1. Introduction

The safety and utility of dobutamine stress testing are well established in the evaluation of patients with known or suspected coronary artery disease [1]. Overall incidence of adverse effects during dobutamine stress testing is about 5–10%. Transient regional wall motion abnormalities of left ventricle and hemodynamic effects of dobutamine infusion during stress testing have been described. However, mechanisms and determinants of various ballooning patterns are unknown.

2. Methods and results

This study was a systematic review of all published case studies and case series from January 2006 to December 2013. We performed a comprehensive literature search using keywords — apical ballooning, dobutamine, stress echocardiogram and stress cardiomyopathy, in Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Cochrane database of systematic reviews. Our search yielded a total of 21 articles of which, 16 were individual case reports and 2 were case series. We compared the baseline characteristics and post stress testing characteristics of our study patients with those with stress cardiomyopathy from other causes. Statistical analysis was performed to calculate mean, median and standard deviation for continuous variables. Categorical variables were expressed as percentages.

The baseline characteristics are summarized in Table 1. Ninety percent were females with mean age of 65 years. Hypertension was the most common risk factor and obesity was least common. Approximately a quarter of study patient had documented psychiatric illness or stressors. Chest pain or exertional dyspnea was the most common reason for evaluation with stress testing. The clinical and imaging characteristics of dobutamine induced stress cardiomyopathy are summarized in Table 2. Chest pain or dyspnea was the leading manifestation. ST segment elevation was common in inferolateral leads. Apical ballooning was noted in 95% of the study patients. Recovery rate was 90% in our analysis and 1 patient died due to sudden cardiac arrest. Time to recovery varied from 1 day to 3 months. Data regarding recurrence was available only for 2 patients. Both patients had no recurrence at one year. Beta blocker was prescribed in over 50% of the patients.

3. Discussion

Main conclusions of this study are: Demographics and risk factor profile of patients with dobutamine stress testing (DST) induced transient cardiomyopathies appear to be very similar to the stress cardiomyopathies where dobutamine is not the inciting factor. Study patients are mostly postmenopausal females with risk factors and clinical presentation similar to the population with coronary artery disease. However coronary angiogram was normal in about three-quarter of the patients. In general the prognosis was good with complete recovery by about 3 months.

Various mechanisms for wall motion abnormalities have been postulated, including catecholaminergic excess, focal myocyte injury, myocardial stunning, and microvascular dysfunction leading to microvascular ischemia, multivessel coronary vasospasm and impaired coronary vasodilatory reserve [3]. Specifically, the development of severe systemic hypertension in patients with left ventricular hypertrophy (LVH), the presence of systolic anterior motion leading to LV outflow tract obstruction (LVOTO) and mitral regurgitation, and mid cavity obstruction leading to dynamic intracavity gradients have been postulated as plausible explanations [4]. However, LVOTO or mid cavity obstruction occurring due to basal hyperkinesia and apical akinesis, increased response of the apex to adrenergic stimulation reflecting a differential beta receptor distribution, base-to-apex perfusion gradient cannot explain mid-ventricular ballooning pattern [5,6]. Transient cardiomyopathy during dobutamine infusion is commonly noted at peak doses ranging from 20 to 50 mcg/kg/min, in some instances, it can develop during recovery. Hence imaging during recovery is as important as obtaining baseline and peak dobutamine infusion images [7]. Significance of atropine administration in this setting is due to lack of data. Parasympathetic withdrawal after atropine administration, creating an imbalance between the parasympathetic and sympathetic influence, is thought to be contributory. In addition, inhalational beta-agonists, centrally acting stimulants such as methylphenidate can contribute to exaggerated sympathetic activity. It is also speculated that such catecholamine-induced myocyte injury is focal, leading to edema and necrosis in the acute phase. This may lead to late gadolinium enhancement (LGE) in the acute phase, but in the healing phase, necrotic areas are replaced by microscars with size below voxel resolution and magnetic resonance imaging (MRI) threshold for detection of fibrous scar [8]. Strain imaging/strain rate curve analysis in patients with stress cardiomyopathy has shown reduced systolic peak and postsystolic thickening in the affected segments.

Recurrence has mostly been associated with pheochromocytoma but isolated cases with no identifiable triggers have been reported. While there have been reports of Takotsubo cardiomyopathy affecting different LV walls with each recurrence [9], such cases would be rare with dobutamine as it would be difficult to re-challenge such patients.

Supportive medical treatment, when instituted in a timely fashion, is lifesaving. In addition to beta-blocker, rehydration and afterload augmentation with phenylephrine are recommended in those with
documented LVOT or mid cavity gradients. Aspirin, angiotensin converting enzyme inhibitors, nitroglycerin, and statins have been prescribed to improve endothelial dysfunction and microvascular coronary vasospasm. In patients with cardiogenic shock, treatment is mainly supportive with intra-aortic balloon pump. Levosimendan is a calcium sensitizer and a non-catecholamine inotrope which has been used successfully in cardiogenic shock related to stress cardiomyopathy [10].

We acknowledge the limitations in our study. First, the descriptive nature and retrospective design of the study prevent us from establishing causal relationships. Nevertheless, the results of this study will enable us to propose hypotheses for the future studies.

Second, the study had a relatively small sample size, probably due to rarity and under reporting of cases. This small sample size and rarity of fatal outcomes precluded us from performing statistical analysis to predict risk factors for poor outcomes and determine statistical differences between control and study groups. Third, the source of data was from published manuscripts and some reports had incomplete data sets. Lastly, long term follow-up was available only in minority of patients.

### 4. Conclusion

In summary, the demographic, clinical and imaging profiles of transient cardiomyopathy from DST are comparable to classical stress cardiomyopathy. Complete recovery is expected in short term but prospective studies are needed to assess long term outcomes. Additional mechanisms such as intracavity gradients in patients with significant LVH, imbalance between parasympathetic and sympathetic stimulation from atropine administration may play a role. Alternative tests for ischemia workup should be considered in susceptible patients.

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The authors report no relationships that could be construed as a conflict of interest.

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