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Feasibility of the Threshold-Based Quantification of Myocardial Fibrosis on Cardiac CT as a Prognostic Marker in Nonischemic Dilated Cardiomyopathy

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Objective: This study investigated the feasibility and prognostic relevance of threshold-based quantification of myocardial delayed enhancement (MDE) on CT in patients with nonischemic dilated cardiomyopathy (NIDCM).

Materials and Methods: Forty-three patients with NIDCM (59.3 ± 17.1 years; 21 male) were included in the study and underwent cardiac CT and MRI. MDE was quantified manually and with a threshold-based quantification method using cutoffs of 2, 3, and 4 standard deviations (SDs) on three sets of CT images (100 kVp, 120 kVp, and 70 keV). Interobserver agreement in MDE quantification was assessed using the intraclass correlation coefficient (ICC). Agreement between CT and MRI was evaluated using the Bland-Altman method and the concordance correlation coefficient (CCC). Patients were followed up for the subsequent occurrence of the primary composite outcome, including cardiac death, heart transplantation, heart failure hospitalization, or appropriate use of an implantable cardioverter-defibrillator. The Kaplan–Meier method was used to estimate event-free survival according to MDE levels.

Results: Late gadolinium enhancement (LGE) was observed in 29 patients (67%, 29/43), and the mean LGE found with the 5-SD threshold was 4.1% ± 3.6%. The 4-SD threshold on 70-keV CT showed excellent interobserver agreement (ICC = 0.810) and the highest concordance with MRI (CCC = 0.803). This method also yielded the smallest bias with the narrowest range of 95% limits of agreement compared to MRI (bias, -0.119%; 95% limits of agreement, -4.216% to 3.978%). During a median follow-up of 1625 days (interquartile range, 712–1430 days), 10 patients (23%, 10/43) experienced the primary composite outcome. Event-free survival significantly differed between risk subgroups divided by the optimal MDE cutoff of 4.3% (log-rank $P = 0.005$).

Conclusion: The 4-SD threshold on 70-keV monochromatic CT yielded results comparable to those of MRI for quantifying MDE as a marker of myocardial fibrosis, which showed prognostic value in patients with NIDCM.

Keywords: Myocardial fibrosis; Myocardial delayed enhancement; Semi-automated quantification; Nonischemic dilated cardiomyopathy

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INTRODUCTION

Myocardial fibrosis is a common consequence of myocardial injury in most cardiomyopathies. It contributes to cardiac remodeling and functional impairment and occurs with distribution patterns distinct for each disease [1,2]. Late gadolinium enhancement (LGE) imaging supported by histopathological validation is a crucial technique for detecting and quantifying myocardial fibrosis [3-5]. LGE imaging provides prognostic information on nonischemic dilated cardiomyopathy (NIDCM), with quantitative data predicting adverse cardiovascular outcomes [1,6]. Semi-automated quantification methods, such as threshold-based quantification and the full-width at half-maximum technique, have proven accurate and reproducible in quantifying LGE in various cardiomyopathies [7].

With robust evidence supporting the prognostic value of LGE on cardiac MRI, efforts have been made to apply this knowledge to CT, aiming to capitalize on advantages of CT such as accessibility, shorter examination times, better suitability for patients with metallic devices, and the opportunity to perform concurrent evaluations of coronary artery disease. Theoretically, myocardial delayed enhancement (MDE) can be assessed using cardiac CT, similar to LGE, because iodinated agents and gadolinium chelates exhibit similar contrast kinetics [8]. Previous studies have demonstrated a good agreement between MRI and CT in determining the pattern and extent of myocardial fibrosis in cardiomyopathies [9-13]. Furthermore, several studies utilizing virtual monochromatic images from dual-energy CT have shown improved MDE assessments, higher contrast-to-noise ratios, and reduced beam-hardening artifacts [11-15]. However, only a few studies have applied semi-automated quantification methods for MDE assessment on cardiac CT. Therefore, our study aimed to investigate the feasibility and prognostic value of threshold-based quantification, a representative semi-automated method, of MDE on CT in patients with NIDCM.

MATERIALS AND METHODS

Study Population

This was a retrospective analysis of data acquired from two prospective studies. The Institutional Review Board approved these studies (IRB Nos. 4-2010-0210 and 1-2014-0047), and all study participants provided informed consent when the previous studies were initiated. The board also approved this retrospective investigation and waived the requirement for further consent (IRB No. 1-2022-0060).

