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Original article

Eccentricity index as an adjunctive indicator of coronary ischemia: Correlation with ischemic burden based on myocardial perfusion imaging

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ABSTRACT
BACKGROUND: One of the main challenges in managing CAD is the measurement of ischemic burden experienced by patients, which can influence therapy decisions and prognosis. The Left Ventricular Eccentricity Index (EI) has become a potential additional indicator for assessing the severity of ischemia in CAD patients.
OBJECTIVES: This study aims to analyze the correlation between the Left Ventricular EI and ischemic burden measured using myocardial perfusion imaging (MPI) in CAD patients.
METHODS: This retrospective cohort study was conducted at Dr. Hasan Sadikin Hospital in Bandung from August 2023 to June 2024. Data were collected using MPI with 99mTc sestamibi gated SPECT. Statistical analysis was performed using the Mann-Whitney U test and Spearman's correlation.
RESULTS: A total of 78 patients who met the inclusion and exclusion criteria were included in this study. The analysis showed that EI values in both the stress and rest phases were significantly higher in the group with ischemic burden ≥10%. The median ejection fraction value in the stress phase was also lower in this group ($p = 0.013$). Correlation analysis revealed a significant relationship between EI and ischemic burden ($p < 0.05$).
CONCLUSION: This study demonstrates that EI can be used as an additional indicator to assess the severity of ischemia in CAD patients. Integrating EI into routine MPI protocols can improve the accuracy of risk stratification and management of CAD patients.

KEYWORDS: Eccentricity Indeks; coronary artery disease; myocardial perfusion imaging.

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INTRODUCTION

Coronary artery disease (CAD) has now grown into a major health problem worldwide, as its prevalence, incidence, and mortality rates are steadily on the rise.[1] This is a condition that constitutes about 31 percent of the global deaths Every year, it occurs in both developed and developing countries.[2] Some of its key risk factors include the following: hypertension, diabetes mellitus, smoking, and increased cholesterol level, among others.[3] However, these traditional factors are not entirely representative of the ischemic burden that patients with coronary artery disease suffer.[4,5] Hence the deeper interpretation of ischemic burden, and one promising emerging tool in this regard is the Left Ventricular Eccentricity Index (EI).[6] It has been known to measure the geometric changes in the left ventricle as a consequence of ischemia, giving a picture of the changes in shape that the ventricle may undergo, which may not be captured through conventional perfusion analysis.[7] Understanding how its EI unit functions under the headings of CAD is necessary to promote accuracy in ischemic assessments and prognosis.[1,8]

EI measures the deviation of the left ventricle from the ideally spherical shape which reflects ventricular remodeling, in response to ischemia.[9] This remodeling is more related to the stresses of high burden of ischemia which can eventually be detrimental to the cardiac functionality and compromise ejection fraction while predisposing to heart failure.[10] Studies have shown that the increased EI values showed a more ischemic burden in CAD patients, correlating to reduced left ventricular functioning and rising sudden cardiac death risk.[11] However, some of these have also shown conflicting results as some studies have failed to show a significant association.[12] Such discrepancies could arise from differences in study populations, imaging methods, or other factors.[13,14] Hence, our study aims to understand the association of EI with ischemic burden and the role of EI in assessing CAD as a potential supplementary diagnostic. The results expected from this study are likely to prove that EI could be a good marker for assessing ischemic severity in CAD patients while enhancing diagnostic accuracy, improving risk stratification, and giving better insights to manage CAD in the practice.

METHODS

Design

This study was a retrospective cohort study conducted at Dr. Hasan Sadikin Hospital, Bandung, from August 2023 to June 2024. The study aimed to evaluate the association between Left Ventricular EI and ischemic burden (IB) in patients with suspected CAD using MPI with 99mTc sestamibi SPECT. A semi-quantitative visual analysis was used, employing a five-point scoring system on a 17-segment model. Ischemic burden was measured using the percentage difference of summed defect (SD%). The study protocol adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Ethical approval

The research protocol was deemed ethically appropriate. The study was conducted following the principles of the Declaration of Helsinki. Before participation, all subjects were provided with a detailed explanation of the study's purpose, potential risks, and benefits, and they voluntarily provided written informed consent. Participants had the right to withdraw from the study at any time without consequences. No financial incentives were provided to the participants.

