

A Rare Cardiovascular Complication of Covid-19, Takotsubo Cardiomyopathy – Review

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ABSTRACT

As the COVID-19 cases are anticipated to rise globally, there may be rise in associated cardiovascular complications. COVID-19 could trigger several cardiomyopathies, including a rare complication of Takotsubo Cardiomyopathy (TCM). It is often presumed that mental trauma, elevated catecholamine's excessive immune responses, and viral cytotoxicity could be pathways for inducing TCM. Health professionals should be familiar with different cardiovascular complications and appropriate screening tools, which include cardiac ultrasound and bedside echocardiography. In high-risk COVID-19 patients, a simple history of previous psychiatric conditions and some other possible risk factors for the Takotsubo syndrome could assist in screening. Besides, the diagnosis must be considered, and efficient management should be initiated. There can be multiple direct and indirect factors manifesting as Takotsubo cardiomyopathy in COVID-19 patients. On other hand, Takotsubo cardiomyopathy may also be observed in the non-COVID-19 patients due to other stressors. Therefore, more extensive research work and further studies are required to learn more about the exact mechanism and relation between Takotsubo cardiomyopathy and COVID-19. Here, we aim to complete a literature review of suspected or known Takotsubo cardiomyopathy related to COVID-19. The main objective of this manuscript is to provide information reported by healthcare providers across the globe on reported comorbidities, potential pathophysiology, and optimal management of stress cardiomyopathy that generally has a favorable outcome.

Keywords

SARS-CoV-2, COVID-19, Coronavirus, Cardiomyopathy, Takotsubo.

Introduction

In December 2019, in Wuhan, Hubei, China, an outbreak of unusual pneumonia, now known as, Coronavirus Disease 2019 (COVID-19) caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was brewing the pandemic [1]. As further information about the novel Coronavirus keeps evolving it has come to light that COVID-19 infection has potential adverse cardiovascular consequences [2]. Two main questions may arise are how and why is the SARS-CoV-2 affecting the cardiovascular

system so aggressively? The answer lies with the Angiotensin-converting enzyme 2 (ACE2), which is a membrane-bound amino-peptidase [2]. ACE2 has been identified as one of the target functional receptors for coronaviruses, including SARS-CoV and SARS-CoV-2. ACE2 has a vital role in the cardiovascular and immune systems [2]. The Spike (S) protein of the SARS-CoV-2 binds to the ACE2 receptor on the host cell, which is highly expressed in the heart and lungs [2]. It is therefore very crucial to take into consideration that if a patient with COVID-19 is on anti-hypertensive, either Angiotensin-converting Enzyme Inhibitors (ACEIs) or Angiotensin Receptor Blockers (ARBs), should be carefully monitored [2].

Now besides the direct injury to the cardiovascular system, the COVID-19 is associated with an increased incidence of stress-induced cardiomyopathy or Takotsubo cardiomyopathy [3]. This further explains the indirect psychological, social, and economic pandemic-related stress mechanism which leads to the COVID-19 disease process [3]. *Jabri, A, Kalra, A, Kumar, A, Alameh, A, Adroja, S, Bashir, H, et al.* (2020) conducted a cohort study in which their principal finding showed a significant increase in the incidence of stress cardiomyopathy during the pandemic [3].

There was a significantly longer length of hospital stay observed in patients hospitalized for stress cardiomyopathy [3]. Further learned about the impact of stress and anxiety associated with stress cardiomyopathy [3]. Researchers also discovered that more than just the direct viral involvement, one's psychological, social, and economic distress during the time of the pandemic may contribute to stress cardiomyopathy [3]. *Sattar, Y, Connerney, M, Ullah, W, Philippou, A, Slack, D, McCarthy, B, et al.* (2020) [4] mentioned COVID-19 may have several different early extrapulmonary cardiovascular manifestations; acute coronary syndrome, stress cardiomyopathy, myocardial injury, heart failure, arrhythmias, pericardial effusion, cardiac tamponade, thromboembolic complications, and cardiogenic shock [4]. However, Dr. Finsterer responded to *Sattar, Y, Connerney, M, Ullah, W, Philippou, A, Slack, D, McCarthy, B, et al.*'s (2020) notes by suggesting that cardiovascular (CVS) manifestations could have been psychological or emotional stress therefore it is not justified to say that SARS-CoV-2 is the causative trigger for these manifestations [4].

