Can CT measured LA diameter predict the presence and the degree of LV Diastolic Dysfunction?

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Running title: CT measured LA diameter and diastolic dysfunction
Abstract

Objective: This study was conducted to determine whether the presence and the degree of left ventricular diastolic dysfunction (LVDD) can be predicted by the simple LA diameter measured on computed tomography (CTLAD).

Methods: Among adult patients who underwent both chest CT and echocardiography in the emergency department from January 2020 to December 2021, a retrospective cross-sectional study was conducted on patients in whom the time interval between the two tests was less than 24 hours. Receiver operating characteristic curve analysis was used to evaluate the diagnostic power of CTLAD for echocardiographic LVDD.

Results: In a study involving 373 patients, 192 (51.5%) had LVDD. Among them, 122 (63.5%) had grade 1, 61 (31.8%) had grade 2, and 9 (4.7%) had ≥grade 3 LVDD. Median CTLAD values were 4.1cm for grade 1, 4.5cm for grade 2, and 4.9cm for ≥grade 3 LVDD. The AUC value of CTLAD in distinguishing LVDD of ≥grade 1, ≥grade 2 (optimal cutoff ≥4.4cm), and ≥grade 3 (optimal cutoff ≥4.5cm) were 0.588, 0.657 (with sensitivity 61.4%, specificity 66.0%, positive predictive value [PPV] 29.5%, negative predictive value [NPV] 88.1%, odds ratio [OR] 3.1), and 0.834 (with sensitivity 88.9%, specificity 70.1%, PPV 6.8%, NPV 99.6%, OR 18.7), respectively.

Conclusion: CTLAD ≥4.4cm can be used as a rough reference value to distinguish LVDD of ≥grade 2, and CTLAD ≥4.5cm can be very reliably distinguish LVDD of ≥grade 3. CTLAD might be very useful parameter in predicting LVDD in environments where echocardiography is not available.

Keywords: Computed Tomography; Echocardiography; Heart Failure, Diastolic; Ventricular Dysfunction, Left; Left Atrium
Capsule summary

What is already known?
Echo measured LA size (LA volume index or LA diameter) can predict LVDD. However, information on CT measured LA diameter can predict LVDD is limited.

What is new in the current study?
CT measured LA diameter ≥4.4 cm can be used as a rough reference value to distinguish ≥grade 2 LVDD, and CT measured LA diameter ≥ 4.5 cm can very reliably distinguish ≥grade 3 LVDD. CT measured LA diameter might be used to predict LVDD in environments where echocardiography is not available.
Introduction

Traditionally, heart failure (HF) refers to a clinical syndrome in which symptoms occur due to a decrease in left ventricular systolic function, represented by ejection fraction (EF) [1]. However, since the 1990s, it has been recognized that HF can occur even without a decrease in EF [2]. Currently, HF is divided into HF with reduced EF (HFrEF) with an EF of 40% or less, HF with midrange EF (HFmrEF) with an EF of 41-49%, and HF with preserved EF (HFpEF) with an EF of 50% or more [3]. The reason why symptoms of HF appear in HFpEF is because of the left ventricular diastolic dysfunction (LVDD). In other words, to diagnose HFpEF, it is essential to identify LVDD [4, 5]. Practically, the fundamental elements of HFpEF are clinical signs or symptoms of HF, evidence of preserved or normal EF and evidence of abnormal LVDD that can be determined by doppler echocardiography or cardiac catheterization [5]. The prevalence of HFpEF is gradually increasing, and some studies show that it accounts for more than half of all HF [6, 7]. In addition, the hospitalization rate and mortality rate due to worsening of HF in HFpEF are also known to be similar to those in HFrEF, traditional HF [8, 9].