Participants & eligibility criteria

The study involved 78 patients who underwent MPI with 99mTc sestamibi gated SPECT, using either physical or pharmacological stress tests (dobutamine or adenosine), and met the inclusion and exclusion criteria. Inclusion criteria included male or female patients of any age with suspected or diagnosed coronary artery disease. Exclusion criteria included patients with uncontrolled arrhythmias, incomplete MPI data, normal perfusion, a history of myocardial infarction, previous heart surgery, atrial fibrillation, ventricular pacemaker implantation, malignancy, or prior hemodialysis.

Data collection

Data collection was performed at the Department of Nuclear Medicine and Molecular Diagnostic Radiology, Dr. Hasan Sadikin General Hospital, Bandung, from August 2023 to June 2024. Data collection utilized MPI with 99mTc sestamibi gated SPECT, including stress and rest phases. Data were analyzed by experts using a semi-quantitative visual scoring system on a 17-segment model. Inter-rater differences in data interpretation were minimized by following standard protocols and consistent training. The data collection process was conducted by AA, BB, and CC.

Covariates

In this study, the main variables were Left Ventricular EI and IB. EI was defined as a measure of left ventricular elongation, calculated from the major and minor axes of the ellipsoid on the left ventricular myocardium in three dimensions (Figure 1). EI measurements were made assuming both minor axes had the same length and were calculated using specific formulas. EI values ranged from 0 to 1, with values close to 0 indicating a spherical shape and values close to 1 indicating an elongated shape. Ischemic burden was measured by the percentage difference (SD%) in myocardial perfusion defects. The variable interpretation was based on median values and interquartile ranges.

Statistical analysis

Data were presented as mean ± standard deviation (SD) if normally distributed or median ± interquartile range (IQR) if the data distribution was not normal. Normality testing was performed using the Shapiro-Wilk test. Comparisons between groups based on ischemic burden (SD% < 10% and SD% ≥ 10%) were conducted using the Mann-Whitney U test to determine the difference in median EI between the groups. The correlation between EI and IB was analyzed using Spearman's correlation. A p-value of < 0.05 was considered statistically significant. Data analysis was performed using SPSS version 25 software.

RESULTS

Baseline characteristics of patients included in the study

A total of 68 patients were included in this study, with an average age of 60.75 ± 11.75 years and a female proportion of 57.35%. The average Body Mass Index (BMI) was 25.68 ± 4.65 kg/m², and the resting heart rate was 74.20 ± 14.41 bpm. The average systolic and diastolic blood pressure were 141.25 ± 22.51 mmHg and 81.38 ± 12.9 mmHg, respectively. Most patients had a history of hypertension (60.2%) and diabetes (20.5%). Medications used included ACE inhibitors or ARBs (54.4%), beta-blockers (75%), and calcium channel blockers (38.23%). Most patients underwent stress testing with adenosine (69.11%), while 20.58% used physical stress tests, and 8.82% used dobutamine. The average SSS, SRS, and SDS values were 12.42 ± 7.38, 6.9 ± 5.86, and 5.0 ± 4.36, respectively. The average TID was 1.06 ± 0.20. The left ventricular end-diastolic volume (LVEDV) post-stress and at rest were 60.86 ± 33.64 ml and 58.25 ± 35.11 ml, respectively, while the left ventricular end-systolic volume (LVESV) post-stress and at rest were 24.94 ± 27.25 ml and 23.52 ± 28.32 ml, respectively. The left ventricular ejection fraction (LVEF) post-stress and at rest were 65.13 ± 14.11% and 66.72 ± 14.53%, respectively. No significant differences were found in the baseline characteristics between groups, indicating homogeneous data. The p-values for the main characteristics were > 0.05, indicating no significant differences between groups at baseline.

Differences analysis

A differences analysis was performed between the groups with ischemic burden <10% and ≥10%. A total of 45 patients were included in the SD% <10% group, and 23 patients were in the SD% ≥10% group. The median eccentricity index values during stress (Ecc_S) and at rest (Ecc_R) were significantly higher in the SD% ≥10% group (Ecc_S: 0.83 ± 0.04 vs. 0.80 ± 0.06, p = 0.038; Ecc_R: 0.83 ± 0.03 vs. 0.80 ± 0.06, p = 0.009). The ejection fraction during stress (EF_S) was lower in the SD% ≥10% group (62.00 ± 14.00

vs. 67.00 ± 17.00, p = 0.013), while at rest (EF_R), no significant difference was observed between groups (p = 0.179). The TID ratio tended to be higher in the SD% ≥10% group (1.11 ± 0.24) compared to the <10% group (1.00 ± 0.18), but it did not reach statistical significance (p = 0.053).