Also, Dr. Finsterer stated that angiography was not performed to rule out Acute Coronary Syndrome (ACS) to comply with the Mayo clinic's inclusion criteria for making a diagnosis of Takotsubo Cardiomyopathy [5]. Dr. Finsterer concluded with the suggestion of triple therapy to patients with Takotsubo Cardiomyopathy [5]. Dr. Sattar and the team responded saying that diagnosis of TTS requires ruling out myocarditis and ACS as per the American College of Cardiology and Mayo clinic criteria. However, an obstructive coronary artery disease does not rule out Takotsubo cardiomyopathy because arterial occlusion can cause mechanical stress, which can lead to Takotsubo cardiomyopathy [6].

Therefore, there is no clarity in the exact mechanism of how and why COVID-19 may lead to Takotsubo cardiomyopathy. There can be multiple direct and indirect factors manifesting as Takotsubo cardiomyopathy in COVID-19 patients. On other hand, Takotsubo cardiomyopathy may also be observed in the non-COVID-19 patients due to other stressors. Therefore, more extensive research work and further studies are required to learn more about the exact mechanism and relation between Takotsubo cardiomyopathy and COVID-19.

Here, we aim to complete a literature review of suspected or known Takotsubo cardiomyopathy related to COVID-19. The main objective of this manuscript is to provide information reported by healthcare providers across the globe on reported comorbidities,

potential pathophysiology, and optimal management of stress cardiomyopathy that generally has a favorable outcome.

Takotsubo Cardiomyopathy and COVID-19 link

Takotsubo cardiomyopathy (TCM) is a left ventricular (LV) apex motion impairment preceded by physical or emotional distress that commonly improves eventually. This cardiomyopathy has been referred to by other terms, including transient LV apical ballooning syndrome and broken heart syndrome. The following general manifestations are particularly characteristic of TCM: (1) abrupt and stress-induced onset; (2) ECG findings: even though the initial findings may be nonspecific, the elevation of the ST segment has been observed in precordial leads in 50 percent of patients along with reciprocal ST-segment depression, inverted T waves, and q waves abnormalities. (3) A minor rise in the amount of the cardiac enzymes at admission which then declines at a rapid pace and does not appear to be of prognostic value. (4) Lack of coronary artery abnormality, so coronary angiography should also be performed to exclude acute coronary syndrome. (5) balloon-like ventricular dilation [7].

COVID-19 could trigger several cardiomyopathies, including Takotsubo Cardiomyopathy. It is often presumed that mental trauma, elevated catecholamines, excessive immune responses, and viral cytotoxicity could be pathways for inducing TCM. Health professionals should be familiar with different cardiovascular complications and appropriate screening tools, which include cardiac ultrasound and bedside echocardiography. In high-risk COVID-19 patients, a simple history of previous psychiatric conditions and some other possible risk factors for the Takotsubo syndrome could assist in screening. Besides, the diagnosis must be considered, and efficient management should be initiated [8].

The pathophysiology of myocardial injury in COVID-19 patients is poorly known. The proposed mechanisms suggest cytokine-mediated trauma, oxygen insufficiency, development of micro vascular thrombi, and specific myocardial viral interference. TCM might evolve from micro vascular disturbance caused by catecholamine due to COVID-19-related metabolic, immune, and psychological trauma. Comparison to patients with non-TCM myocardial damage to those with TCM displayed contrasting lab manifestations, such as higher levels of cardiac enzymes but lesser tiers of inflammatory and prothrombotic markers, indicating that TCM might constitute a different mechanism in COVID-19 as documented in other groups of seriously ill patients [9].

