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Assessment of Left Ventricular Ejection Fraction by Thallium-201 Myocardial SPECT-CT in Patients with Angina Pectoris: Comparison with 2D Echocardiography

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Abstract

Purpose Left ventricular (LV) ejection fraction (EF) is an important parameter for assessing cardiac systolic function and predicting prognosis in patients with cardiovascular disease. The aim of this study was to evaluate the feasibility of assessing LVEF by Tl-201 hybrid myocardial single-photon emission computed tomography (SPECT)/CT using two attenuation correction methods in patients with angina pectoris.

Methods A total of 339 patients with angina pectoris (62.8 ± 12.9 years, male:female = 206:133) were analyzed. All patients underwent Tl-201 myocardial SPECT/CT and transthoracic two-dimensional (2D) echocardiograph. We compared LVEF assessed by SPECT/CT using two attenuation correction methods: CT-based attenuation correction (CTAC) and non-attenuation correction (non-AC) methods and 2D echocardiography.

Results LVEF assessed by either of the two attenuation correction techniques and 2D echocardiography showed moderate correlation in all patients with angina pectoris ($r = 0.487$ for CTAC and $r = 0.473$ for non-AC, $p < 0.001$). Results were similar in the subgroup of patients with perfusion abnormalities on myocardial SPECT/CT images. Overall diagnostic performances were similar for the CTAC and non-AC methods for evaluating normal and decreased LVEF by myocardial SPECT/CT.

Conclusion LVEF measured by the CTAC method of Tl-201-gated myocardial SPECT/CT was comparable with the conventional non-AC method in patients with angina pectoris and in the subgroup of patients with perfusion abnormality. Tl-201-gated myocardial hybrid SPECT/CT can be a reliable tool in the assessment of LVEF in clinic.

Keywords Left ventricular ejection fraction · Angina pectoris · Thallium-201 · Myocardial SPECT/CT

Introduction

Systolic left ventricular (LV) function can be reliably determined by multiple non-invasive modalities such as echocardiography, radionuclide angiocardiography, computed tomography (CT), and magnetic resonance imaging [1–3]. LV systolic function estimated from the left ventricular ejection fraction (LVEF) is an important variable in patients with angina pectoris because it can predict myocardial injury and regional myocardial wall motion abnormalities before coronary angiography [4]. Tomographic methods rather than planar imaging are usually used to measure parameters of LV function in blood pooling or myocardial perfusion studies because of the three-dimensional nature of the above methods [5, 6]. Thallium (Tl)-201 single-photon emission computed tomography (SPECT) allows clinicians to simultaneously assess myocardial perfusion, LV volume, ejection fraction, regional wall motion, and wall thickening. SPECT also enables clinicians to measure post-stress LV volume and LVEF so they can detect transient dilatation induced by coronary artery disease or stress [7]. Previous studies have reported that LVEF assessed by gated Tl-201 myocardial SPECT is as reliable as

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gated Tc-99m sestamibi SPECT [8] and significantly correlated with measurements by other modalities [9–12]. Two-dimensional (2D) echocardiography can be a comparative standard for measuring LVEF in the clinical field. However, 2D echocardiography has limitations such as underestimation of LV volume and restricted repeatability. Hybrid SPECT/CT [13] systems equipped with multislice CT are currently used for nuclear cardiac imaging. These hybrid systems obtain attenuation maps from low-dose CT images. Advantages of CT-based attenuation correction (CTAC) methods include higher quality maps due to high photon flux, less noise, and resolution improvement [14]. Therefore, CTAC methods can improve the diagnostic accuracy of myocardial SPECT imaging [13, 15]. However, comparisons of LVEF assessed by hybrid SPECT/CT using a CTAC method with assessments by conventional measurements using a non-attenuation correction (non-AC) method or 2D echocardiography have been limited. We hypothesized that CTAC methods would not be inferior to the other two methods. Therefore, we evaluated the correlation between LVEF assessed by CTAC or non-AC methods of Tl-201 myocardial SPECT/CT and 2D echocardiography. We compared the diagnostic performance of these two attenuation correction methods for identifying abnormal LVEF in patients with angina pectoris and in a subgroup of patients with perfusion abnormalities on myocardial SPECT/CT images.