Table 1. Baseline characteristics of patients included in our study

Characteristics	n = 68
Age (years)	60.75 ±11.75
Female genders (%)	57.35
BMI (kg/m2)	25.68±4.65
Resting heart rate (beats/min)	74.20±14.41
Systolic blood pressure (mmHg)	141.25±22.51
Diastolic blood pressure (mmHg)	81.38±12.9
Hypertension (%)	60.2
Diabetes (%)	20.5
Medication	
ACEis or ARB (%)	54.4
Beta-blockers (%)	75
Calcium channel blockers (%)	38.23
Type of Stress test	
Physical stress test (%)	20.58
Dobutamine (%)	8.82
Adenosine (%)	69.11
SPECT Variables	
SSS	12.42±7.38
SRS	6.9±5.86
SDS	5.0±4.36
TID	1.06±0.20
Post-stress LVEDV (ml)	60.86±33.64
Post-stress LVESV (ml)	24.94±27.25
Rest LVEDV (ml)	58.25±35.11
Rest LVESV (ml)	23.52±28.32
Post-stress LVEF (%)	65.13±14.11
Rest LVEF (%)	66.72±14.53
Post stress end-systolic LVSI	0.46±0.10
Post stress end-diastolic LVSI	0.66±0.08

Note, Data were presented in mean ± SD or n (%); BMI, body mass index; ACEis, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; SPECT, single photon emission computed tomography; SSS, summed stress score; SRS, summed rest score; SDS, summed difference score; TID, transient ischemic dilation; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LVSI, left ventricular stroke index.

Correlation analysis

Correlation analysis revealed a significant positive relationship between the eccentricity index both during stress (Ecc_S) and at rest (Ecc_R) with ischemic burden percentage (SD%). The correlation between Ecc_S and SD% was r = 0.265 (p = 0.029), while the correlation between Ecc_R and SD% was r = 0.307 (p = 0.011). These findings suggest that a higher left ventricular eccentricity index is associated with a greater ischemic burden experienced by patients, both during stress and at rest.

DISCUSSION

This study demonstrates a significant correlation between the Left Ventricular EI and IB, indicating that changes in ventricular shape are associated with the severity of myocardial ischemia.[15] Patients with high ischemic burden (SD% ≥ 10%) showed significantly higher EI and lower ejection fraction, especially under stress conditions.[16]

These findings align with previous studies that highlight the impact of ischemia on left ventricular (LV) remodeling and function.[17] The direct reason is that prolonged ischemia leads to increased wall stress and neurohormonal activation, which contribute to progressive ventricular dilation and spherical remodeling.[18] Thus, our results emphasize that EI can be used as an additional parameter to detect coronary ischemia.

Table 2. Differences analysis

Covariates	< 10 % Median (IQR)	> 10 % Median (IQR)	P
Ecc_S	0.80±0.06	0.83±0.04	0.038
Ecc_R	0.80±0.06	0.83±0.03	0.009
EF_R	71.00±16.00	67.00±10.00	0.179
EF_S	67.00±17.00	62.00±14.00	0.013
TID	1.00±0.18	1.11±0.24	0.053

Note, Ecc_S, echocardiographic stress; Ecc_R, echocardiographic rest; EF_R, ejection fraction rest; EF_S, ejection fraction stress; TID, transient ischemic dilation.

Our results show that EI, both during stress and rest phases, is higher in the SD% ≥ 10% group.[19] Ejection fraction during stress is also significantly lower in the SD% ≥ 10% group.[20] The transient ischemic dilation (TID) ratio tends to be higher in the SD% ≥ 10% group, although it did not reach statistical significance.[21] These findings are consistent with previous cardiac imaging research that shows ischemic injury induces ventricular remodeling and geometric changes.[17] The main reason is that ischemic myocardium segments contribute to adverse ventricular remodeling, leading to contractile dysfunction, ventricular dilation, and impaired systolic performance.[22] Therefore, the geometric changes measured by EI can reflect the severity of ischemia.[23]

Table 3. Correlatian analysis

Parameters		Correlation Coefficient	P
Ecc_S	SD%	0.265	0.029
Ecc_R	SD%	0.307	0.011

Note, Ecc_S, echocardiographic stress; Ecc_R, echocardiographic rest; SD%, standard deviation percentage.

