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ORIGINAL ARTICLE

Resting echocardiographic parameters can exclude significant coronary artery disease: A comparison with coronary computed tomography angiography

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Abstract

Introduction: Coronary computed tomography angiography (CCTA) is known to have a high negative predictive value (NPV) in identifying coronary artery disease (CAD). This study aimed to examine whether resting echocardiographic parameters could exclude significant CAD on CCTA.

Methods: We recruited 142 patients who had undergone both CCTA and echocardiography within a 3-month window. Based on the CCTA findings, patients were divided into two groups: Group A (non-significant CAD, defined as all coronary segments having <50% stenosis) and Group B (significant CAD). Resting echocardiographic parameters were compared between the two groups to identify predictors of non-significant CAD on CCTA.

Results: A total 92 patients (mean age, 68 ± 13 years; males, 62%) were eligible for this study; 50 in Group A and 42 in Group B. Among the various echo parameters, left atrial volume index (LAVI) and left ventricular (LV) global longitudinal strain (GLS) were significantly lower in Group A (23.5 ± 7.6 vs. 33.6 ± 7.4 mL/m^2, $p < .001$; −20.2 ± 1.8% vs. −16.8 ± 2.0%, $p < .001$, respectively). Analysis of the receiver operating characteristic curve revealed that the cutoff value to exclude significant CAD on CCTA was 29.0 mL/m^2 for LAVI (NPV 80.8%) and −18.1% for GLS (NPV 80.7%). The NPV increased to 95.0% when these parameters were combined (LAVI < 29.0 mL/m^2 and GLS < −18.1%).

Conclusion: The combination of resting LAVI and GLS was clinically useful in excluding significant CAD via CCTA.

KEYWORDS
coronary artery disease, coronary computed tomography angiography, global longitudinal strain, left atrial volume index

1 | INTRODUCTION

Coronary computed tomography angiography (CCTA) is a highly recommended non-invasive anatomical imaging modality for diagnosing stable coronary artery disease (CAD) and stratifying its prognostic risk.[1] Conversely, resting echocardiographic parameters can predict CAD. Normal resting left atrial volume index (LAVI < = 28 mL/m^2), which reflects left ventricular (LV) diastolic function, is strongly predictive of a normal stress echocardiogram.[2] Nowadays, global longitudinal strain (GLS), derived from two-dimensional (2D) speckle-tracking echocardiography, is widely used as a more sensitive and predictive echo index for detecting subclinical LV dysfunction prior to reduction in LV ejection fraction (LVEF).[3] In patients without regional wall motion abnormality, GLS at rest can detect > 50% coronary stenoses with a sensitivity of 74% and a specificity of 72%.[4] This study aimed to examine whether resting echocardiographic parameters and their combination were clinically useful in predicting non-significant CAD on CCTA.

2 | METHODS

2.1 | Study patients

We examined all the patients who underwent both CCTA and echocardiography within 3 months of each other between October 2018 and August 2021. The purpose of CCTA examination was to rule out significant CAD in patients with chest pain including atypical symptoms or asymptomatic with non-specific ECG findings on preoperative assessment for non-cardiac surgery. A total of 142 patients remained after excluding those with atrial fibrillation, paced rhythm, history of myocardial infarction/CAD, significant valvular heart disease, and reduced LVEF (<50%).

2.2 | Echocardiography/echocardiographic analyses

Conventional 2-dimensional echocardiographic examinations were performed using Vivid E95 (GE Vingmed Ultrasound, Horten, Norway) with an M5Sc-D (1.4–4.6 MHz) transducer. Examinations included measurements of cardiac dimensions, volumes, LVEF, and Doppler parameters, performed according to the recommendations of the American Society of Echocardiography (ASE).[5,6] Left atrial volume was measured by the biplane disks method using apical four- and two-chamber views at the end-systolic frame preceding mitral valve opening and was indexed to body surface area to derive LAVI.[5] GLS was measured using stored images from apical long axis, four-chamber, and two-chamber views. All images were obtained at a frame rate of 60–80 frames/s. Three consecutive cardiac cycles were saved in digital format and the one most suitable for GLS analysis was analyzed. An analyst unaware of the angiographic results performed strain analysis offline using EchoPAC PC (ver. 204, GE Vingmed Ultrasound, Horten, Norway) with AFI LV. In the apical long-axis view, we defined the aortic valve closing time, which was also used as a reference value in two-chamber and four-chamber views. After adjusting the region of interest to include the entire myocardial layer, we validated the tracking quality throughout the cardiac cycle.

