Troponin: 15.4 µg/L, NT-pro-BNP: 4473 pg/mL	tamponade	renal failure; survived	
	71-year-old woman with a history of breast cancer		1) Vital signs:	1) Diffuse inverted T waves and elongated	Infero-septal and infero-apical LV wall hypokinesia, LVEF= 56%, and a		
16	treated with surgery, chemotherapy, radiotherapy, and hormonotherapy	Flu-like symptoms, mild fever (38 °C), chest pain,	SpO2: 91%, T: 38 °C	QT up to 700 ms	moderate pericardial effusion	Acute myopericarditis (moderate pericardial effusion); survived	N/A
		_		2) High-sensitivity troponin T: 60 ng/L, BNP: 474 ng/L			
17	78-year-old man with hypertension	chest pain and dyspnea	N/A	1) AF with 150 beat/ min and concave ST elevation except for aVR lead	N/A	Acute respiratory distress, mild pericardial effusion;	Intubation, Furosemide, beta- blocker, ACE inhibitor,
	nypertension	ypertension		2)Troponin T: 998.1 ng/L		survived	COVID-19 specific therapy

				1) Sinus tachycardia, ST elevation in II, III, and	Severe global LV systolic dysfunction,	ACS, purulent fulminant myopericarditis, cardiac tamponade, circulatory shock, acute hypoxemic	
18	50-year-old man with hypertension and past history of ischemic stroke	fevers, chills, generalized malaise, non- productive cough, dyspnea for 3-4 days	N/A	aVF and ST- depression in I and aVL	RV enlargement and systolic dysfunction, Moderate-to-large pericardial effusion anterior to the RV with	respiratory failure, AKI, gastro- intestinal bleeding, multi-organ failure; Expired	Intubation, Mechanical ventilator, Pericardiocenentesis, vasopressin, norepinephrine, dobutamine, HCQ, azithromyci,
		and an episode of near- syncope		2) LDH: 3332 U/L, high	organizing material (suggesting an inflammatory process),		Vancomycin, Cefepime, IVIg, methylprednisolone, Methylene blue, Remdesivir
				sensitivity troponin: 544 ng/L, creatine kinase: 2135 U/L, CK-MB: 54.3 ng/mL	intermittent RV impaired filling and collapse suggestive of tamponade physiology		
19	53-year-old woman with no comorbidities	Fever, dry cough, severe fatigue, without chest pain, dyspnea, and further symptoms. The patient did not show any respiratory involvement during the clinical course.	1) Vital signs:	1) Low voltage in the limb leads, minimal diffuse ST- segment elevation (more prominent in the inferior and lateral leads), and	Regional wall motion abnormalities, normal LV dimensions with increased wall thickness	Acute myopericarditis (pericardial effusion) with systolic dysfunction; survived	Dobutamine, antiviral drugs (lopinavir/ ritonavir),
			BP: 90/50, HR: 100 bpm, SpO2: 98%, T:36.6 °C	ST-segment depression with T-wave inversion in V1 and	(interventricular septum: 14 mm, posterior wall: 14 mm),		steroids, chloroquine, kanrenone, furosemide, bisoprolol, kayexalate, glucose and insulin solution, sodium bicarbonate, aspirin
				aVR	diffuse echo-bright appearance of the myocardium, diffuse hypokinesis, estimated LVEF= 40%., no evidence of heart valve disease,		
				2) Troponin T: 0.24	midly impaired LV diastolic function with		
				ng/mL, CK-MB: 20.3 ng/mL, NT-pro-BNP: 5647 pg/mL	mitral inflow patterns, an E/A ratio of 0.7 and an average		
					E/e' ratio of 12, circumferential pericardial effusion most notable around the right cardiac chambers (maximum, 11 mm), without signs of tamponade.		

