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Review Article

Stress cardiomyopathy of the critically ill: Spectrum of secondary, global, probable and subclinical forms

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ABSTRACT

Stress cardiomyopathy (SC) typically presents as potential acute coronary syndrome (ACS) in previously healthy people. While there may be physical or mental stressors, the initial symptom is usually chest pain. This form conforms to the published Mayo diagnostic criteria, is well reported and as the presentation is initially cardiac, is considered primary SC. Increasingly we see SC develop several days into the hospitalization secondary to medical or surgical critical illness. This condition is more complex, presents atypically, is not easy to recognize and carries a much worse prognosis. Label of Secondary SC is appropriate as it manifests in sicker hospitalized patients with numerous comorbidities. We review the limited but provocative literature pertinent to SC in the critically ill and describe important clues to identify global, subclinical and probable forms of SC. We illustrate the several unique clinical features, demographic differences and propose a diagnostic algorithm to optimize cardiac care in the critically ill.

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1. Introduction

Stress cardiomyopathy (SC) was first described in Japanese literature in 1990.[1] The number of publications about this condition has exploded over the last 2 decades.[2–4] As there are several causes and morphological variants, our understanding of SC is continuing to evolve. SC occurs much more frequently in the critically ill than the medical community recognizes.[5,6] The diagnosis of SC is challenging in the critically ill and does not conform to the published criteria. Several important critical care publications evaluating a spectrum of cardiac abnormalities over the last few decades have labelled SC variably, thus significantly limiting our current understanding. We offer a provocative broader understanding of SC gleaned from the published critical care literature and cardiac imaging studies to optimize the diagnosis of SC in the critically ill.

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2. Defining SC

Originally described as Tako-tsubo cardiomyopathy (TC) and apical ballooning syndrome (ABS), we have subsequently included many morphological variants like basal and mid-ventricular forms under the umbrella of SC.[7,8] There are still no definite criteria for the diagnosis of Stress Cardiomyopathy. The pathogenesis remains unknown and thus the diagnosis is not definitive for the majority of patients.

Based on our evolving understanding, the following clinical framework appears to encompass the broad spectrum of SC: *Stress cardiomyopathy (SC) is acute reduction in cardiac function oftentimes due to mental or physical stress with spontaneous complete normalization of cardiac function within days to weeks.* This describes a clinical phenomenon that arises from a variety of causes and a myriad of clinical presentations but overlaps with some specific causes of cardiac dysfunction.[9]

The emphasis of this simple definition of SC is on regional wall motion abnormality (RWMA) and its spontaneous recovery. The clinical presentation can vary from asymptomatic to crushing substernal pain and cardiogenic shock. Electrocardiogram (ECG) may include a wide range of abnormalities from sinus tachycardia, ventricular ectopy, ischemic ST depressions and deep T inversions to ST elevation myocardial infarction (STEMI) patterns.[10] Mayo criteria for SC diagnosis requires coronary angiogram to confirm absence of culprit lesions that may account for the RWMA.[7,11] Our interest is in early non-invasive diagnosis of SC in the critically ill. We have reviewed the various etiologies of cardiac dysfunction in the critically ill[12] and highlighted management issues specific to the critically ill.[13,14] We routinely encounter potential SC in various ICU settings and have published our algorithm to definitively diagnose SC without catheterization.[9] This requires clinical suspicion, good quality echocardiographic windows to characterize the RWMA and repeat echocardiogram in about 5–7 days to confirm normalization/improvement of cardiac function. Recently, the European society of cardiology has published a position statement where they have differentiated primary SC presenting to the ER with chest pain from secondary takotsubo syndrome that develops during the course of hospitalization for another medical, surgical, anaesthetic, obstetric, or psychiatric condition.[15]