The connected functionality of the brain and the heart is recognized as an essential element in TCM pathophysiology. The basic explanation is suspected to be excessive sympathetic stimulation. Elevated plasma cortisol and enhanced sympathetic stimulation will pose a risk to the myocardium. Abrupt mental or physical strain induced by the catecholamine's and cortisol could therefore lead to risks for TCM. Besides, local variations in myocardial presentation of the concentration of β_2 -adrenergic receptors have been found to trigger the pathological effects of elevated blood

levels of catecholamine and justify the stunning of the local left ventricular myocardium. Thus, the immense emotional pressure imposed by COVID-19 on the population will stimulate the neuro-cardiovascular axis and function as a major TCM stimulus. The COVID-19 outbreak has triggered an ongoing health crisis with evolving cardiovascular effects culminating in personal and social panic and distress [10].

Minhas, A. S, Scheel, P, Garibaldi, B, Liu, G, Horton, M, Jennings, M, et al. (2020) [11] reported the case of a 58-year-old woman who presented with COVID-19 symptoms of productive cough, fatigue, fever, and diarrhea for the past 5 days. This was possibly the first known case in the United States of takotsubo cardiomyopathy potentially related to COVID-19. During the physical exam, the physician noted tachycardia (130 beats/min) and low oxygen saturation (82%) with diffuse rhonchi on lung examination. As soon as the chest radiograph confirmed bilateral lower lobe infiltrates, which is typical of COVID-19, she was intubated for hypoxic injury from SARS-CoV-2. The ECG showed sinus tachycardia with 1-mm up sloping ST-segment elevations in leads I and aVL, diffuse PR depression, and diffuse ST-T wave changes with peaked troponin I level (11.02 ng/ml). A transthoracic echocardiogram showed akinetic anterior, anteroseptal, and anterolateral apical segments with apical ballooning and reduced ejection fraction (20%). The patient was admitted to ICU. Due to positive COVID-19, coronary angiography was deferred and the patient was treated with conservative therapy for ACS (antiplatelet, anticoagulation, IV heparin) and hydroxychloroquine for COVID-19, which was later discontinued after echocardiography results received. The patient was determined to have stress cardiomyopathy based on clinical signs, but also because she had rapid recovery over the next few days [11].

Roca, E, Lombardi, C, Campana, M, Vivaldi, O, Bigni, B, Bertozzi, B, et al. (2020) reported a case of an 87-year-old female with severe SARS-CoV-2 with confirmed nasopharyngeal swab and images [12]. The patient was initially admitted to the clinic with a 2-week history of fever, fatigue, and shortness of breath, and no known history of travel to high-risk COVID-19 regions or comorbidities such as HTN, DM, or obstructive pulmonary disease. After admission, she was immediately placed in an isolation ward and received supplemental oxygen through a face mask with the standard of care (azithromycin, ceftriaxone, methylprednisolone for shortness of breath). The patient experienced an episode of tachycardia on the second day of the admission with elevated cardiac enzymes: Troponin I (5318 ng/l; normal value <6) and CK-MB was 55 µg/l (normal value <3). The echocardiogram showed apical LV akinetic expansion (ballooning) and hypokinesia with slightly reduced ejection fraction (48%); diagnostic for a clinical, laboratory, and radiographic picture of Takotsubo syndrome. The patient was treated with bisoprolol and fondaparinux as the coronary angiography is contraindicated for her age.

Chadha, S. (2020) also presented a case of an 85-year-old female without cardiac history, who presented to the ER with sudden

onset chest pain. The patient denied any recent travel or exposure to COVID-19 and any related symptoms such as cough, fever, or SOB. Upon completion of imaging in the ER, the ECG showed a septal q-ST pattern in leads V1-V3 with elevated troponin T (112 pg/ml). An urgent catheterization was performed, which showed basal hyperkinesis of LV and ballooning, consistent with the diagnosis of Takotsubo cardiomyopathy. The patient was stable over the next 5 days and was discharged once the LV systolic function had recovered, which was initially at 35% [13].