		Dry cough, fatigue,	1) Vital signs:	1) Diffuse ST elevation	Enlarged heart with a marked decrease in ventricular	Fulminant	HCQ,
20	51-year-old man with a history of hypertension.	dyspnea, fever, multiple episodes of	T: 39.6 °C, RR: 26, BP: 141/89, HR: 97 bpm, SpO2: 91%	2) Troponin: 18 ng/ mL, CK-MB: 14.7 ng/mL, BNP: 1,287 pg/mL	systolic function (EF= 20%)	myopericarditis, ARDS with bilateral pleural effusion; expired	azithromycin, dobutamine, remdesivir, ventilatory support,
		epigastric pain and nausea partially improved with omeprazole treatment two days prior to	2) Lungs: bilateral wheezing and rhonchi, agonal respiration, and a symmetrical decrease in chest				acetaminophen IV drip, ceftriaxone, vancomycin, remdesivir, dobutamine, indomethacin, Intravenous
		hospitalization. No chills,	expansion.				methylprednisolone, and colchicine
		diaphoresis, chest pain, or change in bowel or urinary habits.	3) Heart: pericardial friction rub (in day 7 of hospitalization)				
	58-year-old woman on a background of	Fever, diarrhea and vomiting and poor oral intake	1) Vital signs:	1) N/A	1.5 cm pericardial effusion initially, over	Cardiogenic shock, and	Pericardial drain, vasopressor support in the ITU,
	type 2 Diabetes and Hypertension	with no respiratory symptoms	BP: 85/45, RR: 18, SpO2: 96%, HR: 91 bpm, T: 34.7 °C	2) Raised LDH, High sensitivity troponin: 388.8 ng/L,	7 hours the effusion progressed to 3–4 cm with evidence of cardiac tamponade	cardiac tamponade; survived	IV Amoxicillin and oral Doxycycline initially, then escalated to Piperacillin/ Tazobactam,
			2) Heart: raised JVP and pulsus paradoxus				furosemide
			3) Abdomen: generalized				
			abdominal tenderness				
		5 days of		1) Diffuse concave elevation of the ST segment	Day 1: Severe RV dysfunction with paradoxical movement of the septum due to overload of the right chambers,	Acute myopericarditis.	
22	61-year-old man with obesity	progressive dyspnea leading to respiratory failure and severe hypoxemia	Hemodynamic and pulmonary instability	2) N/A	in addition to severe TR suggesting pulmonary embolism	severe COVID-19 pneumonia, massive pulmonary thromboembolism of both main pulmonary arteries;	ICU admission, O ₂ supplementation
					Day 7: Normal LVEF with		
					Mild to moderate pericardial effusion		

23	82-year-old woman with hypertension, hyperlipidemia, iron-deficiency anemia, and paroxysmal AF, tachycardia -bradycardia syndrome	5 days of productive cough, fever with chills, intermittent diarrhea, without angina symptoms	1) Vital signs: afebrile, hemodynamically stable, and in no respiratory distress	1) Atrial paced rhythm with diffuse new, prominent T-wave inversions and a prolonged QT interval (>500 ms) 2) mildly elevated troponin I (peaked at 0.037 ng/ml)	Day 1: LVEF= 55%, small circumferential pericardial effusion, and apical hypokinesis Day 6: a moderately enlarging pericardial effusion with left pleural effusion Day 8: circumferential pericardial effusion that had further enlarged since the previous study, a RV pacemaker wire 'piercing' the RV apex alongside early diastolic collapse of the right ventricle, suggesting echocardiographic tamponade	COVID-19-induced inflammatory myopericarditis and pericardial effusion, cardiac tamponade; survived	No ICU admission or mechanical ventilation; physical isolation, antipyretics, hydration, and O ₂ supplementation
	5 patients	5 patients Respiratory failure requiring invasive ventilation (Age, gender, omorbities: N/A)		1) No significant characteristics of a myopericarditis	Pericardial effusion without signs of cardiac tamponade located predominantly around the right atrium and ventricle, presence of a quasi-floating	COVID-19 associated myopericarditis, n=5;	
24	(Age, gender, comorbities: N/A)		invasive ventilation	2) Increased high- sensitivity troponin I: 5/5	fiber-like structure within the right- sided segment of the atrioventricular sulcus, and RV dilatation in 3/5 cases with PAP of 39, 35, 30 mmHg,	Survived, n=3, Expired, n=2	ICU admission
				1) Sinus tachycardia	respectively	Expired, II-2	
			1) Vital signs:	and diffuse ST- segment elevation;			Ceftriaxone, LMWH, acetylsalicylic acid, pantoprazole, HCQ, lopinavir/ritonavir (antiviral and HCQ therapy was discontinued after 2 days because of nausea, diarrhea and anemia) Colchicine
			HR: 120 bpm,	2) Troponin 1: 367 ng/L			
			T: 38.5 °C, SpO.: 97% in				
			ambient air				
25	19-year-old woman with no comorbidities	ear-old Fever, chest n with no pain and rbidities cutaneous rash	abdominal examination: normal.		Normal ventricular function, with no signs of pericardial effusion		
			3) Skin examination: showed a rash consisting in slightly erythematous confluent macules, involving the trunk and the limbs. On the palms and soles the macules merged into sharply edged areas of erythema with islands of spared skin			COVID-19 associated acute myopericarditis; survived	

