Reliability in Using Routine Coronary CT Angiography with Retrospective Electrocardiographic Gating for the Comprehensive Functional Evaluation of the Left Ventricle

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Purpose To evaluate the feasibility of comprehensive left ventricle (LV) functional parameters on routine coronary computed tomographic angiography (CCTA) based on two-dimensional echocardiography (2DE).

Materials and Methods Ninety-nine patients who underwent CCTA accompanied by 2DE were included in the study. The volumetric LV systolic functional parameters were acquired from 10-phase reconstruction of CCTA data. By differentiating the time-LV volume curve by time domain and measuring mitral valvular orifice areas, transmirtal time-velocity curves were drawn and the early (E) to late (A) mitral inflow peak velocities ratio (E/A ratio) was acquired. By measuring a longitudinal jerking velocity of the mitral valvular annulus on a four-chamber view, the mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E') ratio (E/E' ratio) was evaluated. All functional parameters were compared with the 2DE results.

Results The LV end diastolic volume, LV end systolic volume, ejection fraction, stroke volume, cardiac output, and LV myocardial mass measured by CCTA and 2DE showed moderate to strong correlations (r = 0.732, 0.821, 0.416, 0.394, 0.328, and 0.764, respectively; p < 0.05). The E/A and E/E' ratios showed strong correlation between CCTA and echocardiography (r = 0.807 and 0.751, respectively; p < 0.05).
Conclusion When CCTA is performed with retrospective electrocardiographic gating, additional information about the LV function can be acquired as reliably as with echocardiography.

Index terms Multidetector Computed Tomography; Echocardiography; Systole; Diastole; Heart Ventricles

INTRODUCTION

The evaluation of the function of the left ventricle (LV) by using LV volume and ejection fraction (EF) has been a mainstay in the assessment of patients with an ongoing or suspected cardiovascular disease. Variable modalities such as two-dimensional echocardiography (2DE), cardiac angiography, and cardiac magnetic resonance image (CMR) have been used to assess the LV function, and each technique has its own advantages and limitations (1-4). 2DE is the most commonly performed method and the easiest for the anatomic and functional analysis of the heart. However, it may have limitations for use with patients with obesity or chronic obstructive pulmonary disease; furthermore, it is highly operator-dependent and has a limited number of anatomical views in clinical settings. By contrast, coronary computed tomographic angiography (CCTA) has been increasingly performed in daily medical practice owing to remarkable technical advances (5). In cases of retrospective electrocardiographic (ECG) gating, CCTA can measure the LV volume with systolic function, with outcomes that are highly in agreement with those of other imaging modalities such as 2DE or CMR (6-8). LV diastolic dysfunction is increasingly being recognized as an early marker of cardiac disease. Therefore, the evaluation of the LV diastolic function is of interest to clinicians (9-10). 2DE represents the most commonly used approach for evaluating the diastolic function. Generally, transmitral valvular velocity (‘E’, peak transmitral velocity in early diastole; ‘A’, peak transmitral velocity in late diastole) has been used as a non-invasive marker for evaluation of the LV diastolic function (11-12). However, several confounding factors may influence the transmitral velocity. Therefore, combined assessment with early peak mitral septal velocity (E’) has been recommended (12). In a recent study (13, 14), CCTA could also evaluate the LV diastolic function, and the results showed good correlations for transmitral velocity, mitral septal tissue velocity, and estimation of LV filling pressures when compared with 2DE with tissue Doppler imaging.

Therefore, we presume that CCTA can provide comprehensive functional parameters of LV with both systolic and diastolic functions on a single scan with additional anatomical information of coronary arteries. However, to our knowledge, no prior studies have simultaneously evaluated the systolic and diastolic LV functions with CCTA. Therefore, the present study evaluated the functional parameters for both systolic and diastolic LV functions with CCTA in the same group of patients and validated the clinical feasibility of this method by comparing its outcomes with the 2DE results. Our Institutional Ethics Committee approved this study (KNUH 2015-12-028), and written informed consent was waived.

