Two-dimensional speckle tracking echocardiography derived post systolic shortening in patients with unstable angina and normal left ventricular systolic function

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ABSTRACT

Objective: Post-systolic shortening (PSS) has been shown to be sensitive in detecting ischemia on stress echocardiography. In this study, we aimed to assess the diagnostic potential of resting PSS and post-systolic index (PSI) in patients with suspected unstable angina (UA).

Methods: A total of 159 participants with suspected UA without any wall motion abnormalities were recruited. They all underwent speckle tracking echocardiography (STE) and coronary angiogram (CAG). Global longitudinal strain (GLS); presence or absence of pathological PSS; PSI in left anterior descending, left circumflex, and right coronary artery territories were assessed. On the basis of CAG, those who had more than 70% stenosis were labelled to have obstructive CAD.

Results: Obstructive disease was noted in 54.7% patients. The prevalence of PSS (62.1% vs. 13.9%), mean PSI (5.4 vs. 3.3), and PSI (6.2 vs. 3.7) were significantly higher in those with CAD compared with patients without obstructive disease. Both PSS (odds ratio (OR) 10.145; 95% confidence interval (CI) 4.577–22.489; p=0.001) and PSI (OR: 1.217; 95% CI: 1.064–1.393; p=0.004) were predictors of CAD by multivariate regression analysis. PSS had a sensitivity of 62.1% and specificity of 86.1% with a positive predictive value of 84.4%. PSI (area under curve (AUC): 0.637; p=0.003) and PSI (AUC: 0.661; p=0.001) have moderate accuracy in identifying obstructive CAD.

Conclusion: In patients presenting with suspected UA, STE derived PSS has reasonable sensitivity and good specificity in diagnosis of obstructive CAD. Patients identified to have PSS can be subjected to CAG without further stress testing because of its high positive predictive value.

Keywords: post-systolic shortening, speckle tracking echocardiography, unstable angina

Introduction

Coronary artery disease (CAD) is the most common cause of mortality both worldwide and in India (1). Unstable angina (UA) constitutes an important sub-group among patients with CAD presenting with chest pain to both the emergency room (ER) and outpatient department. In patients with definite acute coronary syndrome (ACS), resting ECG may be non-diagnostic in more than half of the patients. Hence, several non-invasive investigations are used in the diagnosis and risk stratification of suspected UA without any high-risk features before subjecting them to an invasive investigation, such as coronary angiogram (CAG), although patients with high-risk features such as ongoing pain, dynamic ECG changes, and regional wall motion abnormalities (RWMA) undergo CAG
without any non-invasive testing (2). Except for stress ECG which has limited sensitivity and specificity, the use of other imaging modalities (single photon emission computed tomography/computed tomography/magnetic resonance imaging) is restricted in developing countries like ours owing to financial constraints, availability, and lack of technical expertise. This potential gap in resources has always propelled clinicians to search for a point of care and cost effective tool to diagnose CAD.

Impairment in several 2-dimensional and 3-dimensional strain parameters have been shown to have a role in predicting obstructive CAD, both in stable ischemic heart disease (3) and non-ST elevation myocardial infarction (NSTEMI)/ST elevation myocardial infarction (STEMI) patients (4). Kukulski et al. (5) first described the diagnostic superiority of tissue Doppler derived post-systolic index (PSI) over conventional strain parameters in identifying ischemia during coronary angioplasty. Speckle tracking echocardiography derived rest post-systolic shortening (PSS) was reported to be a promising marker in detecting myocardial ischemia (6). Myocardial shortening that happens after aortic valve closure is defined as PSS. It is easily identifiable by STE and observed during isovolumic relaxation. PSS can be measured and quantified objectively by PSI. Not only is PSS a marker for detecting myocardial ischemia, but also elevated PSI values in segments with RWMA represent actively contracting myocardium and hence correlates well with viability (7). However, the use of PSS has not been described in patients with UA with normal left ventricle (LV) function presenting to the ER. In this study, our objective was to document the role of STE derived PSS and PSI at rest in the diagnosis of CAD among patients with suspected UA and in their risk stratification.

**Methods**

**Study population**

This was a prospective study with 159 patients, older than 18 years of age with suspected unstable angina and normal LV systolic function who were admitted for a coronary angiogram. All those included had no RWMA on echocardiogram and negative highly sensitive troponin assay result.

