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Left Ventricular Sphericity Index is a reproducible bedside echocardiographic measure of geometric change between acute phase Takotsubo's syndrome and acute anterior myocardial infarction

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ABSTRACT

Background: Left ventricular sphericity index (LVSI) is a simple, quick and reproducible measure to evaluate LV geometric changes. The aim of our study was to evaluate the utility of LVSI as a rapid discrimination tool in two disease processes; Takotsubo's Syndrome (TS) and Anterior Myocardial Infarction (AMI), in the absence of significant left ventricular systolic dysfunction.

Methods: Consecutive patients with acute phase TS admitted to our institution (Jan 2013 - Dec 2018) were evaluated (n=66). Patients with a comprehensive two-dimensional transthoracic echocardiogram were included in primary analysis (n=50) and age-matched with a cohort of patients with acute anterior AMI (n=50). Appraisal of demographic, clinical and echocardiographic parameters of patients was undertaken. Biplane LVSI was calculated as an average of the short- and long-axis length in the 4- and 2-chamber apical views.

Results: A total of 50 TS patients (64.3±13.7 years, 18% men) were matched with 50 AMI (62.10±12.84 years, 74% men) patients. There was no significant difference in baseline cardiovascular risk factors other than diabetes mellitus (AMI 34% vs TS 17%, p = 0.034). There was also no difference in LV mass (p=0.10) or LVEF (p=0.52) between the two groups. Interestingly, there was a significant difference in mean LVSI between TS (0.60±0.06) vs AMI (0.52±0.07) (p<0.01) reflecting a more spherical shaped left ventricle in the acute TS group.

Conclusions: LVSI is reflective of geometric changes in the left ventricle and may be helpful as a rapid and reproducible diagnostic tool in differentiating between TS and AMI in the acute phase.

1. Introduction

Takotsubo's syndrome (TS) has historically been defined as a transient myocardial disease process resulting in a classical apical hypokinesis with a reversible regional dilatation of the left ventricle [1]. The pathogenesis of this entity is attributed to a catecholamine surge, usually secondary to a physical and/or emotional stressor [1,2]. The presentation of acute TS can be similar to that of an acute anterior myocardial infarction (AMI) [2]. Despite well-established pathognomonic morphological features defining TS, distinguishing between the two conditions may not be straightforward [3]. Both these conditions have very different pathophysiological processes, though distinguishing between the two conditions in the acute phase can be challenging especially in more subtle cases where left ventricular systolic dysfunction is not significantly impaired. We hypothesise that different LV geometric shape changes may be associated with the different pathophysiological processes hence could potentially be used to help differentiate between both conditions with similar clinical acute presentations.

Transthoracic echocardiography (TTE) is a simple and readily available bedside tool which can provide first line imaging and valuable information in patients with acute TS or AMI. However, traditional echocardiographic measures of such as LV ejection fraction (LVEF) and indexed LV mass (LVMI), can frequently be insufficient to differentiate between the two different pathologies in the acute phase [4]. LVSI is an underutilised measurement of LV geometry, a marker of LV remodelling, that can be easily obtained from standard echocardiographic images [5,6]. LVSI has been validated

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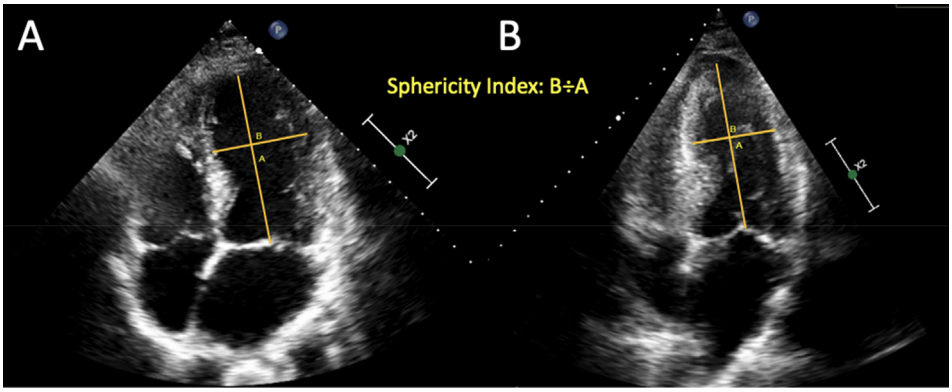

Fig. 1. (A) (Left): Left Ventricular Sphericity index in Takotsubo's Syndrome (4.6/7.6 cm = 0.61). (B) (Right): Left Ventricular Sphericity index in Anterior Myocardial Infarction (4.2/8.5 cm = 0.49).

as a direct measure of LV remodelling in patients with idiopathic dilated cardiomyopathy (IDCM) and correlated with outcomes in ACS populations [6–10]. However, the utility and value of this imaging parameter in differentiating between acute phase TS and AMI has never been studied. Hence the aim of our study was to characterise the geometric changes between acute TS and AMIs using LVSI.