MATERIALS AND METHODS

This retrospective study was performed at a single institute from April 2010 to May 2015.
All patients examined using both retrospectively ECG-gated CCTA and 2DE within a 1-month period were consecutively included in the study. The exclusion criteria were cardiac surgery (include coronary arterial bypass graft, valve replacement, or pacemaker insertion), percutaneous coronary intervention, and age under 15 years. In total, 99 patients who met these criteria constituted the study population; 44 men and 55 women with a mean age of 62 years (range; 22 to 91 years) were recruited. ECG-gated cardiac imaging was performed using a 64-slice CT scanner, i.e., Aquilion 64 (Toshiba Medical Systems, Otawara, Japan) and Optima CT660 (GE Healthcare, Milwaukee, WI, USA). The CT parameters were as follows: collimation 64.0 × 0.5 mm, gantry rotation time 400 msec, and temporal resolution 200 msec for Aquilion 64; collimation 64.0 × 0.625 mm, gantry rotation time 350 msec, and temporal resolution 175 msec for Optima CT660.

One hour prior to the CT exam, beta-adrenergic receptor blocker (Indenol; 40 mg propranolol hydrochloride, Dong Kwang Pharm, Seoul, Korea) was administered orally when the patient’s heart rate was over 70 beats per minute. Immediately before starting the CT scan, nitroglycerin spray (two puffs) was administered intraorally. The protocols of cardiac CT exam were set as: slice thickness 0.5 or 0.65 mm; pitch, 1.4–1.7; no reconstruction interval; tube voltage, 100–120 kVp; and tube current-time product, 300 mAs. The iodine concentration of the contrast media was 400 or 370 mg/mL. The total volume of contrast media was calculated as (scan time) × (injection rate) × 1.2 mL. The upper limit of the total contrast volume (mL) was set as double values of the patient’s body weight (kg). The contrast injection was done through a superficial vein in right upper arm at the rate of 3–4 mL/min. The bi-phase contrast enhancement was performed by adding 20 mL normal saline infusion subsequently to the contrast bolus at the same infusion rate. The scan ignition timing was selected by tracking the contrast bolus arrival at the aortic root level. The scan was performed along the crano-caudal direction. Due to the inherent limitation of the machines, automatic dose modulation such as ECG-padding could not be applied. During the image reconstruction in the console of one CT machine (Optima CT660), an iterative reconstruction algorithm could be applied. The products of the dose length product were recorded by the CT system, and the effective doses were calculated using a conversion coefficient for the chest \[ k = 0.014 \text{ mSv/ (mGy cm)} \] (15).