Patients with a previous history of myocardial infarction, known CAD, presence of significant valvular heart disease, patients on chemotherapy, those with stage 4 and 5 chronic kidney disease, presence of left bundle branch block/pacemaker, and atrial fibrillation were excluded. The study was approved by the Institutional Ethics Committee, Mahatma Gandhi Medical College and Research Institute (Date: 21.05.2020). All the participants signed an informed consent form.

Baseline parameters like the patients’ age, sex, body mass index (BMI), presence of risk factors such as diabetes mellitus, systemic hypertension, dyslipidaemia, obesity, current smoking status, and other relevant clinical data were collected.

**Speckle tracking echocardiogram**

All the study participants underwent echocardiogram in a Vivid E-95 system (GE healthcare) equipped with a 4V phased array matrix transducer (1.5–4.0 MHz) just before the coronary angiogram. Echocardiographic measurements were obtained according to American Society of Echocardiography guidelines (8). The images were stored and later analysed by a single cardiologist experienced in strain echocardiogram, who was blinded to the patient’s clinical and angiographic details. Cine loops with 3 cardiac cycles in apical 3 chamber, apical 4 chamber, and apical 2 chamber views were recorded at a frame rate of 50–80 fps and stored. In each of the apical planes, tracing of LV myocardium was automatically performed by the software. Manual adjustments were made by the investigator whenever tracking the region of interest was inadequate. The longitudinal strain curves were generated, and the presence of PSS was categorised on the basis of the criteria laid out by Voigt et al. (9). The PSI was derived from the strain curve as $\left(\frac{\text{peak negative strain in cardiac cycle} - \text{peak negative strain in systole}}{\text{peak negative strain in cardiac cycle}}\right) \times 100$ (see Fig. 1). A 17 segment bulls’ eye map with PSI of individual segments was generated automatically by the software, and the mean PSI was calculated as an average of the individual segments. The patients were determined to have PSS if PSI in any one of the 17 segments was more than 20%. PSI$_{LV}$ was derived manually from 6 basal and 6 mid-ventricular segments. On the basis of the standardised model of myocardial perfusion territories (10), region-specific PSI was calculated as the average value of the segments belonging to each perfusion territory in the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA), respectively. For example, the region specific PSI of RCA was calculated manually by averaging the PSI values of the 5 segments perfused by the RCA (basal inferior and inferoseptal, mid inferior and inferoseptal, and apicoinferior). Similarly, the region specific PSI of LCX territory was calculated from the following 5 segments - basal and mid inferolateral, basal and mid anterolateral, and apicolateral.

**Coronary angiogram**

The decision to catheterize a subject with UA was made by the admitting clinician. The research group had no role in deciding the need for invasive strategy. Only after the patient was admitted for CAG were they included in the study and after signing the informed consent. The decision to perform CAG was based on the clinical
presentation (typical angina), risk factors, and ECG changes and was not based on the STE results. Angiographic images were studiously assessed by an interventionist who was blinded to the patient data. The study participants were divided into 2 groups on the basis of CAG results. The patients were diagnosed to have obstructive CAD if they had a lesion of >70% stenosis in one or more major epicardial coronary vessels or 50%–70% stenosis but with less than TIMI 3 flow. Participants with normal coronaries and non-obstructive disease were taken as the control group. Patients with >70% stenosis in obtuse marginal, posterior descending artery, posterolateral branch, and ramus were considered obstructive only if the vessel diameter was >2.25 mm. SYNTAX I score was calculated using the standard online calculator from the website http://www.syntaxscore.com/calculator/start.htm.

Statistical analysis

The data analysis was performed using Statistical Package for Social Sciences for Windows, version 16.0 (SPSS Inc., Chicago, USA). Quantitative variables were expressed as mean ± standard deviation, whereas categorical variables were expressed as numbers and percentages. Continuous variables were compared using independent samples t-test. Pearson chi-squared test and Fisher exact tests were used for categorical variables. A value of p<0.05 was considered to indicate a statistically significant difference. Binary logistic regression analysis was done to study the predictors of obstructive CAD. Linear correlation between PSI and SYNTAX score was measured by Spearman S rank correlation coefficient. Receiver operator characteristic curves (ROCs) were constructed for strain parameters to detect their sensitivity and specificity in identifying obstructive CAD.