Cases in which cross-sectional images suitable for GLS measurements could not be obtained were excluded.

2.3 | CCTA protocol/analyses

A 320-slice CT (Aquilion ONE, Canon Medical Systems, Otawara, Japan) was performed in all patients, with a collimation of 320 × 0.5 mm, rotation speed of 275 or 350 ms, scanner settings of 300–580 mA depending on body weight, and a voltage of 100–135 kV. To evaluate coronary artery stenosis, a non-enhanced scan was performed using a prospectively electrocardiography-triggered scan protocol, with a detector configuration of 320 × 0.5 mm and a rotation time of 275 ms.[7] For the contrast-enhanced scan, 20.4 mgI/kg/s of contrast medium was injected for 12 s followed by 20 mL of saline at 3.0 mL/s. Axial scan was performed with prospective gated scan in one heartbeat with a heart rate < 65 bpm for half reconstruction and in two or three beats with a heart rate ≧ 65 bpm for segmental reconstruction. Before imaging, in patients without contraindications, oral metoprolol and/or intravenous landiolol (Ono Pharmaceutical Co., Ltd., Osaka, Japan) was administered if the heart rate was > 65 bpm. Nitroglycerin (0.3 mg) was administered to all subjects immediately before CT imaging. The raw data of the CT scans were reconstructed using algorithms optimized for electrocardiography-gated reconstruction and transferred to a computer workstation for post-processing (ZIOSTATION2, ZIOsoft Inc., Tokyo, Japan). CCTA images were evaluated on axial, coronal, sagittal, cross-sectional, and curved multiplanar reformation images. Coronary arteries with a diameter greater than 2 mm were evaluated for luminal stenosis. Stenotic lesions were quantified for lumen diameter stenosis by visual estimation and graded as normal (absence of plaque and no luminal stenosis), minimal

TABLE 1 Clinical characteristics.

	Group A ($n = 52$)	Group B ($n = 40$)	p-value
Male, n (%)	24 (46.2)	33 (82.5)	<.001
Age (year)	63.0 ± 14.0	74.3 ± 7.7	<.001
Weight (kg)	57.4 ± 11.9	60.6 ± 9.8	.153
Height (cm)	158.8 ± 9.1	161.9 ± 8.6	.075
Body mass index (kg/m^2)	22.6 ± 3.4	23.1 ± 3.1	.457
Risk factors			
Diabetes, n (%)	10 (19.2)	11 (27.5)	.351
Hypertension, n (%)	25 (48.1)	30 (75.0)	.008
Dyslipidemia, n (%)	19 (36.5)	17 (42.5)	.562
Chronic kidney disease, n (%)	13 (25.0)	13 (32.5)	.429
Smoking, n (%)	6 (11.5)	10 (25.0)	.092
Systolic blood pressure (mm Hg)	139.2 ± 18.1	148.1 ± 18.6	.023
Diastolic blood pressure (mm Hg)	78.4 ± 14.3	80.9 ± 11.8	.412
Heart rate (bpm)	76.4 ± 14.5	77.9 ± 15.1	.862

Data are expressed as number (percentage) or mean ± standard deviation.

(plaque with < 25% stenosis), mild (25%–49% stenosis), moderate (50%–69% stenosis), severe (70%–99% stenosis), or occluded, as per the guidelines of the Society of Cardiovascular Computed Tomography.[8] Stenoses of the moderate and higher grades (≥50%) were defined as significant stenoses. All images were assessed by two experienced cardiologists who were blinded to each other and to the clinical data. Diagnosis was made by consensus in case of disagreement. Based on the CCTA findings, patients were divided into two groups: Group A (non-significant CAD, defined as all coronary segments having stenosis < 50%) and Group B (significant CAD). Resting echocardiographic parameters were compared between the two groups to exclude significant CAD on CCTA.

2.4 | Statistical analysis

JMP Pro software (version 17.0.0, SAS Institute, Cary, North Carolina, USA) was used for all statistical analyses. Two-sided p values < .05 were considered statistically significant. Data are presented as means ± standard deviations or as frequencies (percentage). The Shapiro–Wilk test was used to assess the normality of continuous data, compared using Student's unpaired t test for normally distributed variables or Wilcoxon signed rank test for nonparametric data. Categorical variables were compared using the chi-squared test or Fisher's exact test. Receiver operating characteristic (ROC) curve analysis was used to identify parameters that best predicted the presence of CAD. We performed multivariate analyses to examine the associations between CAD and resting echocardiographic parameters selected by ROC analysis after adjusting the confounding factors associated with CAD with a p-value < .05 on univariate analysis. Nominal logistic analysis was used for univariate/multivariate analyses.