From the raw data of cardiac imaging with retrospective ECG gating, 10 phase image sets were reconstructed with even time intervals during one cardiac cycle. The reconstructed data sets were transferred to an independent post-processing workstation (Aquarius iNtuition Edition Ver. 4.4.11, TeraRecon Inc., Foster City, CA, USA) for the quantitative evaluation of the cardiac function. During each phase, semi-automatic segmentation of LV endocardial and epicardial borders (papillary muscles were excluded) was performed limited between the mitral valvular annulus and cardiac apex. An LV time-volume curve was acquired from 10 phase image sets (Fig. 1). Based on the time-volume curve, LV systolic functional parameters such as left ventricular end diastolic volume (LVEDV, mL), end systolic volume (LVESV, mL), stroke volume [SV (mL) = LVEDV − LVESV], EF [%] = SV × 100/LVEDV, and cardiac output [CO (L/min) = heart rate × SV]. The LV myocardial mass [LVMM (g) = (epicardial volume − endocardial volume) × 1.04 g/mL] was calculated on end diastolic phase. Based on the LV time-volume curve, the LV volume differences between neighboring image sets were mea-
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sured. Inter-phase time interval was calculated from simultaneously recorded heart rates. Subsequently, the transmitral unit flow (mL/s) was measured as the inter-phase LV volume difference divided by the time interval (Fig. 1). The mitral valvular orifice areas (cm²) were manually measured at distal end level of valvular leaflets on neighboring phase images (Fig. 2A). The mean value of the two neighboring mitral valvular orifice areas was used for flow velocity calculation. Finally, transmitral valvular velocity (cm/s) was acquired as a unit flow volume divided by mitral valvular orifice area at the same phase [transmitral flow (mL/s) / mitral valve area (cm²)]. The calculated transmitral valvular velocity was defined as ‘estimated transmitral valvular velocity’, and its time-velocity curve was acquired (Fig. 2A). The ratio between estimated transmitral valvular velocity at early diastolic (E) and late diastolic (A) phases was calculated as the ‘E/A ratio’. To evaluate early-diastolic mitral septal annular velocity (E’, cm/s), the traveling distance of mitral septal annulus was calculated for 10 phases with the changes in longitudinal LV length (mm, the distance between the annular attachment site of septal mitral valve leaflet and cardiac apex) between the consecutive phases (Fig. 2B). For each phase, the mitral septal annular velocity was computed using traveling distance of the mitral septal annulus and heart rate. Finally, the mitral septal annular velocity at early diastole was represented as E’, and the ‘E/E’ ratio’ was acquired by dividing the early diastolic transmitral valvular velocity (E) by the mitral septal annular velocity (E’). For the evaluation of inter-observer agreement, two radiologists (J.M.L with 27-years’ experience in cardiac imaging and J.H.H with 4-years experience in cardiac imaging) independently measured each parameters of randomly selected 10 cases of CT image sets.

Fig. 1. The systolic functional analysis of the LV with CCTA. From CCTA with retrospective ECG gating, the LV volume is plotted along 10 phases during one cardiac cycle. Based on the LV time-volume curve (upper graph), LV volume differences between neighboring image sets were measured. Inter-phase time interval was calculated from simultaneously recorded heart rate. Subsequently, transmitral unit flow (mL/s, lower graph) was measured as inter-phase LV volume difference divided by time interval. A = peak trans-mitral velocity in late diastole, CCTA = coronary computed tomographic angiography, E = peak transmitral velocity in early diastole, ECG = electrocardiography, EDV = end diastolic volume, ESV = end systolic volume, LV = left ventricle.
2DE was performed by a cardiac sonographer using commercial echocardiographic machine. The LV systolic functional and volumetric parameters were measured by the modified Simpson's method, and the diastolic functional parameters were measured with pulsed-wave Doppler imaging and color-coded tissue Doppler imaging as recommended by the American Society of Echocardiography (16).

The correlation and limits of agreement for the LVEDV, LVESV, LVEF, SV, CO, and LVMM between CCTA and 2DE were determined using Pearson’s correlation linear regression and Bland-Altman analysis. Spearman’s Rho (correlation coefficient) of 0.10–0.30 was interpreted as a weak correlation, 0.30–0.50 as a moderate correlation, and greater than 0.50 as a strong correlation. The 95% limits of agreement were defined as the range of values ±2 standard deviations from the mean value of the differences. A paired t-test was applied to compare means.
of the parameters between CCTA and 2DE. The inter-observer agreement was assessed using intraclass correlation coefficient (ICC). ICC values of 0.0–0.20 were indicative of poor agreement; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good agreement; and 0.81 or more, very good agreement. p-values less than 0.05 were considered significant. The SPSS software package (Version 20.0, IBM Corp., Armonk, NY, USA) was used for all the statistical analyses.