Results

A total of 159 patients with suspected UA were included for final analysis after excluding 16 patients owing to issues with image quality. The clinical details stratified by presence or absence of PSS are provided in Table 1. The mean age was 55.9 years, and only 22.7% were women. The GRACE score of the included participants ranged from 35 to 126 suggesting that the study participants predominantly had low-risk unstable angina. Thirty-five patients (21.8%) had ischemic changes on ECG, whereas the rest had normal or non-diagnostic changes. Only 17.6% (n=28) had non-invasive ischemia testing with another 12 patients (7.5%) undergoing CT-CAG before conventional CAG.

Of the 159 patients studied, 54.7% (n=87) had obstructive disease and 45.3% (n=72) had normal/non-obstructive disease. Single vessel involvement was noted in 43.7% (n=38). Double vessel and triple vessel disease were noted in 31% (n=27) and 20.7% (n=18), respectively. Only 4.6% (n=4) of those with obstructive CAD had left main disease. Of the 87 with obstructive disease, 9 patients were put on medical management, and the rest were advised to undergo revascularisation (22 for CABG and 56 for PCI).

Among the risk factors, patients with PSS more often had diabetes and hypertension, and they were more frequently on beta-blockers and statin therapy (see Table 1). Furthermore, higher systolic blood pressure, E/e', and significantly altered global longitudinal strain (GLS) (less negative) were noted in those with PSS. The mean LV ejection fraction was 64.2% suggesting that the study group had only patients with normal LV systolic function, and there was no significant difference between those with or without PSS. Those with PSS had higher occurrence of obstructive disease overall and also had significant lesions in LAD, LCX, and RCA than those without PSS. The prevalence of PSS and the mean PSI17 and PSI12 were all significantly high in patients with obstructive lesions (Table 2).

Both PSI17 and PSI12 were predictors of obstructive CAD (Table 3) by regression analysis after adjusting for baseline clinical and echocardiographic variables. Categorical PSS was the strongest predictor of CAD (OR=10.1; 95% CI=4.58–22.49;
Presence of PSS had a reasonable sensitivity with good specificity and positive predictive value (Table 4).

Both PSI\textsubscript{17} and PSI\textsubscript{12} had modest accuracy in diagnosing obstructive CAD with an area under the curve (AUC) of 0.637 (95% CI: 0.551–0.723; p=0.001) and 0.661 (95% CI: 0.576–0.745; p=0.001), respectively (Fig. 2a and 2b). A mean PSI\textsubscript{17} of more than 3.1 had a sensitivity and specificity of 61% and 53.5%, respectively, whereas mean PSI\textsubscript{12} >3.1 had a sensitivity and specificity of 70.1% and 50.7%, respectively. The accuracy of territorial PSI (PSI LAD) in identifying significant lesions of LAD (Fig. 2c) was poor with an AUC of 0.575 (95% CI: 0.484–0.665; p=0.112). Similarly, both PSI LCX

### Table 1. Baseline characteristics stratified by presence or absence of PSS

<table>
<thead>
<tr>
<th>Presence of PSS (n=64)</th>
<th>Absence of PSS (n=95)</th>
<th>Total patients (n=159)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57±9.1</td>
<td>54±10.0</td>
<td>55.9±8.9</td>
</tr>
<tr>
<td>Male</td>
<td>44 (68.8%)</td>
<td>63 (66.3%)</td>
<td>107 (67.3%)</td>
</tr>
<tr>
<td>Body mass index, kg/m(^2)</td>
<td>25.3±3.1</td>
<td>24.4±2.5</td>
<td>24.8±2.8</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>41 (64.1%)</td>
<td>46 (48.4%)</td>
<td>87 (54.7%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>48 (75%)</td>
<td>50 (52.6%)</td>
<td>98 (61.6%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>15 (23.4%)</td>
<td>23 (24.2%)</td>
<td>38 (23.9%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>7 (10.9%)</td>
<td>14 (14.7%)</td>
<td>21 (13.2%)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>138±20.8</td>
<td>131±17.9</td>
<td>134±19.3</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>84.5±8.9</td>
<td>81.8±10.4</td>
<td>83±9.9</td>
</tr>
</tbody>
</table>

**Treatment details**

- **ACE I**: 26 (40.6%) vs 34 (35.8%); 60 (37.7%); 0.537
- **Statin**: 55 (85.9%) vs 69 (72.6%); 124 (78.1%); 0.047
- **Beta-blocker**: 39 (60.9%) vs 43 (45.3%); 82 (51.6%); 0.052