Nguyen D, Nguyen T, De Bels D, & Castro Rodriguez J. (2020) reported a case of TTS in a 71-year-old female who presented with complaints of fainting [14]. The patient was a confirmed case of COVID-19 as evidenced by the positive SARS-CoV-2 Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test [1]. The patient was dyspneic on rest on presentation with a past medical history of arterial hypertension, hypercholesterolemia, and normotensive hydrocephalus treated with ventriculoperitoneal shunt. Her EKG showed Sinus rhythm with prolonged QT interval; QTc of 521ms. The patient was mechanical ventilated due to persistent hypoxemia despite 100% O₂ inhalation. Troponin-T was elevated and Coronary angiography showed lesions in proximal LAD and first diagonal arteries; Drug-eluting stents (DES) were placed in both the arteries. Ventriculography showed LV wall motion abnormalities discordant with coronary artery disease, leading to a diagnosis of TTS [14].

Another case of COVID-19 related TTS was described by *Bernardi N, Calvi E, Cimino G, Pascariello G, Nardi M, Cani D, et al.* (2020); a 74-year-old male with presenting complaints of fever, cough, and dyspnea, complained of retrosternal chest pain on the fifth day of hospitalization [15]. EKG showed ST elevation in the anterior leads and coronary angiography showed non-significant atherosclerotic changes in coronary arteries. He had a past medical history of arterial hypertension, dyslipidemia, and deranged blood glucose levels. Laboratory results showed elevated troponin-T, D-dimer, and Pro-BNP levels. A transthoracic echocardiogram showed dilated left ventricle, akinetic mid and apical left ventricle sections, hyperkinetic basal segments, and severe LV systolic dysfunction with an LV ejection fraction of 30%. Moderate to severe mitral regurgitation with systolic anterior motion causing partial left ventricular outflow tract obstruction was also noted on the echocardiogram. Moreover, two thrombi were also noted in the apex of LV. Furthermore, the patient underwent cardiac magnetic resonance imaging which showed an LV ejection fraction of 22%, with hypokinetic medio-apical segments and a typical apical ballooning of LV; suggestive of TTS [15].

Pasqualetto M.C, Secco E, Nizzetto M, Scevola M, Altafini L, Cester A, et al. (2020), described COVID-19 related TTS in 3 patients who were being treated for COVID-19 pneumonia [16]. All three of the patients had a past medical history of either arterial hypertension or diabetes mellitus, but no previous history of cardiovascular disease. RT-PCR of the nasopharyngeal swab for SARS-CoV-2 infection was positive in all three patients, with

typical findings of COVID-19 pneumonia on chest CT. EKG in all three patients showed QT interval prolongation and T-wave inversions in precordial leads. The echocardiogram showed typical LV apical ballooning due to dyskinetic LV apex and hyperkinesia of the basal segment along with severe systolic dysfunction suggestive of TTS [16].

Giannitsi S, Tsinivizov P, Poulimenos L.E, Kallistratos M.S, Varvarousis D, Manolis A.J, et al. (2020) [10] reported a case of a 79-year old female presenting with acute chest pain while watching TV showing the death toll of the COVID-19 pandemic. Her medical history was significant for arterial hypertension treated with Angiotensin-Converting Enzyme inhibitors (ACEi). On admission, she was hemodynamically stable with a blood pressure of 130/70 mmHg, heart rate of 75 beats/min in sinus rhythm, and oxygen saturation of 99% in room air [10]. Her physical examination and body temperature were normal; however, the electrocardiogram recorded diffuse ST-segment elevation. Hence, she underwent emergency coronary angiography, which ruled out stenotic lesions as shown in the images in the case report as the vessels filled without any obstruction. Her left ventriculography was also carried out to reveal severe hypokinesia as shown in the image in the mid-apical segments, hyper dynamic basal segments, and impaired left ventricular systolic function with an ejection fraction of 35%. She also had highly sensitive troponin-T wave elevated peaking after 12 h on the other hand routine blood work including inflammatory markers were normal.