3 | RESULTS

3.1 | Clinical characteristics

Among the 142 patients that were included initially, 50 patients were excluded because of inadequate echo image quality for LAVI and/or GLS measurements. As a result, a total of 92 patients were eligible for this study (mean age 68 ± 13 years, 38% female); 52 in Group A and 40 in Group B (Table 1). Group B included a significantly higher percentage of males (46.2% vs. 82.5%, $p < .001$) and patients in Group B were older than those in Group A (63.0 ± 14.0 vs. 74.3 ± 7.7 years, $p < .001$). Hypertensive patients more frequently segregated into Group B (48.1% vs. 75.0%, $p < .001$), and systolic blood pressure was also higher in this group (139.2 ± 18.1 vs. 148.1 ± 18.6 mm Hg, $p < .001$). Weight, height, body mass index, diastolic blood pressure, other risk factors, and heart rate did not differ significantly between the two groups. The median time between the examinations of echocardiography and CCTA was 12 days (interquartile range, 6–22).

3.2 | Echocardiographic data

Table 2 shows the 2D echocardiographic data. Indicators related to myocardial thickness (LV anteroseptal and inferolateral wall thickness, mass index) were significantly higher in Group B, while LVEF was slightly higher in Group A (61.2 ± 3.4% vs. 58.8 ± 4.5%, $p = .020$). No significant difference was found between groups in terms of LV end-diastolic volume (72.0 ± 16.0 mL vs. 77.8 ± 23.5 mL, $p = .311$) and end-systolic volume (28.0 ± 7.1 mL vs. 32.4 ± 12.0 mL, $p = .130$). Furthermore, LAVI was significantly smaller in Group A compared with

TABLE 2 2-dimensional echocardiographic parameters.

	Group A ($n = 52$)	Group B ($n = 40$)	p-value
LVIDd (mm)	44.1 ± 4.0	45.1 ± 4.7	.331
LVIDs (mm)	28.8 ± 4.0	30.4 ± 5.0	.142
IVSd (mm)	9.0 ± 1.4	9.6 ± 1.2	.029
LVPWd (mm)	9.1 ± 1.2	9.7 ± 1.1	.014
LAD (mm)	32.5 ± 4.6	34.5 ± 4.3	.019
LVEDV (mL)	72.0 ± 16.0	77.8 ± 23.5	.311
LVESV (mL)	28.0 ± 7.1	32.4 ± 12.0	.130
LVEF (%)	61.2 ± 3.4	58.8 ± 4.5	.020
LAVI (mL/m^2)	23.6 ± 7.5	33.9 ± 7.5	<.001
LVMI (g/m^2)	84.0 ± 19.1	96.0 ± 23.8	.014
RWT	.41 ± .06	.43 ± .07	.127

Note: Data are expressed as mean ± standard deviation.
Abbreviations: IVSd, interventricular septal dimension in diastole; LAD, left atrial dimension in systole; LAVI, left atrial volume index; LVIDd, left ventricular internal dimension diastole; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVIDs, left ventricular internal dimension systole; LVMI, left ventricular mass index; LVPWd, left ventricular posterior wall dimension in diastole; RWT, relative wall thickness.

TABLE 3 Doppler echocardiographic parameters and GLS.

	Group A ($n = 52$)	Group B ($n = 40$)	p-value
Peak E-wave velocity (cm/s)	64.2 ± 13.8	61.9 ± 14.4	.385
Mitral DT (ms)	215.5 ± 48.2	219.1 ± 49.8	.643
Peak A-wave velocity (cm/s)	71.3 ± 16.5	85.8 ± 17.4	<.001
Mitral E/A ratio	.9 ± .3	.7 ± .1	<.001
Septal e' velocity (cm/s)	6.9 ± 1.8	5.6 ± 1.5	<.001
Septal a' velocity (cm/s)	9.6 ± 2.3	9.6 ± 2.1	.944
Septal s' velocity (cm/s)	7.7 ± 1.4	7.0 ± 1.6	.019
Lateral e' velocity (cm/s)	9.8 ± 2.7	7.5 ± 2.0	<.001
Lateral a' velocity (cm/s)	11.2 ± 2.2	10.5 ± 2.6	.076
Lateral s' velocity (cm/s)	9.9 ± 2.2	8.7 ± 2.1	.008
Average E/e'	8.1 ± 2.6	9.9 ± 3.0	.004
GLS (%)	−20.1 ± 1.8	−16.8 ± 2.1	<.001

Note: Data are expressed as mean ± standard deviation.
Abbreviations: DT, deceleration time; GLS, global longitudinal strain.