**Echocardiogram**

- **EF**: 64.4%±3.5 vs 64.1%±4.5; 64.2 5±4.1; 0.601
- **E/e’**: 12±4.6 vs 10.3±3.0; 11±3.8; 0.015
- **LV mass index**: 102.7±24.6 vs 97.0±23.3; 99.3±23.9; 0.145
- **GLS**: -14.7±10.7 vs -18.5±8.6; -16.9±9.7; 0.021

**CAG**

- **Obstructive CAD**: 54 (64.4%) vs 33 (34.7%); 87 (54.7%); 0.001
- **LAD disease**: 37 (57.8%) vs 29 (30.5%); 66 (41.5%); 0.001
- **LCX disease**: 27 (42.2%) vs 8 (8.4%); 35 (22.0%); 0.001
- **RCA disease**: 27 (42.2%) vs 9 (9.5%); 36 (22.6%); 0.001

Continuous data are expressed as mean ± standard deviation. Categorical data are presented as n (%).

PSS - post-systolic shortening; ACE - angiotensin converting enzyme inhibitor; LV - left ventricle; EF - ejection fraction; E -transmitral early diastolic velocity; e’ - early myocardial diastolic velocity; GLS - global longitudinal strain; CAG - coronary angiogram; CAD - coronary artery disease; LAD - left anterior descending artery; LCX - left circumflex artery; RCA - right coronary artery.

### Table 2. Baseline characteristics of PSS/PSI stratified by CAD

<table>
<thead>
<tr>
<th></th>
<th>Obstructive CAD (n=87)</th>
<th>Non-obstructive CAD (n=72)</th>
<th>Total (n=159)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorical PSS</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>PSI\textsubscript{17}</td>
<td>54 (62.1%)</td>
<td>10 (13.9%)</td>
<td>64 (40.3%)</td>
<td></td>
</tr>
<tr>
<td>PSI\textsubscript{12}</td>
<td>5.4±5.5</td>
<td>3.3±2.5</td>
<td>4.5±4.5</td>
<td>0.002</td>
</tr>
<tr>
<td>PSI LAD</td>
<td>6.2±6.1</td>
<td>3.7±2.9</td>
<td>5.1±5.0</td>
<td>0.001</td>
</tr>
<tr>
<td>PSI LCX</td>
<td>5.6±6.9</td>
<td>3.2±2.9</td>
<td>4.5±5.6</td>
<td>0.003</td>
</tr>
<tr>
<td>PSI RCA</td>
<td>7.1±9.2</td>
<td>4.2±5.1</td>
<td>5.8±7.8</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean ± standard deviation. Categorical data are presented as n (%).

PSS - post-systolic shortening; PSI - post systolic index; LAD - left anterior descending artery; LCX - left circumflex artery; RCA - right coronary artery.

### Table 3. Logistic regression analysis for predicting obstructive CAD

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI\textsubscript{17}</td>
<td>1.217 (1.064-1.393)</td>
<td>0.004</td>
</tr>
<tr>
<td>PSI\textsubscript{12}</td>
<td>1.191 (1.049-1.353)</td>
<td>0.007</td>
</tr>
<tr>
<td>PSI LAD</td>
<td>1.171 (1.052-1.304)</td>
<td>0.004</td>
</tr>
<tr>
<td>PSI LCX</td>
<td>1.069 (1.000-1.143)</td>
<td>0.049</td>
</tr>
<tr>
<td>PSI RCA</td>
<td>1.067 (0.973-1.171)</td>
<td>0.169</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, blood pressure, presence of hypertension, diabetes, and echocardiographic parameters (E/e’, left ventricle mass index, and global longitudinal strain).

OR - odds ratio; CI - confidence interval; CAD - coronary artery disease

Cl: 0.551–0.723; p<0.003) and 0.661 (95% CI: 0.576–0.745; p=0.001), respectively (Fig. 2a and 2b). A mean PSI\textsubscript{17} of more than 3.1 had a sensitivity and specificity of 61% and 53.5%, respectively, whereas mean PSI\textsubscript{12} >3.1 had a sensitivity and specificity of 70.1% and 50.7%, respectively. The accuracy of territorial PSI (PSI LAD) in identifying significant lesions of LAD (Fig. 2c) was poor with an AUC of 0.575 (95% CI: 0.484–0.665; p=0.112). Similarly, both PSI LCX
and PSI RCA had only moderate accuracy in pointing out obstructive diseases of respective coronary territory with AUC of 0.602 (95% CI: 0.493–0.711; p=0.065) and 0.624 (95% CI: 0.522–0.725; p=0.024), respectively (Fig. 2d and 2e).

