South Afr J Anaesth Analg. 2023;29(2):56-58
https://doi.org/10.36303/SAJAA.2979

South Afr J Anaesth Analg
ISSN 2220-1181 EISSN 2220-1173

GUEST EDITORIAL

Stress cardiomyopathy, Takotsubo cardiomyopathy, or acute neurocardiogenic heart failure syndrome?

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Since its first description in Japan in 1990, Takotsubo syndrome, or stress cardiomyopathy (sCMO), goes by many monikers.[1] The sCMO syndrome is characterised by a form of acute reversible myocardial injury characterised by transient regional systolic left ventricular (LV) dysfunction in a non-coronary distribution.[2] The current definition is that of a clinical syndrome characterised by i) an acute and transient (< 21 days) LV dysfunction that ii) may be related to an emotional or physical stressful event, and iii) the presence of LV regional wall motion abnormalities extending beyond a single coronary artery distribution. This syndrome is now recognised with increasing frequency, with a prevalence of 1–2% of patients presenting with an acute coronary syndrome (ACS).[2,3]

The most common and best-recognised form is systolic apical ballooning of the LV, with basal hyperkinesia seen in 80% of patients. Atypical forms such as the mid-LV cavitary variant (15% of cases) or basal (reverse) variant (5% of cases) have also been described. A localised or focal type that may mimic myocarditis is also recognised (1–2%).[2,3]

sCMO is suspected based on clinical presentation, echocardiography (ECG) changes, mild elevation of serum cardiac troponin, significant elevation in serum natriuretic peptide levels and typical ECG findings as described above. Coronary angiography is usually performed to exclude an acute coronary event. In some instances, the typical wall motion abnormalities of sCMO may co-exist with the presence of non-culprit coronary lesions and the diagnosis of sCMO still prevails, with the extant obstructive coronary disease being a bystander, but not culpable in the clinical presentation. Approximately 15% of patients were noted to have co-existing coronary artery disease (CAD).[4,5]

Complications of sCMO, such as acute heart failure (HF), left ventricular outflow tract obstruction (LVOTO), and mitral regurgitation (MR) leading to cardiogenic shock are not infrequent. In the medical intensive care unit (ICU) in patients that have infections or sepsis syndromes, it may be seen in a quarter of patients. Little data exists in the surgical intensive care or operating suites. The two cases accompanying this editorial delineate the challenges in diagnosing and managing sCMO, in particular during the perioperative period.[6,7]

A few diagnostic criteria have been described, but there is an overlap between these criteria. The most widely used diagnostic criteria are the Heart Failure Association of the European Society of Cardiology diagnostic criteria for Takotsubo syndrome, which have revised the earlier Mayo Clinic Criteria.[3,8] Recently, the International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria), which can be deployed to create a risk score, has been described. This has added value by using a point system that can either rule in or rule out sCMO with a high degree of certainty.[9]

While ECG changes predominantly show ST-segment elevation, one study found that the combination of ST-segment depression in a VR and the absence of ST-segment elevation in V1 has a high likelihood of diagnosing sCMO, with 91% sensitivity, 96% specificity, and 95% predictive accuracy.[10] While other studies show an absence of reciprocal changes and Q-waves with the ST-elevation ratio in leads V4–6 to V1–3 > 1, and also the absence of ST-depression or following inferior ST-elevation.[11]

The pathophysiology of sCMO is not completely understood, but several lines of evidence suggest a catecholamine surge atop a hyper catecholamine state. The resultant catecholamine cardiotoxicity and microvascular dysfunction, as part of a neuro-pituitary-adrenal axis, cause injury and microvascular dysfunction at the myocyte level.[4,5] Several mechanisms may be involved in the pathophysiology that result in the syndrome of sCMO. The link between the brain and heart has long been known.[12-14] More recently, the brain-heart or neurocardiac axis has been studied using a neuro-imaging approach.[15,16] The central autonomic nervous system is known to control and regulate all of the cardiovascular functions; this is part of the sympathetic neuronal control. It has been well known that cardiac dysfunction ensues and may occur in patients with stroke or subarachnoid haemorrhage or intracranial bleeding, or after electroconvulsive therapy. This usually manifests as ECG changes and may be accompanied by transient cardiac dysfunction. This phenomenon is referred to as "neurogenic stunning myocardium".[17]

An increase in cerebral blood flow in the hippocampus, brainstem, and basal ganglia can be seen on neuro-imaging during the acute phases of sCMO in patients versus control subjects, which then returns to normal after the acute

syndrome resolves.[12,13] That is the case for a more "unified" name for sCMO and its several monikers that it is known by and should be: acute neurocardiogenic heart failure. Management is a challenge, especially in the more critically ill patients. Initially, the clinical scenario is that of an ACS, this mandates management as an ACS with oxygen supplementation, aspirin, heparin, and possibly beta-blockers if stable. With the first imaging, either by cardiac catheterisation or ECG, the diagnosis can be made and an ACS excluded; the aspirin may then be discontinued if haemodynamically stable beta-blockers can be instituted. However, in the 10% of cases where cardiogenic shock ensues, management is more challenging as highlighted in the two case presentations in this issue of the journal.[6,7]

As per guidelines, angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin receptor blocker (ARB) may be used as part of regional wall motion abnormality (RWMA) and LV dysfunction management after the acute phase. Anticoagulation therapy should be continued, especially if an akinetic or dyskinetic apical segment is noted to prevent LV apical thrombus, which is likely to occur within the first five days.[18] It can be continued for four to six weeks or less if complete LV function and apical wall motion recovery and contractility have occurred.

Patients with haemodynamic instability or cardiogenic shock pose a greater challenge as seen in the accompanying cases in this issue. The challenges are in both recognition of the disease in the hyperacute setting as well as the management in the perioperative period. Haemodynamic instability is the biggest challenge, because it may be due to concomitant dynamic LVOTO or significant MR.

In patients with congestion diuretics, nitroglycerin may show benefit, since 20% of patients with sCMO will have congestive heart failure (CHF).[18] This treatment cannot be given to patients in shock or those with LVOTO as it may worsen the haemodynamic status. Therefore, unstable patients or patients in shock need to be dichotomised at the earliest opportunity soon after diagnosis, with repeat echocardiography as necessary so that triage to inotropic support is the main form of therapy versus mechanical cardiopulmonary support.[3,8,9]

Arrhythmias occur in approximately 25% of sCMO patients. Atrial fibrillation, which is most prominent especially in severe LV dysfunction, can be seen in 5–15% of patients and is associated with a higher incidence of cardiogenic shock.[19-23] Ventricular arrhythmias occur in 49% of patients.[10,11] Torsade de pointes may supervene in sCMO, especially if the QT interval is > 500 ms.[22] Other arrhythmias are less frequent.[11] These arrhythmias are managed expectantly and in accordance with guidelines. In addition to decongesting the lungs and reducing myocardial stress and left atrial stretch, anti-arrhythmic therapy or DC cardioversion may be necessary. Amiodarone is a good option for both atrial and ventricular arrhythmias in these high-acuity emergencies and in cases of shock-synchronised DC cardioversion per guidelines.

The complicated acute neurocardiogenic HF patient can be a challenge to manage. Prompt recognition of the syndrome in the medical or surgical intensive care or operating room is imperative and predicates the likelihood of success with timely and appropriate intervention, after identifying the subtype of the sCMO. The two case presentations and successful outcomes attest to the prompt recognition and appropriate management strategies. The ECG findings discussed, echocardiographic phenotype and InterTAK Diagnostic Criteria scores, when familiar, will allow for prompt recognition.[9]

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