During acute exacerbations of HFpEF, patients usually visit emergency department (ED), but it is not easy to evaluate LVDD using a bedside portable sonography in the ED setting. To evaluate LVDD, it is necessary to measure mitral inflow velocity (E/A ratio), mitral annular motion velocity (E'/A' ratio), and E/E' using doppler and tissue doppler [4], while systolic function can be evaluated to some extent by relatively simple visual estimation EF by bedside sonography [10]. Technical skills are required to accurately measure LVDD-related indicators, and even if the values are accurately measured, background knowledge of echocardiography and cardiac pathophysiology are required for correct interpretation. Unfortunately, according to one study, despite receiving training on measuring LVDD right before the study, the accuracy of emergency physicians in distinguishing the presence and degree of LVDD using
echocardiography was about 87% compared to those of cardiologists [11, 12]. Additionally, many ED may not be equipped with echocardiography itself, and often only have bedside sonography. For these reasons, ED physicians may not recognize LVDD, even though a patient’s cause of symptom is quite advanced LVDD, until formal echocardiography results are reported by a cardiologist.

As LVDD progresses, it affects the left atrium (LA) and ultimately increases LA size [13-15]. Since the use of computed tomography (CT) in the ED has recently increased dramatically [16], this study was conducted to determine whether the presence and degree of LVDD could be predicted using the LA diameter measured on CT (CTLAD).
Methods & Patient Selection

A retrospective cross-sectional study was conducted on adult patients aged 18 years or older who visited our ED and underwent both chest CT (contrast-enhanced or non-contrast-enhanced) and echocardiography with the time interval between the two tests of less than 24 hours. We arbitrarily assumed that the cardiac function may have been changed (by the effect of vasoactive medications or fluids etc.) if the time interval between the two tests exceeded 24 hours, and therefore were excluded from the study. Cases with severe thoracic deformity or spinal abnormality that prevented LA size measurement on chest CT were also excluded. Additionally, cases where LA size or LVDD were omitted from the report were also excluded (Fig. 1). Before conducting the study, the Institutional Review Board (IRB) approval was obtained (2022-06-058), and written informed consent exempted by the IRB. All personal information such as patient name, hospital registration number, date of birth, and national resident registration number was deleted after assigning a research subject number to ensure anonymity. This study was conducted in compliance with the ethical regulations of the World Medical Association Declaration of Helsinki [17].

Data Acquisition

To measure LA diameter on CT, the anteroposterior diameter of the LA midline was measured on the axial view of chest CT (Fig. 2). A Brilliance iCT–SP 128 (Philips Medical Systems, Best, Netherlands) was used during the study period. LA diameter was measured using the length measurement tool built into the picture archiving and communication system viewer program in a 27-inch full high definition (1920x1080) resolution monitor environment. The LA diameter was measured by continuously moving the longitudinal image in the mediastinal setting and selecting the image in which the anteroposterior diameter of the LA appeared the longest. One emergency physician with 14 years of clinical experience measured
LA diameter on chest CT without knowing the echocardiography results. The presence and degree of LVDD were retrieved from formal report of echocardiogram which were measured by echocardiographer and confirmed by a cardiologist. According to the results of the cardiologist’s formal report, if LVDD was present, it was classified as grade 1 (relaxation abnormality), grade 2 (pseudonormal) or ≥grade 3 (restrictive) LVDD.

**Statistical Analysis**

The STATA for Windows ver. 15.1 (Stata Corp., College Station, TX, USA) was used for statistical analysis. The data did not follow a normal distribution and therefore were expressed as median with interquartile range. Kruskal-Wallis H-test was performed for comparison between groups, and Dunn test was performed as a post hoc analysis. P<0.05 was considered to indicate statistical significance. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic power of CTLAD for LVDD confirmed by echocardiography, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratio (OR) were calculated according to the best cutoff value.
Results

From January 1, 2020, to December 31, 2021, a total of 1,118 adult patients aged 18 years or older underwent chest CT and echocardiography in the ED (Fig. 1). The study was conducted on a total of 373 patients, excluding 684 patients in whom the interval between chest CT and echocardiography was more than 24 hours, and 61 patients in whom there was no reports on LA size or LVDD in the formal echocardiography report. There were no cases of thoracic deformity or spinal abnormalities severe enough to prevent LA size measurement on chest CT. The median age of the study subjects was 78 years (66, 84), and 188 (50.4%) were women (Table 1). The median time interval between Chest CT and echocardiography was 6 hours (2, 15).