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26	73-year-old man with hypertension, dyslipidemia, type 2 diabetes mellitus, COVID-19 pneumonia and	Pressure-like, non-radiating and constant chest pain, 7 out of 10 in severity, started 3 hours prior arrival, worsened by deep breathing	1) Vital signs: within normal limits except for heart rate fluctuating between 100 to	1) Concave shaped ST elevations in leads I, II, aVF, V2-V6 of different magnitudes, with reciprocal ST depression seen in lead aVR, PR segment depression, Spodick's sign on V3 to V5	Small pericardial effusion,	COVID-19 associated acute myopericarditis (6-8 weeks after COVID-19 positive test); survived	N/A
	former nicotine dependence	and movement, dyspnea on minimal exertion	, 110 bpm ,	2) Elevated troponin I	grade I diastolic dysfunction, LVEF between 40- 50%, increased wall thickness, and concentric hypertrophy		
27	45-year-old woman with no comorbidities	Progression of dyspnea, fever, myalgia and postural hypotension	Vital signs:	1) N/A	Normal biventricular function, with moderate pericardial effusion and diastolic restriction of the right ventricle	Fulminant COVID-19 associated myopericarditis, pleural effusion, cardiac tamponade	Antibiotic therapy with azithromycin, piperacillin/ tazobactam and teicoplanin, ICU admission, unsuccessful pericardiocentesis followed by emergency thoracotomy, internal cardiac compression and pericardial drainage, noradrenaline, dobutamine, milrinone and vasopressin,
			HR: 125 bpm,	2) Initial troponin I: 867 pg/mL		and arrest; survived	venoarterial ECMO,
			BP: 105/72 mmHg, RR: 26 breaths/min and SpO ₂ :100% on room air	peak troponin levels reached 14,000 pg/ mL			tocilizumab,
				Initial BNP: 1840 pg/mL			immunoglobulin,
							convalescent plasma,
							methylprednisolone, UFH infusion

electrocardiographic and ECG findings, and subsequent complications and management.

Overall, myopericarditis seems to be a rare complication of COVID-19. Direct and indirect mechanisms can explain this pathology in the patients [8,9]. Viral entry through cardiac angiotensin-converting enzyme II (ACE-II) might directly cause myopericarditis [10]. Indirect injuries might result from the cytokine storm precipitated by the immune response to the virus and immune-cell recruitment [9,11]. This condition's incidence was not precisely studied, and future studies need to decipher the unknowns surrounding the subject.

Keywords: Anorectal disorders • Prevalence • Nepal

Abbrevations: ECG: Electrocardiography; HR: Heart rate; BPM: Beats per minute; BP. Blood pressure; SpO2: O2 saturation; T: Temperature; N/A: Not available; LV: Left ventricular; IV: Intravenous; AF: Atrial fibrillation; ITU: Intensive treatment unit; JVP. Jugular venous pressure; BNP. B-type natriuretic peptide; LVEF: Left ventricular ejection fraction; ICU: Intensive care unit; IVIg: Intravenous immunoglobulin; HCQ: Hydroxychloroquine; CK-MB: Creatinine kinase-MB; EF: Ejection fraction; PAP. Pulmonary artery pressure; RV: Right ventricle; ACE: Angiotensin-converting enzyme; ACS: Acute coronary syndrome; AKI: Acute Kidney injury; ARDS: Acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation; LMWH: low-molecular weight heparin; RR: respiratory rate; TR: tricuspid regurgitation; UFH: unfractionated heparin.

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