Methods

Study Population

Between September 2010 and September 2011, 339 consecutive patients underwent Tl-201 myocardial SPECT/CT and two-dimensional (2D) echocardiography within 1 month of a SPECT/CT study evaluating chest pain. These patients were analyzed in this retrospective study. Elective coronary angiography (CAG) was performed in 136 of the 339 patients. Patients were excluded if they experienced acute myocardial infarction or unstable angina within 2 weeks before Tl-201 myocardial SPECT/CT or if they had changes of clinical status between acquisition of SPECT/CT and 2D-echocardiography. We also excluded patients with significant arrhythmia that could interfere with gating techniques.

The study was approved by the institutional review board of our institution (IRB No. 2018-05-026).

Tl-201 SPECT Imaging and Analysis

Patients were asked to not ingest food or caffeine for more than 4 h prior to pharmacologic stress test with 6 min of adenosine (0.14 mg/kg) infusion. After 3 min of adenosine infusion, Tl-201 (111 MBq, 3 mCi) was injected to acquire stress images. During stress tests, patients were monitored by 12-lead electrocardiogram. Throughout the stress protocol and recovery time, serial blood pressure monitoring was carried out. Myocardial perfusion SPECT was performed at rest and 4 h after injection of Tl-201. SPECT was acquired on a 90-configuration dual-head hybrid SPECT/CT system (Infinia Hawkeye 4, GE Medial System, Milwaukee, WI, USA) with a low-energy, high-resolution collimator. The camera obtained data from a 45° right anterior oblique projection to a 45° left posterior oblique projection. The protocol was a 64×64 matrix, 30 projections of 60 s, and 8 frames per cardiac cycle in association with a 15% window centered on 167 keV photopeak of Tl-201 radiopharmaceuticals. At the end of each acquisition, low-dose chest CT scan (140 kVp, 2.5 mA) was acquired to obtain attenuation maps that were used by Xeleris Workstation (GE Medical System, Milwaukee, WI, USA) automatically to correct emission data. To avoid motion artifacts, patients' raw data were reviewed on a cine projection and a sonogram.

Two methods were used to reconstruct images from the projection data using Myovation cardiac software on a Xeleris workstation. CTAC images were processed using the ordered subset expectation maximization iterative reconstruction algorithm (IRAC), and non-AC images were processed using the filtered back projection (FBP) algorithm. Each SPECT reconstruction method was automatic, but reorientation into three orthogonal views was manually performed by nuclear medicine technologists. SPECT data were analyzed with automatic commercial SPECT Quantitative Gated SPECT software (QGS, Cedars-Sinai Medical Center, Los Angeles, CA, USA). The algorithm works in three-dimensional space. Using this algorithm, segmentation of the left ventricle, estimation and display of endocardial and epicardial surfaces for all eight images in the cardiac cycle, and calculation of relative LV volumes and LVEF were performed. We compared LVEF obtained by CTAC (IRAC) and non-AC methods (FBP) with LVEF obtained by 2D echocardiography.

We performed a subgroup analysis of cases whose SPECT/CT results showed ischemia or infarction ($n = 31$) to investigate if perfusion abnormalities affected LVEF measurements by CTAC, non-AC, and 2D echocardiography.

Echocardiographic Examination

We performed 2D transthoracic Doppler echocardiography (IE33, Philips Medical Systems, Best, Netherlands) of patients in the left lateral decubitus position. Gain settings were adapted to patient characteristics to obtain the best quality image for measurement accuracy. Transthoracic echocardiography was performed according to American Society of Echocardiography recommendations [16]. Left ventricular and diastolic

Table 1 Clinical characteristics of patients ($n = 339$)

Characteristics	Value
Male	206 (61)
Age (years)	62.8 ± 12.9
Body mass index (kg/m^2)	24.7 ± 3.1
Left atrium size (mm)	40.4 ± 5.8
Hypertension	102 (30)
Diabetes mellitus	44 (13)
Congestive heart failure	52 (15)

Data are presented as *n* (%) or mean ± standard deviation

dimension, left ventricular and systolic dimension, and EF were measured in the parasternal long-axis view. One cardiologist and one trained technician with 21 years of echocardiography experience who were blinded to SPECT/CT results and clinical data performed echocardiography and analyzed the data. Study population was categorized into two groups based on the LVEF as follows: normal (≥ 55%) and decreased (< 55%) according to previous 2D criteria of American Society of Echocardiography [17].