Correlation analysis between CTLAD and echocardiography measured LA diameter showed Pearson’s $r=0.834$ ($P<0.001$), confirming a strong correlation between the two variables (Fig. 3). The median value of echocardiography measured LA diameter was 4.4 cm (4.0, 4.9) and the median value of CTLAD was 4.2 cm (3.6, 4.7) (Table 1). The median value obtained by subtracting the CTLAD from the echocardiography measured LA diameter was 2.1 cm (-0.5, 5.7).

Of the 373 patients, 181 patients (48.5%) had normal diastolic function. There were 192 patients (51.5%) with LVDD, of which 122 (63.5%) had grade 1, 61 (31.8%) had grade 2, and 9 (4.7%) had ≥grade 3. When comparing the CTLAD between each group using the Kruskal-Wallis H-test, there was a statistically significant difference between the four groups ($\chi^2(3)=23.0$, $P<0.001$) (Fig. 4). Post-hoc analysis showed no statistical difference between the patient group without LVDD and grade 1 LVDD ($P=0.124$). There were statistical differences between grade 1 LVDD and grade 2 LVDD ($P=0.011$), grade 2 LVDD and LVDD of ≥grade 3 ($P=0.014$).

The area under ROC curve (AUC) value of CTLAD for distinguishing LVDD of ≥grade 1
was 0.588 (95% CI, 0.528 - 0.648, P=0.004) (Fig. 5). The AUC value of CTLAD for distinguishing LVDD of ≥grade 2 was 0.657 (95% CI, 0.594 – 0.720, P<0.001), and the best cutoff value was ≥4.4 cm (sensitivity 61.4%, specificity 66.0%, PPV 29.5%, NPV 88.1%, and OR 3.1). The AUC value of CTLAD for distinguishing LVDD of ≥grade 3 was 0.834 (95% CI, 0.746 – 0.921, P<0.001), and the best cutoff value was ≥4.5 cm (sensitivity 88.9%, specificity 70.1%, PPV 6.8%, NPV 99.6%, and OR 18.7).

As LVDD progressed, LVEF also tended to decrease, and the Kruskal-Wallis H-test showed statistical significance ($\chi^2(3)= 22.4$, P= 0.0001). Therefore, LVEF was added as a covariate and adjusted using a linear model, and the results are as follows (Fig. 5). The AUC value of CTLAD adjusted for LVEF for distinguishing LVDD of ≥grade 1 was 0.595 (95% CI, 0.536 - 0.654, P= 0.002). The AUC value of CTLAD adjusted for LVEF for distinguishing LVDD of ≥grade 2 was 0.628 (95% CI, 0.557 - 0.699, P<0.001). The AUC value of CTLAD adjusted for LVEF for distinguishing LVDD of ≥grade 3 was 0.795 (95% CI, 0.696 - 0.895, P<0.001).
Discussion

This study confirmed that CTLAD can distinguish LVDD of ≥grade 2 (CTLAD ≥4.4 cm) and LVDD of ≥grade 3 (CTLAD ≥4.5 cm). In the stage of grade 1 LVDD, although LV relaxation is impaired, it is not accompanied by an increase in LV end-diastolic pressure (LVEDP), so left atrial pressure and LA size do not increase, and pulmonary edema rarely occurs. Therefore grade 1 LVDD, which is relatively common in asymptomatic elderly people, has little clinical significance. However, since LVDD of ≥grade 2 is accompanied by an increase in LVEDP, LA pressure and LA size increase, and pulmonary edema may also occur [18]. Therefore, the results of this study that LVDD of ≥grade 2 can be distinguished by CTLAD might be a very clinically meaningful finding.