2. Methods

2.1. Study population

Patients with a clinical diagnosis of acute phase TS infarction between January 2013 to December 2018 that presented to our institution were retrospectively examined. Patients who were >18 years of age presenting with clinical syndrome that is consistent with TS and who underwent coronary angiography and a comprehensive TTE within 72 h of admission which demonstrated normal LVEF were included. These patients were age-matched in a 1 to 1 ratio with patients presenting with an acute ST elevation myocardial infarct (STEMI) within the same period. Patients with ventricular or supra-ventricular arrhythmias, congenital heart disease, significant valvular heart disease or prosthetic valves, missing baseline clinical data or had poor quality echo images were excluded. The study protocol was approved by the Human Research and Ethics Committee of New South Wales (1910-06 QA).

2.2. Transthoracic echocardiography

Standard transthoracic echocardiography was performed using commercially available ultrasound equipment (EPIQ, Philips Medical Systems, Andover, MA; GE E9, GE Healthcare, Milwaukee, WI; GE 95, GE Healthcare, Milwaukee, WI) according to guideline recommendations by the American Society of Echocardiography. All echocardiographic images were saved in digital format and analysis was performed offline by two investigators who were blinded to the clinical data of the patient.

Left ventricular sphericity index (LVSI) was measured offline by two independent researchers, blinded to the patient history and condition. LVSI was calculated as LV basal radial length/longitudinal length, measured in both the apical 4- and 2-chamber views during end-diastole (ED) and end-systole (ES) (see Fig. 1). An average of four measurements of LVSI from 3 cardiac cycles (i.e. ES/ED in apical 4-chamber and ES / ED in apical 2-chamber) was reported.

2.3. Intra- and inter-observer variability

Intra- and inter-observer variability was assessed by repeating LVSI in 20 randomly selected patients from the cohort >4 weeks apart by the same investigator and by a second independent investigator. There was good inter- and intra-observer agreement for the LVSI measurements, with an interclass correlation of 0.96 with a 95% Confidence Interval of 0.90–0.99 and a coefficient of variation of 3.39 with a 95% Confidence Interval of 1.65–5.14.

2.4. Statistical analysis

All statistical analyses were performed using commercially available software (SPSS version 22; SPSS Inc, Chicago, IL, USA). Variable distribution was reported as mean and standard deviation for normally distributed variables, median and interquartile range for non-normally distributed variables or as percentage for categorical variables. Comparison between mean values between TS and AMI groups was performed with Student T test for unpaired data or ANOVA with analysis of variance and Bonferroni correction. Categorical variables were compared with Chi - square test (with Yates correction) or with Fisher test. All tests were 2-tailed. A p value of <0.05 was considered as statistically significant.

3. Results

3.1. Baseline characteristics

The final cohort consisted of 100 patients, which included 50 patients with diagnosed acute TS (64.3 ± 13.7 years, 18% men) and 50 patients with anterior STEMI (62.10 ± 12.84 years, 74% men). Patients in the AMI population had higher rates of diabetes mellitus (p = 0.03) but no other significant differences in the baseline characteristics between groups. See Table 1.

Table 1
Baseline characteristics.

Baseline characteristics	TS (n = 50)	AMI (n = 50)	p value
Age (years)	64.30 ± 13.80	62.10 ± 12.80	0.41
Men	9 (18%)	37 (74%)	**<0.01**
Body mass index (kg/m^2)	26.9 ± 8.3	29.1 ± 6.4	0.19
Peak Troponin Level	5145 ± 5925	27519 ± 33619	**<0.01**
Hyperlipidaemia	11 (22%)	18 (36%)	0.186
Hypertension	25 (50%)	23 (46%)	0.689
Diabetes Mellitus	7 (14%)	17 (34%)	**0.034**
Obesity	11 (22%)	15 (30%)	0.34

Table 2
Echocardiographic parameters.