Statistical Analysis

SPSS (release 17.0, Chicago, IL, USA) was used for analysis. Data are expressed as means ± SDs if continuous, and as counts and percentages if categorical. The paired *t* test was used for the comparison of LVEF between echocardiography and the two attenuation correction methods on Tl-201 myocardial gated SPECT-CT. Pearson's (for total patients) and Spearman's correlation coefficient (for subgroup with perfusion abnormality) was used to evaluate the correlation between LVEF on Tl-201 myocardial SPECT-CT and LVEF on 2D echocardiography. To compare performances of the IRAC and FBP reconstruction methods for evaluating normal (≥ 55%) and decreased (< 55%) LVEF, sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated. P values < 0.05 were considered statistically significant.

Results

Characteristics of Study Population

Patient mean age was 62.8 ± 12.9 years (range 22–93 years). Time between acquisition of SPECT-CT and echocardiography averaged 3 ± 4 days. Table 1 lists clinical characteristics of the enrolled patients. Rates were 30% for hypertension, 13% for diabetes mellitus, and 15% for congestive heart failure. Mean body mass index was 24.7 kg/m^2. Mean size of the left atrium was 40.4 mm by 2D echocardiography.

Comparison of LVEF by Echocardiography and Tl-201 Myocardial Hybrid SPECT/CT

LVEF measurement assessed by the two attenuation correction methods (CTAC and non-AC) was significantly lower than measurement assessed by 2D echocardiography in total patient as well as in subgroup with perfusion abnormality ($p < 0.001$ for all) (Table 2). However, LVEF measurements by the two attenuation correction techniques (CTAC and non-AC) and 2D echocardiography for total patients ($n = 339$; $r = 0.487$ for CTAC and 2D echocardiography, $r = 0.473$ for non-AC and 2D echocardiography, all $p < 0.001$; Fig. 1a, b) were moderately correlated. Moderate correlation was also seen in the subgroup with perfusion abnormalities on myocardial SPECT/CT ($n = 31$) ($r = 0.506$, $p = 0.004$ for CTAC and 2D echocardiography, $r = 0.565$, $p = 0.001$ for non-AC and 2D echocardiography; Fig. 1c, d). Representative cases of LVEF measured by Tl-201 myocardial hybrid SPECT/CT in patients with normal perfusion and abnormal perfusion are presented in Fig. 2.

Overall diagnostic performances of CTAC and non-AC methods for assessing normal and decreased LVEF by myocardial hybrid SPECT/CT were similar. However, in patients

Table 2 Comparison of LVEF assessed by 2D echocardiography and myocardial SPECT/CT in total patients ($n = 339$) and in the subgroup of patients with myocardial perfusion abnormalities ($n = 31$)

	2D echo	CTAC	Non-AC	*p* 2D echo vs. CTAC	*p* 2D echo vs. non-AC
Total patients	67.09 ± 8.32	60.72 ± 12.30	59.63 ± 12.25	< 0.001	< 0.001
Patients with perfusion abnormality	57.52 ± 11.90	44.84 ± 12.79	44.26 ± 12.65	< 0.001	< 0.001

Data are presented as percent ± standard deviation

LVEF left ventricular ejection fraction, *2D echo* 2D echocardiography, *CTAC* CT-based attenuation correction, *Non-AC* non-attenuation correction