Although patients with diastolic HF may have symptoms such as shortness of breath or chest tightness during exercise, these are not disease-specific symptoms that only appear in diastolic HF. In addition, the current diagnostic guidelines for diastolic HF require doppler echo to be performed to measure and interpret mitral inflow velocity and mitral annular motion velocity [4, 5]. Therefore, even if patient’s cause of symptom is quite advanced diastolic HF, LVDD may not be diagnosed without objective tests such as echocardiography. The results of this study showing that LVDD of ≥grade 2 might be distinguished using CTLAD should be of great help to clinicians who are unfamiliar with echocardiography or in environments where echocardiography cannot be used.

Increased LA size can be evaluated by echocardiography measured LA diameter or volume index, and using this, LVDD can be indirectly diagnosed and classified [13-15]. However, echocardiogram is often unavailable (especially during night times and holidays), and many EDs are not even equipped with echocardiogram, this study focused on CTLAD. CTLAD was 2.1 cm shorter than the echocardiography measured LA diameter in this study. This is thought to be because echocardiography uses electrocardiogram to measure largest LA diameter by the
LV end-systole, but CT does not consider this timing. Although CTLAD was 2.1 cm shorter than the echocardiography measured LA diameter, the measurement values of the two methods showed a strong correlation, and it was confirmed that LVDD of ≥grade 2 might be recognized using CTLAD. CTLAD of ≥4.4 cm can serve as a rough reference value for distinguishing LVDD of ≥grade 2 and CTLAD of ≥4.5 cm can very reliably distinguish LVDD of ≥grade 3.

One noteworthy finding in the results of this study is the high negative predictive value of the CTLAD. If the CTLAD is less than 4.4 cm, the likelihood of LVDD of ≥grade 2 is significantly lower considering the negative predictive value of 88.1%, and if the CTLAD is less than 4.5 cm, the negative predictive value is 99.6%, meaning that LVDD of ≥grade 3 can be virtually excluded. The authors suggest that the LA diameter must be checked without omission after a chest CT scan, if patient has HF relevant symptoms.

There is one previous study by Lick et al. which reported CTLAD to predict LVDD in patients who underwent CT and echocardiography within 48 hours, and the median time interval between CT and echocardiography was 15.5 hours. They reported that CTLAD of ≥4.0 cm can discriminate LVDD of ≥grade 2 with 68% of sensitivity and 74% of specificity [19]. In our study, the best CTLAD value for distinguishing stage 2 or higher LVDD was 4.4 cm, whereas in their study it was 4.0 cm, which is 0.4 cm shorter. Authors do not have answer to explain this difference, however, we do believe that limiting the time interval between CT and echocardiography to less than 24 hours (median of 6 hours) is one of the biggest strengths of this study. As the interval between CT and echocardiography increases, LVEDP, LA pressure, and LA size at each time point may vary due to the influence of intravenous fluids or use of HF treatment medications. Therefore, the results of this study, where the time interval between the two tests was only about 6 hours, are considered to be very reliable.

This study has several limitations. First, this study was a retrospective cross-sectional study including only patients who visited the ED and underwent both CT and echocardiography
within 24 hours. If two tests were performed intensively at the same time, included patients are likely to be more seriously ill, which may result in selection bias. Second, CTLAD is not as accurate as the LA volume index in reflecting true LA size. The actual appearance of LA is a complex shape with a curved outer margin, the volume index is known to be more accurate for measuring the true LA size [20, 21]. To measure the LA volume index, the area-length method or Simpson's method should be used in the apical 4-chamber or 2-chamber view at the LV end-systole, when LA size is largest. It is difficult to measure the LA volume index in the ED where visual estimation is mainly performed using portable sonography. Although CTLAD does not reflect the true LA size like the LA volume index, it is an index that indirectly suggests LA enlargement, and since CT is available in most EDs, it was used in this study as an alternative parameter to measure LA enlargement. Third, there is a possibility that fluids or specific medications administered to patients in the ED may have affected the patient's actual degree of diastolic HF and LA size. A drawback of this retrospective study is that the analysis did not reflect whether and how much fluid was administered, as well as the medications used for the patient. However, short time interval between CT and echocardiography in this study should have minimized the potential effect of fluid or medications.