**RESULTS**

Based on the CCTA results and the medical records of the 99 participants, 40 patients showed a suspected coronary arterial disease on CCTA, and 13 patients showed significant stenosis (> 50% diameter stenosis by visual estimate) on conventional coronary angiography. Twenty-three patients showed valvular disease (aortic regurgitation, n = 11; mitral regurgitation, n = 15; aortic stenosis, n = 1; mitral stenosis, n = 1) and four patients had cardiomyopathy (stress-induced cardiomyopathy, n = 1; LV noncompaction, n = 1; hypertrophic cardiomyopathy, n = 1; and dilated cardiomyopathy, n = 1). Other findings were as follows: coronary anomaly (n = 3), pulmonary arterial thromboembolism (n = 2), and aortic dissection (n = 1).

**Table 1. Comparison of the Functional Parameters of the LV Between CCTA and 2DE**

| LV Functional Parameters | CCTA (n = 99) | 2DE (n = 99) | Pearson’s Correlation Coefficient | Bland-Altman Analysis |
|--------------------------|--------------|-------------|----------------------------------|------------------------|
| LVEDV (mL)               | 100 ± 25     | 104 ± 28    | 0.732                            | < 0.001                |
| LVEF (%)                 | 67 ± 10      | 57 ± 14     | 0.416                            | < 0.001                |
| LVESV (mL)               | 34 ± 16      | 44 ± 20     | 0.821                            | < 0.001                |
| SV (mL)                  | 67 ± 18      | 58 ± 19     | 0.394                            | < 0.001                |
| CO (L/min)               | 4.5 ± 1.3    | 3.9 ± 1.3   | 0.328                            | < 0.001                |
| LVMM (g)                 | 137 ± 45     | 186 ± 80    | 0.764                            | < 0.001                |
| E/A                      | 1.0 ± 0.5    | 1.0 ± 0.5   | 0.807                            | < 0.005                |
| E/E’                     | 10.7 ± 5.8   | 12.3 ± 6.5  | 0.751                            | < 0.005                |

Data are expressed as the mean ± standard deviation.

**Table 2. Inter-Observer Agreement of LV Functional Parameters of Coronary CT Angiography Between Two Radiologists**

| LV Functional Parameters | ICC      | 95% CI          | p-Value |
|--------------------------|----------|-----------------|---------|
| LVEDV (mL)               | 0.982    | 0.929–0.995     | < 0.001 |
| LVEF (%)                 | 0.973    | 0.896–0.993     | < 0.001 |
| LVESV (mL)               | 0.979    | 0.804–0.946     | < 0.001 |
| SV (mL)                  | 0.923    | 0.722–0.980     | < 0.001 |
| LVMM (g)                 | 0.996    | 0.983–0.999     | < 0.001 |
| E/A                      | 0.976    | 0.908–0.994     | < 0.001 |
| E/E’                     | 0.959    | 0.843–0.990     | < 0.001 |

CI = confidence interval, E/A = early (E) to late (A) mitral inflow peak velocities ratio, E/E’ = mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E’) ratio, ICC = intraclass correlation coefficient, LV = left ventricle, LVEDV = LV end-diastolic volume, LVEF = LV ejection fraction, LVESV = LV end-systolic volume, LVMM = LV myocardial mass, SV = stroke volume.
CCTA heart rates varied from 53 to 97 beats per minute (mean 65 ± 28 beats per minute), and mean heart rate at 2DE was 67 ± 34 beats per minute. No significant difference in the heart rate was noted between CCTA and 2DE (p = 0.255). The overall mean effective dose of CCTA for each participant was 10.64 mSv (range: 3.91–13.70 mSv). Global LV function evaluation was possible in all 99 patients using CCTA. The mean end-diastolic volume was 100.5 ± 24.9 mL, and the end-systolic volume was 34.4 ± 15.5 mL. The mean left ventricular EF was 66.6 ± 10.4% (range: 30.2–91.5%). The stroke volume and CO data are shown in Table 1. The mean LVMM was 136.6 ± 45.3 g. Mean E/A ratio and E/E' ratios were 1.20 ± 0.49 and 10.71 ± 5.83, respectively. The 2DE demonstrated end-diastolic and end-systolic volumes of 104.1 ±
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27.6 mL and 44.1 ± 20.2 mL, respectively. Mean LVEF was 57.1 ± 13.6% (range; 15.2–91.6%). Mean E/A and E/E' ratios were 1.02 ± 0.49 and 12.32 ± 6.51, respectively. The LV muscle mass showed a mean value of 186.1 ± 80.4 g.