This study included 43 patients with NIDCM (59.3 ± 17.1 years; 21 male). NIDCM was diagnosed as unexplained left ventricular (LV) enlargement (diameter > 55 mm in end-diastole) with decreased LV systolic function (ejection fraction < 40%), absence of significant obstructive coronary artery disease, and no prior history of myocardial infarction. Thirteen patients from June 2012 to March 2014 were included in previous studies on the myocardial extracellular volume fraction using dual-energy CT [16] and the utility of monochromatic imaging for myocardial fibrosis [11]. Another 30 patients from January 2014 to June 2015 were included in prior studies on the role of cardiac CT in heart failure [17] and the synthetic extracellular volume fraction (Fig. 1) [18].

Cardiac CT and MRI

All cardiac CT scans were performed using a second-generation, dual-source CT scanner (SOMATOM Definition Flash; Siemens Healthcare, Forchheim, Germany). Dual-energy CT was performed 12 min after injection of the contrast material. A detailed scanning protocol is provided in the Supplementary Materials. From the raw data, 100, 140, and weighted average 120-kVp images (fused images with 60% from the 100 kVp and 40% from the 140 kVp) were automatically reconstructed at the mid-diastolic phase with a 0.75-mm section thickness, 0.5-mm increment interval, and medium-smooth convolution kernel (D30f). Additional 70-keV monochromatic images were created on a commercially available workstation (Syngo MMWP VE23A; Siemens Healthcare) using data from the 100- and 140-kVp images. Finally, three sets of CT images (100 kVp, 120 kVp, and 70 keV) were analyzed.

Cardiac MRI was performed with a 3T system (Magnetom Trio; Siemens Medical Solutions, Erlangen, Germany) and an eight-channel cardiac coil within 3 days (2.0 ± 0.8 days) of the cardiac CT. The scanning protocol and image analysis methods are detailed in the Supplementary Materials.

Cardiac CT Image Analysis

All images were transferred to an offline workstation (Aquarius iNtuition V4.4.13; TeraRecon, Durham, NC, USA) and reconstructed on the short-axis plane with an 8-mm section thickness and without intersection gaps. Two observers (D.J.I. and H.J.L., with 9 and 15 years of experience in cardiac imaging, respectively) independently reviewed the cardiac CT images in random order after

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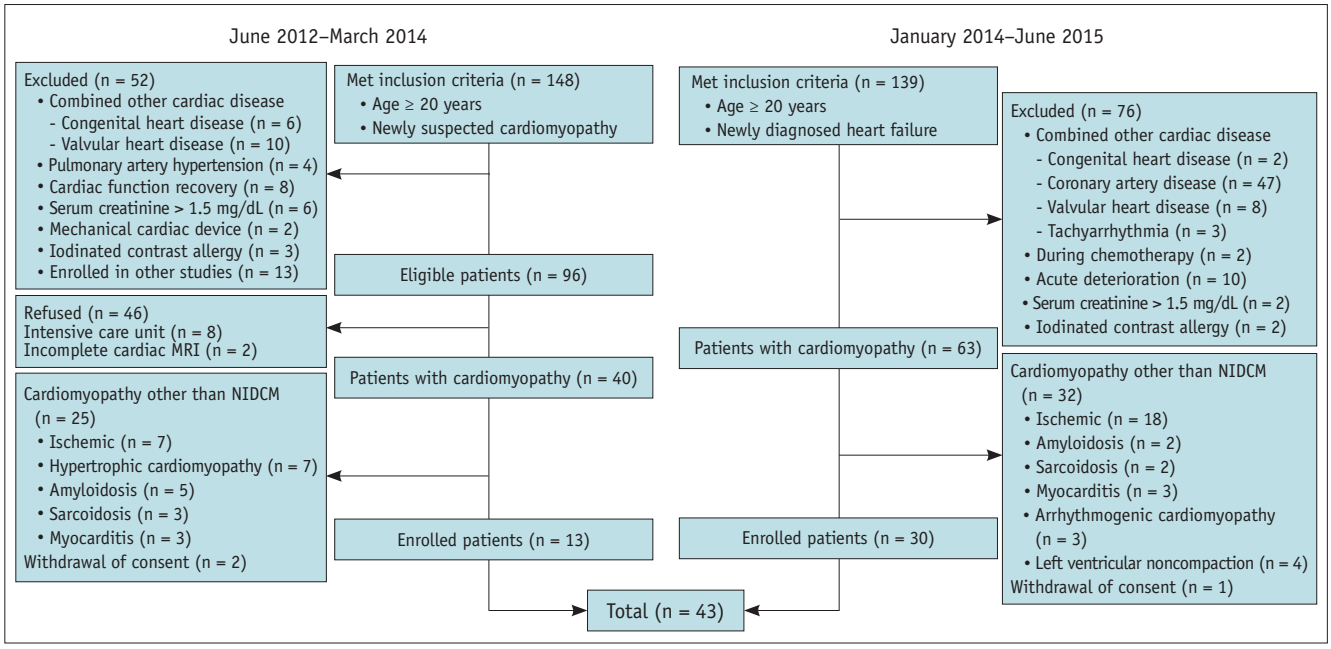