Conclusion

LVDD of ≥grade 2 might be distinguished using CTLAD. CTLAD of ≥4.4 cm can be used as a rough reference value for distinguishing LVDD of ≥grade 2, and CTLAD of ≥4.5 cm can very reliably distinguish LVDD of ≥grade 3. This might be a very helpful finding in the treatment of patients complaining of HF-related symptoms in environments where echocardiography is not possible.
ARTICLE INFORMATION

Ethical statements: This study was approved by the Institutional Research Ethics Committee (IRB No. 2022-06-058). The Institutional Review Board exempted written informed consent due to the retrospective nature of the study.

Conflict of interest statement: The authors declare no conflict of interest.

Funding: This research received no external funding.

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Author contributions: Conceptualization: DHS, JHL; Data curation: GAK, JUN, DHS; Formal analysis: JUN, DHS; Visualization: JUN, JHL; Writing-original draft: GAK, JHL; Writing-review & editing: all authors. All authors read and approved the final manuscript.
References


20. Fu M, Zhou D, Tang S, Zhou Y, Feng Y, Geng Q. Left atrial volume index is superior to left atrial diameter index in relation to coronary heart disease in hypertension patients with

Table 1. Basic characteristics of the patients

<table>
<thead>
<tr>
<th></th>
<th>total (n=373)</th>
<th>normal (n=181)</th>
<th>LVDD grade 1 (n=122)</th>
<th>LVDD grade 2 (n=61)</th>
<th>LVDD of ≥grade 3 (n=9)</th>
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<tr>
<td><strong>Age, year</strong></td>
<td>78 (66, 84)</td>
<td>74 (57, 82)</td>
<td>81 (73, 85)</td>
<td>82 (71, 88)</td>
<td>77 (67, 79)</td>
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<td><strong>Sex</strong></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>185 (49.6%)</td>
<td>103 (56.9%)</td>
<td>53 (43.4%)</td>
<td>24 (39.3%)</td>
<td>5 (55.6%)</td>
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<tr>
<td>Female</td>
<td>188 (50.4%)</td>
<td>78 (43.1%)</td>
<td>69 (56.6%)</td>
<td>37 (60.7%)</td>
<td>4 (44.4%)</td>
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<td><strong>Vital signs</strong></td>
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<tr>
<td>HR, /min</td>
<td>85 (75, 104)</td>
<td>90 (77, 109)</td>
<td>83 (74, 92)</td>
<td>82 (71, 104)</td>
<td>84 (65, 102)</td>
</tr>
<tr>
<td>BT, °C</td>
<td>36.8 (36.3, 37.3)</td>
<td>36.7 (36.2, 37.1)</td>
<td>36.9 (36.4, 37.5)</td>
<td>36.6 (36.2, 37)</td>
<td>36.5 (35.9, 36.7)</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>138 (121, 165)</td>
<td>135 (122, 159)</td>
<td>144 (121, 165)</td>
<td>143 (118, 181)</td>
<td>168 (129, 177)</td>
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<td>DBP, mmHg</td>
<td>77 (66, 89)</td>
<td>80 (69, 90)</td>
<td>75.5 (64, 87)</td>
<td>74 (62, 87)</td>
<td>79 (74, 100)</td>
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<tr>
<td>Oxygen saturation, %</td>
<td>97 (95, 99)</td>
<td>98 (96, 99)</td>
<td>97 (95, 99)</td>
<td>97 (95, 99)</td>
<td>96 (95, 99)</td>
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<td><strong>CT parameters</strong></td>
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<tr>
<td>Left atrial diameter, cm</td>
<td>4.2 (3.6, 4.7)</td>
<td>4.0 (3.3, 4.8)</td>
<td>4.1 (3.8, 4.5)</td>
<td>4.5 (4.0, 4.7)</td>
<td>4.9 (4.7, 5.6)</td>
</tr>
<tr>