Therefore, the diagnosis of Takotsubo (Stress induced-) Cardiomyopathy (TTS) was made. The presentation of TTS is very similar to that of Acute Coronary Syndrome (ACS) [10]. TTS represents acute heart failure with considerable morbidity and mortality [10]. However, left ventricular systolic function usually recovers within four weeks [10]. It has come to the knowledge that the overstimulation of the sympathetic nervous system can be an underlying mechanism in the development of TTS [10]. The higher the stress levels the higher the activity of the hypothalamic-pituitary-adrenal axis (HPA-axis), which leads to high serum cortisol levels. Therefore, high serum cortisol levels alongside the hyper stimulated sympathetic nervous system can cause severe myocardial damage [10]. So, to say the least, the psychological or physical stress-mediated release of catecholamine's and cortisol levels can act as a trigger or TTS [10]. Moreover, there has been a great amount of psychological strain due to the pandemic, which may trigger the brain-heart axis and can act as a potential stressor for TTS [10].

A 76-year-old woman presented with subjective fevers, nonproductive cough, and dyspnea was admitted to the intensive care unit for acute hypoxic respiratory failure secondary to COVID-19 infection as per the case reported by *Khalid, Y, Dasu, N, & Dasu, K.* (2020) [17]. Her blood pressure was 110/53 mm Hg, pulse rate was 124 beats/min and regular, respiratory rate was 31 breaths/min, oxygen saturation was 79% on 10 L oxygen nasal cannula, her temperature was 102.3°F, and she was in severe

respiratory distress. A cardiovascular examination was done, which revealed tachycardia. A lung exam was performed which showed diffusely decreased breath sounds and crackles [17]. The remainder of the physical examination was unremarkable. Her medical history was notable for hypertension, hyperlipidemia, and hypothyroidism. *Khalid, Y, Dasu, N, & Dasu, K.* (2020) had wide differentials with the main concern being COVID-19-induced acute respiratory distress syndrome was a major concern. Other differential diagnoses were acute pulmonary embolism, acute heart failure, septic shock, cardiac tamponade and acute coronary syndrome, viral pneumonia from other pathogens, bacterial pneumonia, and viral cardiomyopathy [17]. A transthoracic echocardiogram (TTE) was performed and it revealed a severely decreased LV systolic function with segmental wall motion abnormalities, akinesis of the distal segments of the left ventricle with relatively preserved function at the base, and akinesis of the mid and distal portions of the right ventricle with preserved function at the base of the free wall as well as an ejection fraction (EF) of 25%–30% (normal range >50%) [17].

The echocardiogram was important and that helped *Khalid, Y, Dasu, N, & Dasu, K.* (2020), to better diagnose their patient and transfer her to a higher level of care [17]. TTS and Myocarditis would've been distinguished with help of biopsy but they avoided it to reduce exposure. Their patient was managed with several medications with anti-inflammatory properties. These treatments helped reduce her myocardial injury and allowed for LVEF recovery [17]. Due to the proposed theory of cytokine storm in the COVID-19, Tocilizumab an immunosuppressive drug and an anti-human IL-6 receptor monoclonal antibody, which blocks IL-6 from binding to its receptor, and as a result stunts the immune-inflammatory response, was used in this patient. After completion of tocilizumab, and within 2 days of completing intravenous immunoglobulin, her LVEF recovered to 50% on TTE, with overall mildly reduced LV systolic function, mid-septal, and apical hypokinesia, and mildly reduced right ventricular function [17]. Blood and respiratory cultures were negative. Inflammatory markers greatly improved but then worsened again. IL-6, however, continued to downtrend from 781.46 mg/L to 171.82 mg/L 2 days after the completion of treatment. A decrease in the level of high-sensitivity troponin from 503 ng/L to 418 ng/L was also observed. She was not a candidate for extracorporeal membrane oxygenation owing to her advanced age. After the improvement of her LVEF, the patient was transferred back to our intensive care unit. They concluded that it is very crucial to recognize COVID-19-associated cardiac complications so early intervention, surveillance, and management of critical patients can be done.