Group B (23.6 ± 7.5 mL/m^2 vs. 33.9 ± 7.5 mL/m^2, $p < .001$). Doppler echocardiographic data and GLS are shown in Table 3. Significant differences were observed in various indices used to assess LV diastolic function. Among them, GLS was significantly more preserved in Group A than in Group B (−20.1 ± 1.8% vs. −16.8 ± 2.1%, $p < .001$).

3.3 | ROC analysis and the diagnosis of significant stenosis of coronary arteries

Figure 1 and Table 4 show the results of ROC analysis for detecting significant coronary artery stenosis. Among the single echo parameters with a significant difference, GLS showed the highest area under the curve (AUC) followed by LAVI. Nevertheless, when GLS and LAVI were combined, it provided superior diagnostic performance for the detection of CAD with even higher AUC (.97, $p < .001$). Each single cutoff value for predicting significant coronary artery stenosis was −18.1% of GLS (negative predictive value [NPV] 82.5%) and 29.0 mL/m^2 of LAVI (NPV 82.7%). When these parameters were combined (LAVI < 29.0 mL/m^2 and GLS < −18.1%), the NPV increased to 97.5%. Combining LAVI and GLS, the NPV almost becomes equivalent to CCTA. Thus, echo can potentially substitute CCTA as an alternative. Of the 40 cases with LAVI ≤ 29.0 mL/m^2 and GLS ≤ −18.1%, 39 had normal coronary arteries. In one solitary case, the distal left circumflex artery was stenosed by 50%–69% (Figure 2).

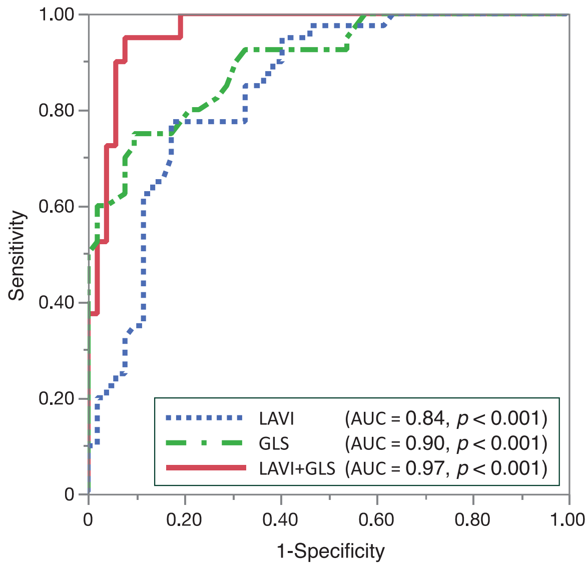

FIGURE 1 ROC curve analysis for the detection of CAD ROC curve analysis for predicting significant stenosis of coronary arteries. AUC, area under the curve; CAD, coronary artery disease; GLS, global longitudinal strain; LAVI, left atrial volume index; ROC, receiver operating characteristic.

3.4 | Univariate/multivariate analyses to examine associations between LAVI/GLS and significant CAD on CCTA

Univariate analyses detected that sex, age, and hypertension showed significant associations with CAD with $p < .05$ among clinical characteristics (Table 5). On multivariate analyses to examine the associations between CAD and LAVI/GLS, both of them demonstrated significant correlations with CAD even after adjusting those confounding factors detected by univariate analyses (Table 6).

4 | DISCUSSION

Our findings demonstrated that while either smaller LAVI (<29.0 mL/m^2) or preserved GLS (<−18.1%) at rest was a

TABLE 4 Predictive characteristics of clinical and echocardiographic variables for the detection of CAD.