<td>Maximum cardiac diameter, cm</td>
<td>13.4 (12.3, 14.5)</td>
<td>13.5 (12.3, 14.7)</td>
<td>13.2 (12.1, 14.4)</td>
<td>13.7 (12.5, 14.7)</td>
<td>13.6 (12.2, 14.9)</td>
</tr>
<tr>
<td>Maximum thoracic diameter, cm</td>
<td>24.2 (22.6, 25.7)</td>
<td>24.5 (23.2, 25.8)</td>
<td>24.1 (22.2, 25.8)</td>
<td>23.1 (22.0, 25.6)</td>
<td>22.8 (22.4, 24.7)</td>
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<tr>
<td>E/A ratio</td>
<td>0.8 (0.7, 1.3)</td>
<td>0.9 (0.6, 1.3)</td>
<td>0.7 (0.6, 0.8)</td>
<td>0.9 (0.7, 1.1)</td>
<td>2.0 (2.0, 2.3)</td>
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<td>LAVI, mL/m²</td>
<td>41.3 (31, 58.9)</td>
<td>33.9 (23.3, 52.1)</td>
<td>38.9 (32.5, 43.9)</td>
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<td>Deceleration time, ms</td>
<td>147.5 (121.2, 199.8)</td>
<td>142.8 (120.0, 181.6)</td>
<td>227.5 (167.1, 254.0)</td>
<td>146.4 (121.7, 231.3)</td>
<td>85.9 (62.6, 111.8)</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>4.4 (4.0, 4.9)</td>
<td>4.0 (3.7, 4.8)</td>
<td>4.40 (4.2, 4.7)</td>
<td>4.9 (4.4, 5.1)</td>
<td>5.2 (5.1, 5.7)</td>
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<tr>
<td>Right atrial diameter, cm</td>
<td>4.4 (4.2, 4.8)</td>
<td>4.5 (4.3, 4.9)</td>
<td>4.2 (3.7, 4.6)</td>
<td>4.3 (4.2, 4.7)</td>
<td>4.5 (4.2, 5.0)</td>
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<tr>
<td>LVEF, %</td>
<td>62.0 (52.6, 69.0)</td>
<td>60.8 (52.6, 67.7)</td>
<td>65.6 (57.1, 70.0)</td>
<td>55.9 (40.0, 66.0)</td>
<td>48.9 (22.5, 62.0)</td>
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<td>RVSP, mmHg</td>
<td>36.0 (29.4, 47.0)</td>
<td>34.0 (28.0, 43.0)</td>
<td>35.0 (30.0, 44.0)</td>
<td>45.0 (34.9, 52.0)</td>
<td>63.0 (57.0, 69.0)</td>
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<td>E/E'</td>
<td>14.3 (9.3, 19.1)</td>
<td>9.8 (7.7, 15.1)</td>
<td>12.3 (8.4, 14.8)</td>
<td>19.1 (15.3, 26.2)</td>
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<tr>
<td>N</td>
<td>90</td>
<td>39</td>
<td>17</td>
<td>31</td>
<td>3</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range), or number (%). LVDD, left ventricular
diastolic dysfunction; HR, heart rate; BT, body temperature; SBP, systolic blood pressure; DBP, diastolic blood pressure; CT, computed tomography; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; RVSP, right ventricular systolic pressure.
Fig. 1. Flow diagram of the study.

ED, emergency department; CT, computed tomography.
Fig. 2. Measuring left atrial diameter on chest computed tomography.

The anteroposterior diameter of the left atrium was assessed using the built-in measurement tool (red line) of picture archiving communication system.
Fig. 3. A scatterplot showing the relationship between CT- and echocardiography-measured left atrium diameter.

CT, computed tomography; LAD, left atrium diameter
**Fig. 4.** A box plot of CT-measured left atrium diameters according to the grade of left ventricular diastolic dysfunction.

The displayed P values are the results of a grade comparison using Dunn's test. CTLAD, CT measured left atrium diameter; LVDD, left ventricle diastolic dysfunction.
**Fig. 5.** Receiver operating characteristic curve analysis of CT-measured left atrium diameter for distinguishing left ventricular diastolic dysfunction.

LVDD, left ventricular diastolic dysfunction; CTLAD, CT measured left atrium diameter; AUC, Area under ROC curve.