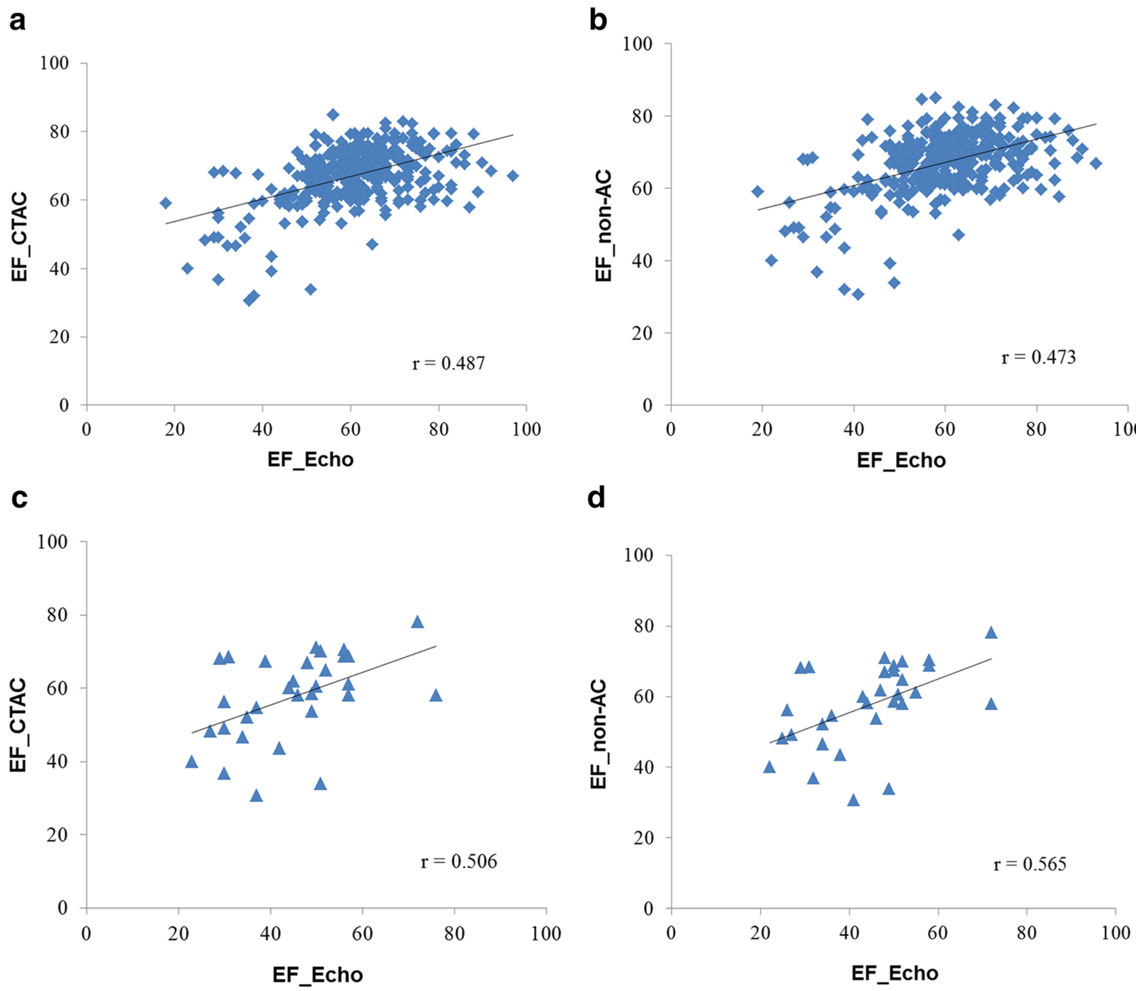


Fig. 1 Moderate correlation of LVEF between the CTAC (**a**, $n = 339$; $r = 0.487$; $p < 0.001$) or non-AC (**b**, $n = 339$; $r = 0.473$; $p = 0.001$) technique and 2D echocardiography in total patients. Correlation of LVEF between the CTAC (**c**, $n = 31$; $r = 0.506$; $p = 0.004$) or non-AC (**d**, $n = 31$; $r = 0.565$; $p < 0.001$) technique and 2D echocardiography in the perfusion abnormality subgroup. *CTAC* CT-based attenuation correction, *LVEF* left ventricular ejection fraction, *Non-AC* non-attenuation correction

with myocardial perfusion abnormalities, sensitivity and accuracy of both CTAC and non-AC methods of hybrid SPECT/CT were lower than sensitivity and accuracy of the total patients (Table 3).