Echocardiographic parameters	TS (n = 50)	AMI (n = 50)	p value
LVEDd (cm)	4.49 ± 0.71	4.56 ± 0.57	0.55
LVESd (cm)	3.03 ± 0.69	3.75 ± 4.62	0.29
IVS thickness (cm)	0.98 ± 0.21	1.10 ± 0.24	**0.01**
PW thickness (cm)	0.96 ± 0.17	1.03 ± 0.19	0.06
LV ejection fraction (%)	54.30 ± 12.01	53.27 ± 13.60	0.69
LVEDv (mL)	94.64 ± 33.57	100.59 ± 30.69	0.36
LVESv (mL)	39.39 ± 15.90	42.92 ± 20.18	0.34
LV mass (g/m^2)	93.15 ± 28.57	93.09 ± 29.18	0.10
Mitral E velocity (cm/s)	0.73 ± 0.26	0.77 ± 0.23	0.51
Mitral A velocity (cm/s)	0.75 ± 0.28	0.82 ± 0.26	0.20
Mitral E/A ratio	1.06 ± 0.50	0.98 ± 0.40	0.45
Deceleration time of E velocity (ms)	0.20 ± 0.08	0.19 ± 0.07	0.50
LVSI (ratio)	0.60 ± 0.06	0.52 ± 0.07	**<0.01**

3.2. Echocardiographic parameters

Baseline TTE data was compared between the two groups. No significant differences were seen between the two groups in terms of LV size and function (TS LVEF 54 ± 12% vs AMI LVEF 53 ± 14%, p = 0.69). There were no significant differences in diastolic parameters (mitral E', A', E/A ratio or deceleration time) between the two groups. However, there was a significant difference in calculated LVSI between the two groups (TS 0.6 ± 0.6 vs AMI 0.5 ± 0.7, p < 0.01) which suggested that patients with acute TS had more spherical shaped left ventricles in the compared to acute anterior MI patients. See Table 2.

4. Discussion

This study attempted to characterise left ventricular geometric changes using a quantitative measure of LV shape i.e. LVSI between acute phase TS and AMI, two fundamentally different cardiac pathologies but with similar clinical presentations. Our results indicate that in acute phase TS process, the LV adopts a more spherical morphology compared to patients with anterior STEMI [11]. Due to large similarities in clinical history, examination, electrocardiography and traditional echocardiographic findings of regional wall motion abnormalities differentiation between the two conditions can be difficult particularly if left ventricular systolic function is within normal limits [12,13]. The present gold-standard investigation which differentiates between these two pathologies is coronary angiography. More recently, echo measures of left ventricular function such as global longitudinal strain, have been proposed to be potentially useful for assisting discrimination between TS and AMI as it is able to provide information segmental wall motion abnormalities [14,15]. However, measurement of longitudinal strain may not be technically possible in situations where there is poor visualisation of the endocardium, and in such situations LVSI may be larger benefit as an additional non-invasive discriminator.

We hypothesised that different patho-physiological processes result in differential LV geometric changes which may then be used to help differentiate between two different conditions with similar clinical presentations. With AMI, early LV remodelling occurs in the left anterior descending coronary artery territory from micro- and macro-vascular ischemia and resultant necrosis. This process typically affects the anterior and apical walls, however does not affect inferior and inferolateral segments as these are typically supplied by the circumflex and right coronary arteries. TS, however, is a result of catecholamine-induced ventricular dysfunction, with a classical apical hypokinesis and basal hyperkinesis appearance. However, the classical pathognomonic morphological appearance which is typically described in TS (with variable sensitivity) is only a qualitative diagnostic assessment for TS [16]. Given the subjective nature of this assessment, there can be difficulty in the diagnosis particularly in subtle cases. Given the relatively higher burden of myocardial involvement not ascribed to a coronary artery territory, there is complete circumferential involvement of the mid-segment including the inferior and inferolateral regions of the left ventricle [17,18]. Therefore, this tool may be of benefit in assisting discrimination of these two pathologies, especially in patients who have contraindications to conventional coronary angiography or are too unstable to undergo procedural therapy.

The major limitations of our study include the small but well-defined sample size and retrospective design of the study. The other limitations included the inability to exclude such morphologic patterns prior to the onset of the acute pathologies and the effect of pre-existing cardiovascular comorbidities (i.e. hypertension) in influencing LV morphological changes.

5. Conclusions

The LVSI parameter provides a simple but more objective quantification of LV geometric changes, and hence could potentially be used as an additional quantitative tool in discriminating these two pathologies in addition to standard diagnostic criteria. Further studies are still required to better characterise the application of this measure in a clinical setting.

Sources of support

Not applicable.

CRediT authorship contribution statement

Shaun Khanna: Methodology, Investigation, Resources, Writing - original draft. **Aditya Bhat:** Writing - review & editing, Formal analysis, Project administration. **Henry H. Chen:** Writing - review & editing, Formal analysis. **Jeremy W.A. Tan:** Investigation, Resources, Validation. **Gary C.H. Gan:** Formal analysis, Data curation, Supervision. **Timothy C. Tan:** Supervision, Project administration, Conceptualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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