The LVEDV, LVESV, SV, CO, and LVMM measured by ECG-gated CCTA and 2DE showed moderate to strong correlations \( (r = 0.732, 0.821, 0.416, 0.394, 0.328, \) and 0.764, respectively; \( p < 0.001 \)). Additionally, between CCTA and 2DE, the E/A and E/E' ratios showed strong correlation \( (r = 0.807 \) and 0.751, respectively; \( p < 0.005 \)). The mean differences in the LV volumes and functional parameters between CCTA and 2DE were -1.0 ± 28.2 mL/m² for LVEDV, -9.7 ± 18.4 mL/m² for LVESV, 0.5 ± 1.5 mL/m² for SV, 8.9 ± 14.6% for LVEF, 0.18 ± 0.3 for E/A ratio, and -1.6 ± 4.4 for E/E' ratio. These results indicated good agreement between the two methods (Table 1). The inter-observer agreement for the measurement of LV
volumes and functional parameters on CCTA were very good (ICC = 0.923–0.996, \( p < 0.001 \)) except for EF which showed good (ICC = 0.797, \( p = 0.002 \)) (Table 2). Excluding LVEDV (\( p = 0.862 \)), paired t-test revealed significant differences in all parameters between CCTA and 2DE. Concordance analysis (Bland-Altman plot) and linear regression equations for the left ventricular function parameters are shown in Figs. 3, 4.

**DISCUSSION**

In the present study, the compatibility of both the systolic and diastolic LV functions acquired from routine CCTA with 2DE was evaluated. Moderate to strong correlations among LVEDV, LVESV, LVEF, SV, CO, and LVMM were observed between CCTA and 2DE. This finding is in line with previous studies that observed good correlation between LV volumetric and functional analysis using 2DE and CCTA (6, 7, 17–21). Despite the significant correlation between CCTA and 2DE, several reports presented an overestimation of the volumetric data by CCTA (20, 22, 23). In this study, overestimation of LVEF was noted on CCTA, a finding that is consistent with those of previous studies. These inter-modality discrepancies may be due to differing volumetric methods. In contrast to 2DE using a modified Simpson’s method based on geometric assumption, CCTA can delineate detailed endocardial borders in consecutive 2D images and allows for measurement of the 3D volume using the classic Simpson’s method. Another cause of the inter-modality discrepancy may be the use of beta-blocker pre-medication during CCTA. Finally, the temporal resolution of CCTA may be limited in demonstrating precise end-systolic and end-diastolic volume, which may be more likely using 2DE (22). However, the CCTA, rather than 2DE, demonstrated closer results to CMR data, which is acknowledged as the gold standard method for evaluation of ventricular function (23).

Prior studies have demonstrated the importance of diastolic function in patients with coronary artery disease (24, 25). According to a recent meta-analysis studying 3396 patients with myocardial infarction, a higher mortality rate was noted in patients with restrictive LV filling pattern than in patients without diastolic dysfunction (28.7% vs. 11.3%, respectively; \( p < 0.01 \)) (25). As an alternative and non-invasive method for diastolic LV filling function, transmitral velocimetry has been performed using 2DE (26, 27). The present study demonstrated that CCTA is comparable to 2DE for assessing LV diastolic function with strong correlation. In terms of the transmitral valvular velocity measurement, 2DE allocates a fixed Doppler signal sampling volume in a post-valvular jet area, where the maximum velocity is depicted. However, this fixed sampling volume cannot negotiate with a longitudinally moving mitral valvular orifice, which may deteriorate reliability of functional parameters (11, 12, 28). CCTA in this study traced the mitral valvular orifice throughout cardiac phases during diastole and measured orifice areas for more reliable velocimetry. This technical detail may lead to the acceptable CCTA results of diastolic function evaluation in spite of its limited temporal resolution. Moreover, the correlation coefficients of both E/A and E/E’ were stronger than that of systolic functional parameters (e.g., EF, SV, and CO). Therefore, the inter-modality agreements of the diastolic parameters were better than that of the systolic parameters, which indicates a more reliable clinical application of this technique.