Discussion

This study showed that LVEF measurement by the CTAC method of Tl-201 myocardial SPECT/CT in patients with angina pectoris was comparable to measurements by a conventional non-AC method. Although the LVEF measurements assessed by the two attenuation correction methods (CTAC and non-AC) were different with measurement assessed by 2D echocardiography, they showed moderate correlation with 2D echocardiography and showed reliable diagnostic accuracy in evaluating normal or decreased LVEF in clinical circumstances. Diagnostic accuracy of myocardial hybrid SPECT/CT in the detection of coronary artery disease (CAD) is superior to that of conventional myocardial SPECT [18, 19]. Use of CTAC images improves normalcy rates (95% for CTAC vs. 76% for non-AC) and diagnostic accuracy in detecting CAD [20]. By providing greater contrast between non-perfused and perfused areas of the myocardium, CTAC methods give better definition of perfusion defect size and severity [21]. However, information is insufficient about the reliability of LVEF measurements by the CTAC method of hybrid SPECT/CT and comparisons with other imaging modalities including conventional 2D echocardiography. In this study, LVEF measured by the CTAC method of hybrid SPECT/CT moderately correlated with measurements by 2D echocardiography. This correlation was

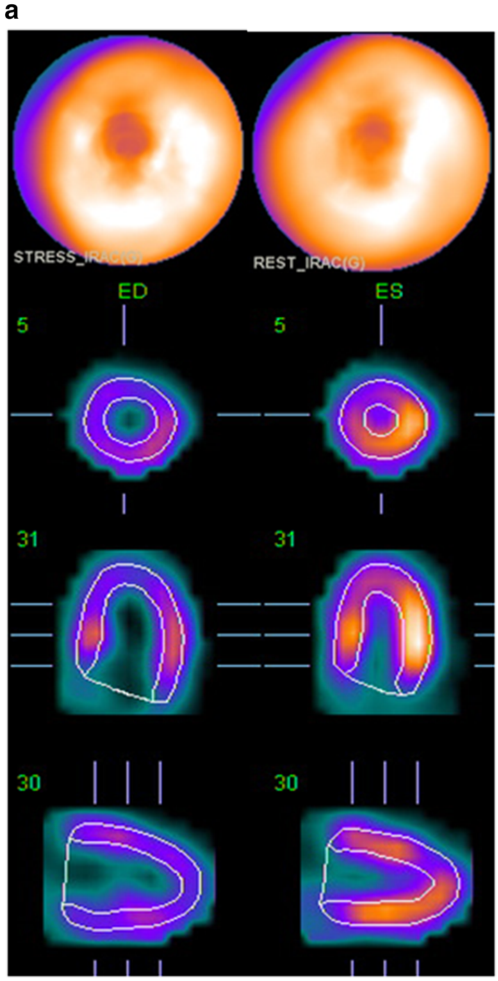


Fig. 2 Representative case of LVEF measured by Tl-201-gated myocardial hybrid SPECT/CT in patients with normal perfusion (**a**, CTAC 53%; **b**, non-AC 52%) or abnormal perfusion (**c**, CTAC 35%; **d**, non-AC 37%). EF measured by 2D echo in patients with normal perfusion was 62%, and that of those with abnormal perfusion was 54%. *CTAC* CT-based attenuation correction, *LVEF* left ventricular ejection fraction, *Non-AC* non-attenuation correction