There was no significant difference in both mean PSI$_{17}$ and PSI$_{12}$ values between those with single and multivessel disease (PSI$_{17}$ - 5.4±6.5 vs. 5.4±3.8, p=0.873; PSI$_{12}$ - 6.1±6.9 vs. 6.5±4.9, p=0.751). As shown in Figure 3, the correlation between SYNTAX score and mean PSI$_{17}$ was weak though being significant statistically ($R^2=0.066$, p=0.004).

**Discussion**

The salient data generated from this study were PSS as depicted by high PSI values was significantly more frequent in patients with obstructive CAD; mean PSI$_{17}$ and PSI$_{12}$ along with territorial PSI of LAD and LCX were statistically higher in those with CAD; multivariate regression analysis suggested high PSI values indicating the presence of PSS to be a strong predictor.

**Table 4. Diagnostic accuracy of PSS in identifying obstructive CAD**

<table>
<thead>
<tr>
<th>Presence of PSS</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>62.1%</td>
<td>86.1%</td>
<td>84.4%</td>
<td>65.3%</td>
<td>73.0%</td>
<td></td>
</tr>
</tbody>
</table>

PSS - post-systolic shortening; CAD - coronary artery disease; PPV - positive predictive value; NPV - negative predictive value
of obstructive disease; although the accuracy of PSS to diagnose CAD is moderate, it has high specificity and positive predictive value. To the best of our knowledge, this is the first study providing information on the diagnostic role of STE derived PSS at rest in patients with UA.

Prior animal studies have demonstrated the sensitivity of post-systolic deformation in acutely ischemic myocardium (11). Post-systolic thickening have been documented in patients with critically stenosed arteries and identified as a sign of myocardial viability (12). A large database exists regarding the role of dobutamine stress echocardiography (DSE) induced PSS in patients with CAD (12, 13). Strain rate imaging during DSE has been investigated, and the ratio of PSS to maximal segmental deformation was found to be the best quantitative parameter in diagnosing stress induced ischemia (14). In another pivotal study using pulse wave Doppler imaging derived PSS, stress-induced PSS was the most sensitive index in the diagnosis of induced ischemia (13). However, there is a paucity of data about the accuracy of post-systolic deformation indices derived with resting STE in patients suspected to have UA.

PSS, albeit a sensitive marker of ischemia, is not 100% specific for it. In a seminal study by Voigt et al. (9), almost one-third patients (31%) in the control group had PSS which was considered to be physiologic. This non-specificity hinders the widespread use of PSS in clinical practice. Hence with an intention to exclude segments showing physiologic PSS, strict criteria of PSI exceeding 20% of the total strain during cardiac cycle as suggested by Voigt et al. (9) was employed in our study. Few other studies have used this threshold to label PSS and reported its role in both stable angina and ST elevation myocardial infarction (15–17). Applying these criteria led to a PSS of 40.3% in our study population (62.1% in CAD group vs 13.9% in control group). The prevalence of CAD was low in our cohort (54.7%) owing to non-availability of non-invasive imaging modalities (such as SPECT, PET, MRI, and CT). All our data were acquired at rest, which lends more clinical relevance as it can be easily performed bedside in an ER setting.

**Study limitations**

The major limitation of our study is that we did not aim to compare post systolic deformation indices with other standard strain parameters. Second, the significance of the lesion was solely on the basis of angiographic criteria and not functionally substantiated (no fractional flow reserve done). Future studies should look into association between functionally significant lesion and PSS. Third, we did not follow up with any of these patients for cardiac events.

**Conclusion**

In patients with low-risk UA and no RWMA, resting PSS by STE has reasonable sensitivity and good specificity in the diagnosis of obstructive CAD. Similarly, higher cut-off values of mean PSS_{17} and PSS_{12} as suggested above has good specificity. Hence, those patients with altered pathologic post-systolic indices can be considered for CAG without submitting them for non-invasive imaging.

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**Conflict of interest:** None declared.

**Peer-review:**Externally peer-reviewed.

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