	AUC	*p*-value	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Age	.75	<.001	64.0 years	92.5	50.0	58.7	89.7
Systolic blood pressure	.64	.027	147.0 mm Hg	57.5	73.1	62.2	69.1
IVSd	.63	.038	9.0 mm	85.0	36.5	50.7	76.0
LVPWd	.64	.016	9.0 mm	92.5	34.6	52.1	85.7
LAD	.64	.037	31.0 mm	85.0	28.5	51.5	76.9
LVEF	.64	.007	55.0%	25.0	98.1	90.9	63.0
LVMI	.65	.012	90.0 g/m^2	60.0	69.2	60.0	69.2
Peak A-wave velocity	.72	.001	77.0 cm/s	77.5	60.8	60.8	77.5
Mitral E/A ratio	.80	<.001	.84	92.5	58.8	63.8	90.9
Septal e' velocity	.72	.001	5.29 cm/s	52.5	84.6	72.4	69.8
Septal s' velocity	.64	.039	6.87 cm/s	60.0	71.2	61.5	69.8
Lateral e' velocity	.75	<.001	8.19 cm/s	70.0	68.6	63.6	74.5
Lateral s' velocity	.66	.016	7.68 cm/s	40.0	92.3	80.0	66.7
Average E/e'	.68	.008	8.64	65.0	66.7	60.5	70.8
LAVI	.84	<.001	29.0 mL/m^2	77.5	82.7	77.5	82.7
GLS	.90	<.001	−18.1%	75.0	90.4	85.7	82.5

Abbreviations: AUC, area under the curve; GLS, global longitudinal strain; IVSd, interventricular septal dimension in diastole; LAD, left atrial dimension in systole; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LVPWd, left ventricular posterior wall dimension in diastole; LVMI, left ventricular mass index; NPV, negative predictive value; PPV, positive predictive value.

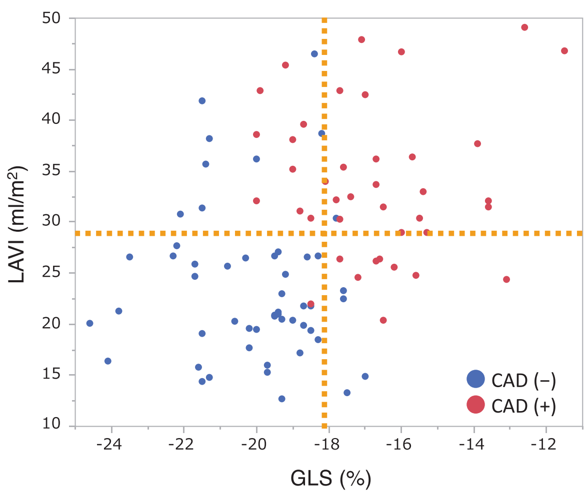

FIGURE 2 Distribution of LAVI and GLS measurements. The distribution of LAVI and GLS. The lines are cut-off values obtained by ROC curve analysis. Blue dots indicate cases with no significant coronary artery stenosis and red dots indicate CAD cases. CAD, coronary artery disease; GLS, global longitudinal strain; LAVI, left atrial volume index; ROC, receiver operating characteristic.

TABLE 5 Univariate analysis of the association between significant CAD on CCTA and clinical characteristics.

	β	95% CI	*p*-value
Male, *n* (%)	.85	.28, 1.37	<.001
Age (year)	.10	.05, .15	<.001
Body mass index (kg/m^2)	.05	−.08, .18	.490
Diabetes, *n* (%)	−.23	−.73, .26	.351
Hypertension, *n* (%)	−.59	−1.05, .15	.010
Dyslipidemia, *n* (%)	−.13	−.55, .30	.562
Chronic kidney disease, *n* (%)	−.18	−.64, .27	.429
Smoking, *n* (%)	−.47	−1.05, .08	.098
Heart rate (bpm)	.01	−.02, .04	.637

Note: Data are expressed as number (percentage) or mean ± standard deviation.
Abbreviation: CI, confidence interval.

clinically useful predictor of non-significant CAD on CCTA, combination of LAVI and GLS was more powerful and almost equivalent to CCTA in ruling out significant CAD.

Noninvasive cardiac imaging is now essential for the diagnosis and management of patients with known or suspected CAD. CCTA has become one of the key modalities for CAD. According to a multicenter study examining the accuracy of 64-row, .5 mm CCTA, it was possible to identify 50% coronary stenoses in patients with suspected CAD with a sensitivity of 85% and specificity of 90%.[9] Conversely, CCTA provides excellent NPV in ruling out significant coronary artery stenosis.[10] In patients with intermediate modified pre-test probability of CAD, CCTA can rule out its possibility with an NPV of 99%,[11] which is associated with significantly improved prognosis compared with > 50% coronary artery stenosis in ≥one proximal segment.[12] Moreover, coronary computed tomography is not only able to visualize and precisely quantify epicardial adipose tissue, but also assess the coronary arteries

TABLE 6 Multivariate analysis of the association between significant CAD on CCTA and resting echocardiographic parameters.