Fig. 1. Flowchart of the patient recruitment process from prior studies. NIDCM = nonischemic dilated cardiomyopathy

blinding the clinical information and cardiac MRI findings, with a 1-month interval between each CT set.

The MDE was defined as an area of apparent high attenuation within the myocardium on visual inspection at a narrow window width and level of approximately 200 Hounsfield unit (HU) and 100 HU, respectively. The MDE was expressed as a percentage of the total LV myocardial volume (MDE%). The total LV myocardial volume was calculated by subtracting the endocardial area from the epicardial area and multiplying that difference by the section thickness. The endo- and epicardial contours of the LV were manually drawn from each section, excluding the papillary muscles and trabeculae. For manual assessment, all hyperenhanced areas of the LV were manually traced and multiplied by the section thickness to calculate the MDE%. Threshold-based quantification of MDE involved the manual delineation of a region of interest, which was drawn on the remote myocardium (defined as a region with no MDE) to generate the mean and standard deviation (SD) used in the 2, 3, and 4-SD thresholds. The region of interest was drawn to avoid the endocardial and epicardial surfaces, and area boundaries determined its size. Subsequently, we used an area histogram based on the HU value at each pixel to quantify the MDE (Supplementary Fig. 1).

In cases of MDE, the contrast-to-noise ratio was calculated using the following formula: (HU on MDE - HU on the remote myocardium)/SD of HU in the blood pool. Working in consensus, the observers drew regions of interest in the center of the MDE, remote myocardium, and blood pool. Using a copy-and-paste function, the sizes and locations of these regions of interest were consistently maintained across each CT set.

Clinical Follow-Up and Cardiovascular Events

Patients were followed up from the date of their cardiac CT until December 31, 2019, through electronic medical record review. The primary composite outcomes included cardiac death, heart transplantation, hospitalization for heart failure, and appropriate implantable cardioverter-defibrillator (ICD) therapy. Cardiac death was defined as death attributable to underlying cardiomyopathy or death due to cardiac dysfunction. Heart failure hospitalization was defined as hospital admission due to signs and symptoms of heart failure and the need for diuretic treatment [19,20]. Appropriate ICD therapy was defined as anti-tachycardia pacing or shock for confirmed sustained fast ventricular tachycardia (R-R interval < 320 ms) or ventricular fibrillation.

Statistical Analysis

All statistical analyses were performed with statistical software (SAS, version 9.2; SAS Institute Inc., Cary, NC, USA). Categorical variables are expressed as frequencies or percentages, and continuous variables are expressed as mean values with SDs or median values with interquartile

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ranges, according to normality confirmed using the Shapiro–Wilk test. For the quantitative analysis of MDE, interobserver agreement was assessed using the intraclass correlation coefficient (ICC). The ICC was interpreted as follows: 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1.00, excellent agreement. Agreements for myocardial fibrosis quantification between MRI and each CT set were evaluated using the Bland–Altman method and the concordance correlation coefficient (CCC). The bias and 95% limits of agreement for the Bland–Altman method were calculated using the least square means of the MDE values measured by each observer, thereby the multi-observer factor was taken into consideration. The CCC was calculated according to previously reported methods, which also considered data collected by multiple observers [21]. CCC was interpreted using the same grading system as that used for ICC. After obtaining the average MDE% measurements on CT from the two observers for each patient, the optimal cutoff value for MDE% that maximized the Youden index was determined using a receiver operating characteristic curve to assess the presence of an event. Kaplan–Meier analysis was used to estimate event-free survival according to the MDE quantification level, and log-rank tests were used to compare the survival curves between the two groups. For all data, $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline Characteristics

Table 1 summarizes the baseline clinical characteristics. Most patients had symptomatic heart failure, with a mean LV end-diastolic diameter of 64.7 ± 8.1 mm and a mean LV ejection fraction of 29.3% ± 9.1% on echocardiography. The volumetric CT dose index for the dual-energy CT was 21.7 ± 2.8 mGy, and the dose-length product was 346.6 ± 45.4 mGy x cm.