3. Literature

There has been an exponential growth in the publications on SC over the last 15 years. Between 2004 and 2014 over half a dozen criteria were published to diagnose SC. The widely used 2004 Mayo criteria were based on 16 patients with 'chest pain – potential ACS' where SC was diagnosed only after catheterization excluded CAD.[11] In 2008 Mayo expanded their criteria to include non-ABS variants and patients with SC due to neurological events.[7] All the published criteria over the past decade stem from clinical experience of high volume centers describing patients presenting with cardiac symptoms initially and undergoing catheterization for potential ACS.[16–19] Thus, all the studies have performed catheterization to exclude ACS and base the diagnosis of SC on excluding CAD. NT-proBNP elevation appears to be more in SC and the ratio of troponin I to LV EF may help differentiate SC from ACS.[20,21] These studies were not been performed in the critically ill and thus may not carry he same diagnostic utility in this population. Higher levels of Interleukin (IL)-6, IL-10 and carbohydrate-antigen (CA)-125 are associate with a more complicated hospital course and risk for recurrence of SC. These inflammatory and cancer biomarkers may be valuable risk markers in SC.[22,23]

We do not have any published diagnostic criteria for secondary SC that develops during the course of medical or surgical critical illness. Extrapolating the 2008 revised Mayo criteria to the critically ill sepsis, surgical and neurological disease populations is difficult and does not serve this population well. Our experience suggests these SC patients will be served better if the emphasis shifts to echocardiographic RWMA recognition instead of relying on catheterization for the diagnosis.[9,24] This non-invasive diagnosis requires clinical suspicion and is imperative in the critically ill given the limitations of catheterization.

3.1. InterTAK registry

The InterTAK registry is the first international multicenter effort to gather data about SC systematically.[8] This registry significantly improves our understanding of SC and its variants. In nearly 44% a physical trigger was identified as potential cause of SC. SC can be fatal as shown by InterTAK, where 4% mortality was noted. For at least 3 reasons, we believe the InterTAK data does not represent the full spectrum of SC, especially the SC developing in critical care settings. Most importantly, the registry inclusion is based on fulfilling the 2008 modified Mayo criteria for SC. As this requires catheterization to exclude CAD, many critically ill SC patients might not undergo catheterization due to their comorbidities and thus fail to qualify for the registry. Secondly, presenting symptoms were uniformly cardiac –namely chest pain (75.9%), dyspnea (46.9%) and syncope (7.7%). In critical care setting, chest pain is not common and majority of SC patients are recognized due to troponin elevation, hypotension, heart failure or tachyarrhythmias. Lastly, among the 1750 SC patients in this registry, global LV dysfunction was not recognized as a variant of SC. This is due to sampling issues and the inclusion criteria requiring catheterization. We believe the 26 collaborating cardiovascular centers in the registry collected their data from cardiology- related hospitalizations for chest pain and catheterization laboratory database of potential ACS. InterTAK is the best available literature currently to understand the clinical presentation and outcomes in SC from the cardiologist viewpoint. However, InterTAK does not adequately address SC that occurs secondarily in the critically ill.

3.2. McMaster series

Lim et al. from McMaster University have published several studies over the last 10 years addressing cardiac injury in the critically ill.[25–31] Troponin levels were followed systematically through the hospitalization and correlated with ECG changes, clinical picture and hemodynamic alterations. Along the lines of several similar but smaller studies over the last 2 decades, the McMaster experience also estimates that troponin elevation occurs in about half of all critically ill patients. Their 2010 series evaluated 103 patients and identified 49 patients with elevated troponins.[28] Authors evaluated patient charts for secondary causes of troponin elevation, namely sepsis (n = 9), left ventricular hypertrophy/strain, intracranial hemorrhage/stroke, cardiac contusion/cardiopulmonary resuscitation (n = 3), cardiac infiltrative disorders, chemotherapy, myocarditis, pericarditis, cardiac surgery, congestive heart failure (n = 2), cardiomyopathy, pulmonary embolism/pulmonary hypertension, chronic obstructive pulmonary disease (n = 3) and renal failure (n = 6). Based on troponin patterns, type II MI (due to hypotension, hypovolemia, supraventricular tachycardia, severe anemia or vasospasm) was identified in 10 (38% of MI) patients. Type I MI due to plaque rupture was determined to have caused the troponin elevation in 16 (62%) patients. A limitation of the series is that the authors did not consider SC in their differential for troponin elevation. Based on the study design and comorbidities of the patients, we suspect SC accounted for a significant portion of the type II MI, resuscitation and COPD groups. As catheterization was not performed in majority of patients, it is likely that some of the troponin elevations attributed to 'plaque

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