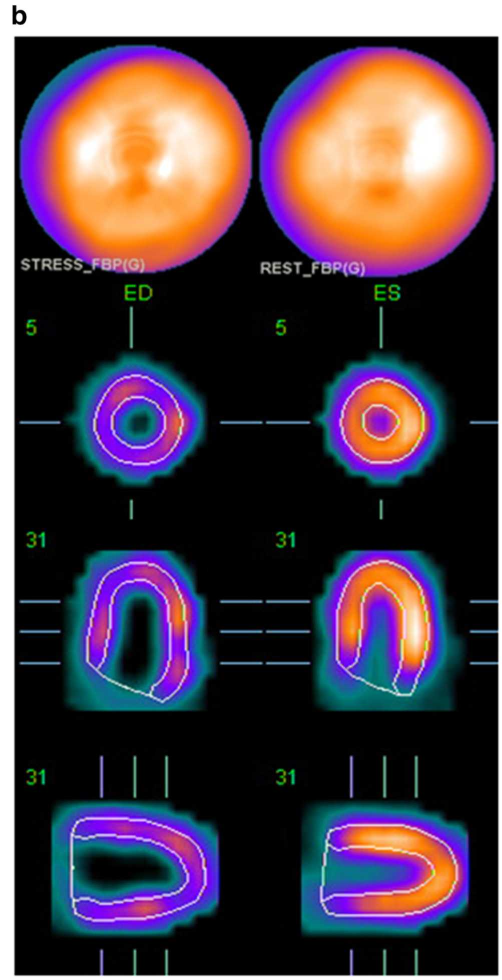
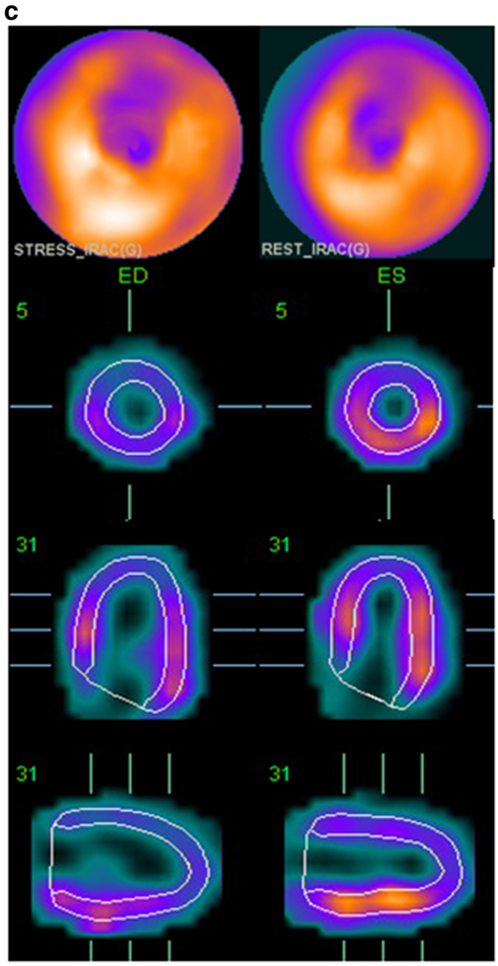


Fig. 2 continued.

maintained in the subgroup of patients with perfusion abnormalities on myocardial SPECT/CT. Thus, LVEF measured by the CTAC method was reliable and could be used in clinical settings.

LVEF measured by both the CTAC and non-AC methods of hybrid SPECT/CT was lower than measurements by 2D echocardiography for the total patient population and was more evident for patients with perfusion abnormalities. There could be several explanations why myocardial perfusion SPECT underestimates LVEF. We performed 8-frame gating during SPECT acquisition, where 8 frames per cardiac cycle underestimated LVEF by 3.7 percentage points compared to gated myocardial perfusion SPECT with 16 frames per cardiac cycle [22]. Although 16-frame to 24-frame gating may provide more accurate estimation of LVEF, it could lead to fewer counts per frame or longer acquisition times. Moreover, the normal range of LVEF and volume varies significantly between commercial SPECT-CT softwares [23]. Hedeer et al. [24] compared four different commercial automated software packages of gated myocardial perfusion SPECT with cardiac MRI. In their result, QGS and GE myometrix showed an underestimation of LVEF, in contrast to Emory Cardiac Toolbox (ECTb) and Exini heart, which were consistent with previous studies [25–28]. We used QGS software and the difference might be greater in the subgroup with perfusion abnormality than total patients.