	B	95% CI	*p* value
LAVI	.14	.06, .23	.001
GLS	1.12	.62, 1.83	<.001

Abbreviations: CI, confidence interval; GLS, global longitudinal strain; LAVI, left atrial volume index.

and pericoronary adipose tissue, inflammation of which has been associated with CAD and major cardiovascular events.[13] However, CCTA cannot be applied to patients with renal dysfunction or allergies to contrast agents. Furthermore, the risk of radiation exposure may induce breast and lung cancer in younger patients.[14] Additionally, CCTA is not suitable for patients with severe coronary calcification.

In contrast, stress echocardiography (SE) is a widely performed non-invasive imaging test that can substitute CCTA. It is simpler, radiation-free, and more applicable to patients with renal dysfunction. A study comparing SE and CCTA in low-risk patients with suspected stable angina showed that initial SE-guided management was similar to CCTA management for detecting obstructive CAD and demonstrated better resource utilization.[15] However, recording acceptable echo images is challenging in a proportion of patients. Additionally, interpretation of SE highly depends on the examiners' skills, causing the sensitivity and specificity of this method to vary across different centers. Besides CCTA and SE, nuclear cardiology and cardiac magnetic resonance also play important roles for the diagnosis and management of patients with CAD. If a patient is suspected of having CAD, the appropriate test should be selected, considering the pros and cons of each noninvasive cardiac imaging technique.[16] Yet, rest echocardiography is the imaging modality to be performed prior to these tests. Although it is considered to have lower diagnostic capabilities for CAD compared with other imaging tests, combining multiple resting echocardiographic parameters has the potential to significantly predict concomitant CAD.

The normal upper limit for 2D echocardiographic LAVI is 34 mL/m^2 for both genders, according to the ASE guideline.[5] Its value is also used to determine LV diastolic dysfunction. LA volume is known to reflect the cumulative effects of increased LV filling pressure and LA pressure over time, and increased LA volume is an independent predictor of cardiac events, including death, heart failure, atrial fibrillation, and ischemic stroke.[17] Although several other echo parameters reflect LV diastolic function, LAVI was the second-best parameter after GLS to rule out CAD in our study. This may be because Doppler parameters reflect real-time hemodynamics whereas LAVI reflects LV diastolic dysfunction over a longer duration. In addition, Doppler parameters are more prone to change with age whereas LAVI is relatively more independent of age and does not differ between genders.[18] In our study, a LAVI cutoff of 29 mL/m^2 was predictive of non-significant CAD on CCTA with a sensitivity of 77.5%, specificity of 82.7%, positive predictive value of 77.5%, and NPV of 82.7%. In their study, Alsaileek et al. reported that LAVI $\leq$ 28 mL/m^{2}at rest indicated negative stress echocardiography even without stress for the diagnosis of CAD.[2]

GLS allows objective quantitative analysis of the complete longitudinal myocardial deformation of the left ventricle throughout the heart cycle and is excellent for detecting microscopic myocardial damage. Strain imaging has been shown to detect subtle systolic dysfunction more sensitively than LVEF,[19,20] presumably due to the compensation of early longitudinal dysfunction by the augmentation of other strain components. This allows the LV to maintain an EF within the normal range.[21] GLS has proven to be a valuable clinical tool to assess various cardiac diseases, such as valvular disease, hypertrophic cardiomyopathy, myocardial infarction, heart failure with preserved LVEF, and amyloidosis, and to manage chemotherapy. GLS is also a prognostic factor in various heart diseases. The LV myocardium has a complex three-layer architecture comprising circumferential fibers in the midwall layer and longitudinal fibers in the endocardial and epicardial layers. Some acquired heart diseases, including CAD, often originate in the endocardium and its fibers. Therefore, GLS, which is closely related to the longitudinal function of the subendocardium and is most susceptible to ischemia, may sensitively detect subtle abnormalities observed in the early stages of myocardial ischemia.[22] GLS is a far more sensitive tool to discriminate between patients with or without CAD. 2D speckle-tracking echocardiography-derived GLS is a standardized indicator with low measurement error and reproducibility.[23] Moreover, beginners can easily learn how to measure GLS by measuring it in 50 cases.[24]