According to previous studies, gated myocardial perfusion single-photon emission com-
Computed tomography (SPECT) correlated well with echocardiography and CMR in evaluating the systolic function with LV volumes and EF (29, 30), although its ability to determine the diastolic function of LV is not well considered yet. Bennett et al. (31) attempted to correlate 16-phase gated SPECT time-volume curves with echo Doppler early/late diastolic flow ratios for diastolic dysfunction, but further studies may be required to validate their clinical applications.

There are some limitations of this study. Since CCTA acquired 10 phase images per cardiac cycle, the data for the calculated velocity were per 10% of the R-R interval. Due to the inferior temporal resolution of CCTA to 2DE, the peak velocity, E/A, and E/E′ may have been underestimated. This limitation may be overcome by increasing the sampling rate or reducing the heart rate, if medically possible (10, 14, 29). Second, we applied simple exclusion criteria for selecting the study population, which consisted of patients who underwent cardiac surgery or coronary intervention. Therefore, the study population was inhomogeneous and patients with various kinds of cardiomyopathy (e.g., hypertrophic cardiomyopathy or dilated cardiomyopathy) or with incidentally founded myocardial infarction were included. Therefore, the ranges of some functional parameters were wide (e.g., EF range; 30.2–91.5%), which may produce a measurement error or influence the statistical analysis.

In conclusion, the systolic and diastolic LV functional parameters acquired from routine CCTA in the present study demonstrated moderate to strong correlations with echocardiographic results, although the absolute values differed. When CCTA is performed with retrospective ECG gating, additional information about the LV function can be acquired as reliably as with echocardiography.

Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

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일상적으로 촬영된 후향적 심전도 동기화 관상동맥전산화단층 영상을 이용한 좌심실 기능의 포괄적 평가

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목적 일상적으로 촬영된 관상동맥전산화단층영상을 이용한 좌심실 기능의 포괄적 평가를 이차원적 심초음파 영상과 비교하여 재현성을 알아보고자 하였다.

대상과 방법 이 연구는 관상동맥전산화단층촬영과 이차원적 심초음파를 모두 시행한 99명의 환자를 대상으로 하였다. 관상동맥전산화단층촬영 영상을 10단계로 재구성하여 좌심실 수축기능과 관련된 인자를계산하였다. 승모판 개방 면적과 시간 영역을 이용하여 좌심실의 시간-용적곡선을 구하고 승모판을 통한 시간-속도곡선을 얻어서 E/A ratio를 계산하였다. 또한 승모판론의 중축 속도를 심방영상에서 측정하여 E/E' ratio를 계산하였다. 얻어낸 모든 기능적 수치들을 이차원 심초음파의 결과와 비교하였다.

결과 좌심실 확장기말 용적, 좌심실 수축기말 용적, 좌심실 박출률, 1회 박출량, 심박출량, 좌심실 심근질량은 중상의 상관성을 보였으며($r = 0.732, 0.821, 0.416, 0.394, 0.328, 0.764; p < 0.05$), E/A 및 E/E' ratio는 강한 상관성을 보였다($r = 0.807, 0.751; p < 0.05$).

결론 후향적 심전도 동기화 방법으로 촬영된 관상동맥전산화단층 영상을 이용하여 얻은 좌심실의 포괄적 기능 수치는 심초음파와 비교하여 신뢰할만한 결과를 얻을 수 있다.

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