Several studies have reported significant positive correlations between LVEF values obtained from 2DE and gated myocardial SPECT with r values ranging from 0.72 to 0.80 [29–33]. However, most of these previous studies used Tc-99m sestamibi tracer. One previous study with Tl-201 tracer described strong correlation between LVEF measurement with 2D echocardiography



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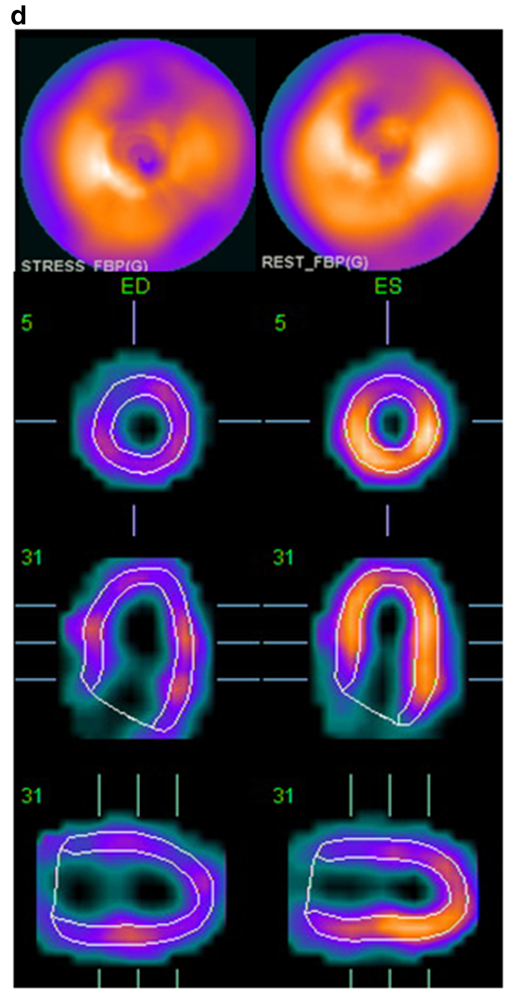

Fig. 2 continued.

and myocardial SPECT (r = 0.7) [34]. Our correlation value (0.4~0.6) seems lower than their result, and it might be caused from different study population and interobserver variability of LVEF caused by two 2D echocardiographers in our institution.

This study had several limitations. First, the study was retrospective and involved a small number of patients with perfusion abnormalities. Second, several studies evaluated the impact of age and gender on the relationship between LVEF and clinical outcomes [35, 36]. We did not take such a point into account in our analysis. In the future research, analyzing whether gender and age influence the relationship between the LVEF measurement assessed by Tl-201 myocardial SPECT/CT and 2D echocardiography would be valuable aspect.

In conclusion, LVEF measured by the CTAC method of Tl-201 myocardial SPECT/CT was comparable to the conventional non-AC method of myocardial SPECT in patients with angina pectoris and in the subgroup of patients with perfusion abnormality. LVEF obtained by both the CTAC and non-AC methods showed moderate

Table 3 Sensitivity, specificity, and diagnostic accuracy of CTAC and non-AC methods of myocardial hybrid SPECT/CT for evaluating decreased or normal LVEF according to 2D echocardiography results

Parameter	CTAC	Non-AC
Total patients (n = 339)		
Sensitivity	76.3 (242/317)	74.8 (237/317)
Specificity	90.9 (20/22)	90.9 (20/22)
Accuracy	77.3 (262/339)	75.8 (257/339)
PPV	99.2 (242/244)	99.2 (237/239)
NPV	21.1 (20/95)	20.0 (20/100)
Patients with perfusion abnormalities (n = 31)		
Sensitivity	35.0 (7/20)	25.0 (5/20)
Specificity	100 (11/11)	100 (11/11)
Accuracy	58.1 (18/31)	51.6 (16/31)
PPV	100 (7/7)	100 (5/5)
NPV	45.8 (11/24)	42.3 (11/26)

CTAC CT-based attenuation correction, *Non-AC* non-attenuation correction, *LVEF* left ventricular ejection fraction, *NPV* negative predictive value, *PPV* positive predictive value correlation with 2D echocardiography and had reliable diagnostic accuracy for evaluating normal or decreased LVEF. Tl-201 gated myocardial hybrid SPECT/CT can be a reliable tool in the assessment of LVEF in clinic.

Compliance with Ethical Standards

Conflict of Interest Ji Young Kim, Hwan-Cheol Park, Soo Jeong Kim, Hyung Seok Chang, Hyung Jin Choi, and Young Hwan Kim declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was not obtained due to retrospective review study.

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