These findings are supported by the theory that myocardial ischemia causes ventricular remodeling, leading to changes in left ventricular shape.[18] Physiologically, the left ventricle maintains an ellipsoid shape, which is crucial for efficient cardiac output.[24] However, under sustained ischemic conditions, increased wall tension and neurohormonal activation contribute to progressive ventricular dilation and spherical remodeling.[18] As a result, the ventricle becomes less efficient at pumping blood, reflected in a decrease in ejection fraction and an increase in EI.[25] Thus, EI can serve as a marker for structural changes due to ischemia.[26]

This study offers several significant clinical implications. First the key results plus further analysis emphasize the promise that EI may present as an additional imaging biomarker potentially augmenting the assessment of ischemic burden in myocardial perfusion imaging (MPI). Second, the routine incorporation of EI parameters into MPI could thereby supplement conventional functional assessments of ischemia with additional data useful in risk stratifying patients with respect to their mechanical effects on LV structure and functioning. Third, the findings from this study may contribute to a higher level of diagnostic accuracy for coronary artery disease, identifying patients at an increased risk of cardiovascular events and thus allowing for refined therapeutic choices. Fourth, this may assist with some diagnostic dilemmas arising from the over-reliance on perfusion assessments, therefore optimizing patient management. Fifth, prospective studies with perhaps more considerable numbers could be designed in future to confirm these findings and explore the role of EI in directing therapy and enhancing clinical outcomes in patients.

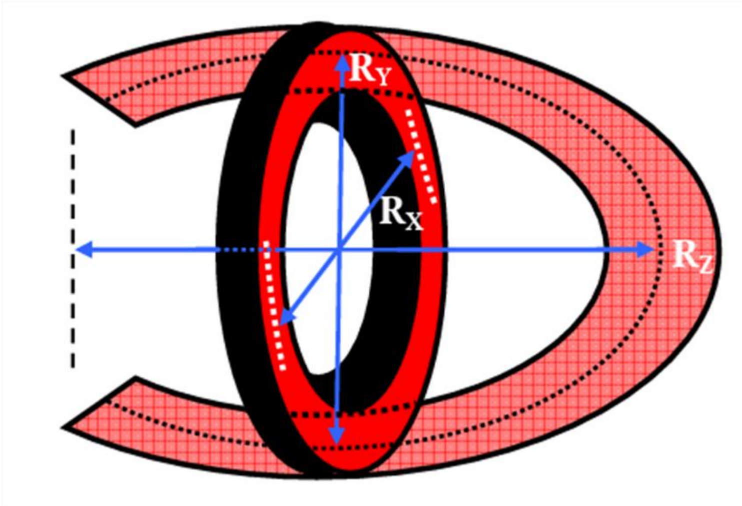

Figure 1. Measurement of left ventricular eccentricity index adapted from the quantitative gated SPECT (QGS) manual, Cedars-Sinai Center.

This study has several limitations. First, the relatively small sample size may limit statistical power and the generalizability of the findings to a larger population. Second, the retrospective design of the study potentially introduces selection bias and does not allow for full control over confounding factors that may influence the relationship between EI and ischemic burden. Third, the study's focus on patients undergoing MPI with 99mTc sestamibi limits the applicability of the findings to other imaging modalities or different patient populations. Fourth, the lack of longitudinal data limits the ability to assess the long-term impact of EI changes on clinical outcomes. Fifth, other limitations include potential variations in measurement techniques and data interpretation that could affect the consistency of the results.

CONCLUSION

This study demonstrates that EI has a significant correlation with IB in CAD patients, indicating that EI can be an additional indicator in detecting ischemia. Further differences analysis shows that EI, both during stress and rest phases, is significantly higher in patients with a greater ischemic burden, and it is associated with a decrease in left ventricular systolic function during stress. Based on these findings, it is hoped that EI can be integrated into routine myocardial perfusion imaging protocols to improve risk stratification accuracy and help optimize the management of CAD patients.

Ethics approval and consent to participate

Our study received approval from the local ethical committee of Hasan Sadikin Hospital Bandung (No: DP.04.03/D.XIV.4.4/999/2024), and informed consent was obtained from all participants.

Conflicts of interest

We have no conflict of interest

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Author contribution
Conceptualization: PHP, EC; Data Curation: PHP, EC; Formal Analysis: PHP; Investigation: PHP; Project Administration: PHP; Resources: PHP; Methodology: PHP; Software: PHP; Visualization: PHP, EC; Supervision: REAS, AHSK; Validation: REAS, AHSK; Writing – Original Draft Preparation: PHP; Writing – Review & Editing: PHP. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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