Meyer, P, Degrauwe, S, Van Delden, C, Ghadri, J.-R, & Templin, C. (2020), reported a case of an 83-year-old female, who was hospitalized for acute chest pain during the beginning of the COVID19 outbreak. She had non-radiating chest pain + mild breathlessness + dry cough, since 3 days before hospitalization. Her nasopharyngeal swab was negative for SARS-CoV-2, but her serology pattern of positive IgA and negative IgG proved

acute infection. Upon hospitalization, her EKG showed ST-segment elevation in all precordial leads with deep T-wave inversions, Echocardiography revealed typical left ventricular apical ballooning with hyperkinetic basal segments, and coronary angiography showed no significant lesion, while ventriculography confirmed typical finding of TTS. The patient recovered progressively on conventional heart failure medications without the need for oxygen or ventilation. The patient was discharged on the 10th day after admission, with Echo showing only mild residual apical hypokinesia [18].

Oyarzabal, L, Gómez-Hospital, J. A, & Comin-Colet, J. (2020) described a case of an 82-year-old male, who tested positive for SARS-Cov-2 by PCR test. The patient presented to the ER with anginal pain which was consistent with his heart failure with a past medical history of hypertension, diabetes, peripheral arterial disease, dyslipidemia, and chronic renal failure. EKG, coronary angiography, and cardiac ventriculography showed changes supportive of TTS (EKG showed ST elevation in leads V2-V3 and AvL, Coronary angiography showed coronary arteries free of any lesion, and ventriculography showed reduced left ventricular ejection fraction with extensive apical akinesia) [19].

Taza, F, Zulty, M, Kanwal, A, & Grove, D. (2020), reported a case of a 52-year-old male, hypertensive, diabetic, schizophrenic; working at a nursing home and tested positive for SARS-Cov-2, presented to the ER with an SOB. He underwent intubation in the ER due to acute respiratory failure and altered mental status and was admitted to ICU for further management. On investigation, his EKG showed ST-segment elevation in leads II, III, avF, coronary angiography showed non-obstructive arteries and ventriculography revealed apical ballooning which was consistent with TTS. His treatment was started with colchicine, methylprednisolone, continuous heparin infusion, and tocilizumab. The patient clinically improved on day 6 and was shifted to the ward. His oxygen demand decreased and was maintaining good saturation. Eventually, the patient was discharged to outpatient rehabilitation [20].

Discussion and Lessons Learned

In general, the incidence of Takotsubo cardiomyopathy is reported to be more common in postmenopausal women (approximately 90% of cases) in comparison to men [21]. Of these confirmed cases, 80% of cases are reported to be related to physical, emotional, or medical stress [21]. The incidence of Takotsubo is reported to be high at 54.9/1,000,000 women in comparison to 3.6/1,000,000 men [21]. Upon our literature review, we came across reported cases that were largely representative of postmenopausal women, and rarely of men. A few of the researchers clearly stated in their case reports whether they had assessed patient-reported stress.

The heightened inflammation-induced due to viral infection can certainly increase the chances of cardiac injury; however, it is not clear whether the cardiac injury seen in COVID-19 patients is primarily due to inflammatory stress alone. If cytokine storm, a sign of hyper inflammation is clinically noted, patients

may be presumed to have stress cardiomyopathy secondary to inflammation [11]. However, it is highly likely that patients had underlying undiagnosed cardiomyopathy. Some studies have suggested the role of endomyocardial biopsy in patients with LV dysfunction.