According to the ASE guidelines, peak GLS is considered normal if it is approximately around −20% in healthy persons. The lower the absolute value of strain, the more likely it is to be abnormal.[5] A systematic review and meta-analysis of several cases with normal LVEFs or normal wall motion showed that the mean value of GLS for patients with CAD was −16.5% (95% confidence interval, −15.8%–17.3%).[4] In addition, the optimal cutoff value of mid- and basal-peak systolic longitudinal strain to detect high-risk CAD (left main or three-vessel) was −17.9% (sensitivity 78.9%, specificity 79.3%).[25] The cutoff value of GLS in our study (−18.1%) was remarkably close to the previously reported cutoff values and could predict non-significant CAD on CCTA (sensitivity 75.0%, specificity 90.4%, PPV 85.7%, and NPV 82.5%) (Figure 2).

LAVI and GLS have been individually reported to be useful indicators in diagnosing CAD, but NPV of significant CAD of each parameter alone cannot exceed that of CCTA, and the predictive power of their combination is unreported yet. Since LAVI is the most stable index of LV diastolic function and GLS is superior in detecting subclinical myocardial dysfunction, the outcome that their combination further improves the NPV of CAD is reasonable. Echocardiography is a non-invasive examination and applies to almost all patients. CCTA and/or coronary angiography (CAG) are still required when a definitive diagnosis of CAD needs to be made. If there is a strong clinical indication for CCTA or CAG for chest pain syndrome, then a normal LAVI or GLS should not exclude the patient from proceeding with these investigations. However, our study has shown that the combination of normal LAVI and GLS may be used to rule out significant CAD with high confidence to avoid unnecessary testing when CCTA and/or CAG are relatively contraindicated in cases such as contrast allergy, renal impairment, and those who needs to minimize radiation exposure.

4.1 | Limitations

First, this study was conducted at a single center and the number of patients was relatively limited. Further prospective studies with larger cohorts will be needed to confirm our findings. Second, patients with atrial fibrillation, atrial flutter, or significant valvular abnormalities were excluded. In these patients, LA dilatation is commonly seen regardless of the LV filling pressure. Third, although abnormal GLS has good predictive power to detect CAD, some patients suffer from myocardial ischemia without abnormal GLS. This is one of the reasons for the moderate sensitivity of GLS. The ischemic burden of patients also varies. Indeed, patients with multivessel disease tend to have reduced GLS compared with those with single-vessel or no CAD.[26,27] GLS in the detection of ischemia may also be influenced by the presence of well-developed collateral vessels. In dogs that have been exposed to repeated cardiac ischemia over a long duration, preservation of ventricular systolic function was correlated with the presence of well-developed collateral circulation.[28] The impact of collateral flows on GLS, therefore, cannot be ignored, particularly in the context of chronic ischemia.[4] Finally, reduction in GLS may be attributed to high blood pressure. Studies have confirmed that even when contractile function is preserved, strain decreases with increasing afterload.[29] In our study, although the mean difference in systolic blood pressure was less than 10 mm Hg, it may affect the results to some extent.

5 | CONCLUSIONS

The combination of resting LAVI and GLS was clinically useful in excluding prognostically significant CAD. Normal LAVI with normal GLS at rest was strongly predictive of excluding significant CAD even without a stress test. These two parameters can easily be incorporated in daily routine echocardiography, and combining them offers an alternative to CCTA when it is contraindicated.

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CONFLICT OF INTEREST STATEMENT

All authors have no financial conflicts of interest.