Uwe, K, Matthias, P, Michel, N, Bettina, S, Thomas, B, Dirk, L, et al. (2005) conducted a study to screen endomyocardial biopsies of 245 patients, whom all tested positive for at least one virus (EV, ADV, HCMV, HSV, EBV, HHV-6, PVB-19, Influenza A, Influenza B), using RT-PCR. At least 45 of these patients had multiple viral infections. The study reported 71% of their patients had detectable cardio tropic viruses upon biopsy and were suspected to play a major role in the pathogenesis of converting myocarditis to dilated cardiomyopathy (DCM) [22]. This shows viruses are capable of damaging the myocardium and it aligns with the molecular biology of SARS-CoV-2, as the S protein of the virus binds to the ACE2 receptor of the human host with high affinity, a receptor that is highly expressed in the heart [12]. The outcome of stress cardiomyopathy is considered favorable, however, the key is to diagnose and manage as early, especially in elderly patients, because they are known to have a high mortality rate during COVID-19 [12].

It is understood that the higher the stress levels the higher the HPA axis activity which will cause high serum cortisol levels alongside stimulated sympathetic nervous system which may cause myocardial damage [10]. In summation, it can be conferred that psychological strain due to the pandemic which triggers the brain-heart axis acts as a potential stressor for the development of TTS [10]. In *Khalid, Y, Dasu, N, & Dasu, K.*'s case report, it was concluded that it is important to identify cardiac complications that may be arising due to COVID-19 so that early intervention, proper surveillance, and management can be undertaken [17].

Huge emotional stress at the population level and respiratory infections caused by COVID-19 may represent potential triggers for TTS. Myocardial injury, frequently reported in patients with COVID-19, is usually attributed to sepsis and/or hypoxemia and/or underlying coronary artery disease [18]. It is possible that the cytokine storm associated with the infection can trigger TTS in patients with underlying risk factors for Takotsubo (emotional distress, physical distress, history of psychiatric disorders) [19]. Some studies have shown an elevation in catecholamine plasma levels suggesting this disorder may be caused by diffuse catecholamine-induced micro vascular spasms or direct catecholamine-mediated myocyte injury. It is hypothesized that SARS-CoV-2 elicits an exuberant systemic immune response with a cytokine release syndrome (CRS) characterized by elevated inflammatory markers [20].

LV thrombus formation is a rare complication of TTS. It is more commonly seen in patients with elevated troponin levels and characteristic apical ballooning of LV. The pathogenesis of LV thrombi in TTS is based upon the Virchow's triad i.e. Stasis of

blood, hypercoagulability, and endothelial injury. LV hypokinesia/akinesia and ballooning lead to blood stasis and thus thrombus formation [23]. Endothelial injury may occur as a consequence of a catecholamine surge in circulation [24]. Increased catecholamine levels can also induce a hypercoagulable state and thus lead to thrombus formation [25]. Higher than normal values of overall blood viscosity, von Willebrand factor (vWF) and lower erythrocyte deformability have been seen in patients with TTS [26]. Moreover, LV thrombus formation in TTS is also associated with cerebrovascular thromboembolic events. Oral anticoagulants (OAC) for 3 months are recommended for TTS patients with apical ballooning and increased troponin levels [23].

Conclusion

COVID-19 is associated with a variety of complications, including cardiomyopathy. Takotsubo cardiomyopathy, also known as the stress myocardopathy is potentially a rare complication of COVID-19. As the COVID-19 cases are anticipated to rise globally, there may be rise in associated cardiovascular complications. We recommend clinicians may need to be aware of diverse causal factors of cardiac complications, especially in conjunction with COVID-19. Clinicians will continue to play a major role in early diagnosis and management of this rare yet devastating complication if the diagnosis is delayed.

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