DATA AVAILABILITY STATEMENT

The data analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. Knuuti J, Wijns W, Saraste A, et al. ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. 2020;41:407-477.
2. Alsaileek AA, Osranek M, Fatema K, McCully RB, Tsang TS, Seward JB. Predictive value of normal left atrial volume in stress echocardiography. *J Am Coll Cardiol*. 2006;47:1024-1028.
3. Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: how useful is it in clinical decision making? *Eur Heart J*. 2016;37:1196-1207.
4. Liou K, Negishi K, Ho S, Russell EA, Cranney G, Ooi S-Y. Detection of obstructive coronary artery disease using peak systolic global longitudinal strain derived by two-dimensional speckle-tracking: a systematic review and meta-analysis. *J Am Soc Echocardiogr*. 2016;29:724-735.e4.
5. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1-39.e14.
6. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2019;32:1-64.
7. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15:827-832.
8. Leipsic J, Abbara S, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of cardiovascular computed tomography guidelines committee. *J Cardiovasc Comput Tomogr*. 2014;8:342-358.
9. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med*. 2008;359:2324-2336.
10. Knuuti J, Ballo H, Juarez-Orozco LE, et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. *Eur Heart J*. 2018;39:3322-3330.
11. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (assessment by coronary computed tomographic angiography of individuals undergoing invasive coronary angiography) trial. *J Am Coll Cardiol*. 2008;52:1724-1732.
12. Hadamitzky M, Achenbach S, Al-Mallah M, et al. Optimized prognostic score for coronary computed tomographic angiography: results from the CONFIRM registry (COronary CT angiography evaluation for clinical outcomes: an international multicenter registry). *J Am Coll Cardiol*. 2013;62:468-476.
13. Guglielmo M, Lin A, Dey D, et al. Epicardial fat and coronary artery disease: role of cardiac imaging. *Atherosclerosis*. 2021;321:30-38.
14. Hurwitz LM, Reiman RE, Yoshizumi TT, et al. Radiation dose from contemporary cardiothoracic multidetector CT protocols with an anthropomorphic female phantom: implications for cancer induction. *Radiology*. 2007;245:742-750.
15. Vamvakidou A, Danylenko O, Pradhan J, et al. Relative clinical value of coronary computed tomography and stress echocardiography-guided

management of stable chest pain patients: a propensity-matched analysis. *Eur Heart J Cardiovasc Imaging*. 2020;22:1473-1481.
16. Berman DS, Hachamovitch R, Shaw LJ, et al. Roles of nuclear cardiology, cardiac computed tomography, and cardiac magnetic resonance: noninvasive risk stratification and a conceptual framework for the selection of noninvasive imaging tests in patients with known or suspected coronary artery disease. *J Nucl Med*. 2006;47:1107-1118.
17. Thomas L, Muraru D, Popescu BA, et al. Evaluation of left atrial size and function: relevance for clinical practice. *J Am Soc Echocardiogr*. 2020;33:934-952.
18. Miyoshi T, Addetia K, Citro R, et al. Left ventricular diastolic function in healthy adult individuals: results of the world alliance societies of echocardiography normal values study. *J Am Soc Echocardiogr*. 2020;33:1223-1233.
19. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart*. 2014;100:1673-1680.
20. Morris DA, Ma X-X, Belyavskiy E, et al. Left ventricular longitudinal systolic function analysed by 2D speckle-tracking echocardiography in heart failure with preserved ejection fraction: a meta-analysis. *Open Heart*. 2017;4:e000630.
21. Stokke TM, Hasselberg NE, Smedsrud MK, et al. Geometry as a confounder when assessing ventricular systolic function: comparison between ejection fraction and strain. *J Am Coll Cardiol*. 2017;70:942-954.
22. Ishizu T, Seo Y, Kameda Y, et al. Left ventricular strain and transmural distribution of structural remodeling in hypertensive heart disease. *Hypertension*. 2014;63:500-506.
23. Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging*. 2015;16:1-11.
24. Chan J, Shiino K, Obonyo NG, et al. Left ventricular global strain analysis by two-dimensional speckle-tracking echocardiography: the learning curve. *J Am Soc Echocardiogr*. 2017;30:1081-1090.
25. Choi J-O, Cho SW, Song YB, et al. Longitudinal 2D strain at rest predicts the presence of left main and three vessel coronary artery disease in patients without regional wall motion abnormality. *Eur J Echocardiogr*. 2009;10:695-701.
26. Biering-Sørensen T, Hoffmann S, Mogelvang R, et al. Myocardial strain analysis by 2-dimensional speckle tracking echocardiography improves diagnostics of coronary artery stenosis in stable angina pectoris. *Circ Cardiovasc Imaging*. 2014;7:58-65.
27. Tsai W-C, Liu Y-W, Huang Y-Y, Lin C-C, Lee C-H, Tsai L-M. Diagnostic value of segmental longitudinal strain by automated function imaging in coronary artery disease without left ventricular dysfunction. *J Am Soc Echocardiogr*. 2010;23:1183-1189.
28. Fujita M, McKown DP, McKown MD, Hartley JW, Franklin D. Evaluation of coronary collateral development by regional myocardial function and reactive hyperaemia. *Cardiovasc Res*. 1987;21:377-384.
29. Voigt J-U, Cvijic M. 2- and 3-dimensional myocardial strain in cardiac health and disease. *JACC Cardiovasc Imaging*. 2019;12:1849-1863.

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