Quantification of MDE

On cardiac MRI, the mean LV end-diastolic volume, end-diastolic volume index, and ejection fraction were 233.8 ± 105.5 mL, 134.8 ± 60.1 mL/m^2, and 29.9% ± 11.8%, respectively. The mean right ventricular end-diastolic volume, end-diastolic volume index and ejection fraction were 170.0 ± 91.2 mL, 88.1 ± 31.4 mL/m^2, and 39.0% ± 13.0%, respectively. The 29 patients (67%, 29/43) had LGE, and the mean LGE% quantified by the 5-SD threshold was 4.1% ± 3.6%.

Table 1. Baseline characteristics

Characteristics	All patients (n = 43)
Age, yr	59.3 ± 17.1 (range 22–86)
Sex, male:female	21:22
BMI, kg/m^2	24.1 ± 4.9
NYHA class	
Class I	2 (5)
Class II	28 (65)
Class III	11 (26)
Class IV	2 (5)
Laboratory findings	
eGFR, mL/min/1.73 m^2	89.2 ± 17.8
Creatinine, mg/dL	0.82 ± 0.20
NT-proBNP, pg/mL	5118.0 ± 6930.2
Clinical history	
Hypertension	20 (46)
Diabetes mellitus	11 (26)
Dyslipidemia	3 (7)
Ever-smoker	10 (23)
Echocardiography findings	
LVEDD, mm	64.7 ± 8.1
LVEF, %	29.3 ± 9.1
Fractional shortening, %	15.9 ± 7.7

Data are mean ± standard deviation for continuous variables and the number with percentage in parentheses for categorical variables. BMI = body mass index, NYHA = New York Heart Association, eGFR = estimated glomerular filtration rate, NT-proBNP = N-terminal pro b-type natriuretic peptide, LVEDD = left ventricular end-diastolic diameter, LVEF = left ventricular ejection fraction

The observers concluded that the quality of the CT images was acceptable for MDE quantification in all patients. On cardiac CT, the mean attenuations of MDE were 121.8 ± 9.7 HU, 107.3 ± 9.5 HU, and 123.4 ± 9.1 HU, and the mean attenuation of the remote myocardium were 82.7 ± 4.7 HU, 79.6 ± 3.9 HU, and 83.5 ± 4.3 HU at 100 kVp, 120 kVp, and 70 keV, respectively. The mean SDs of the remote myocardium were 10.2 ± 3.4 HU, 7.7 ± 1.9 HU, and 8.5 ± 2.6 HU at 100 kVp, 120 kVp, and 70 keV, respectively. The contrast-to-noise ratio of the 100 kVp, 120 kVp, and 70 keV were 3.63 ± 0.59, 3.81 ± 0.64, and 4.10 ± 0.95, respectively.

The mean MDE% assessed by each observer for each CT set is presented in Table 2. Examples of LGE and MDE quantification are shown in Figure 2. All CT sets showed excellent interobserver agreement for manual quantification (ICC = 0.812, 0.804, and 0.833 for 100 kVp, 120 kVp, and 70 keV, respectively). Among the threshold-based quantification methods, only the 4-SD threshold on 70-keV CT showed excellent interobserver agreement (ICC = 0.810), while the other thresholds showed fair or good degrees of

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Table 2. Interobserver agreements for MDE% on cardiac CT

CT	Methods	MDE%		ICC (95% CI)
		Observer 1	Observer 2	
100 kVp	Manual	4.57 ± 4.65	4.83 ± 4.84	0.812 (0.678, 0.894)
	2 SD	13.09 ± 7.34	12.07 ± 8.45	0.413 (0.132, 0.632)
	3 SD	6.82 ± 3.36	7.50 ± 5.10	0.568 (0.326, 0.741)
	4 SD	2.77 ± 2.15	3.76 ± 2.64	0.582 (0.344, 0.749)
120 kVp	Manual	4.82 ± 5.55	4.86 ± 4.82	0.804 (0.666, 0.889)
	2 SD	14.27 ± 7.43	14.13 ± 6.88	0.490 (0.226, 0.687)
	3 SD	7.99 ± 5.28	9.06 ± 5.02	0.635 (0.417, 0.785)
	4 SD	3.49 ± 3.99	5.21 ± 4.07	0.694 (0.500, 0.822)
70 keV	Manual	4.43 ± 4.78	4.41 ± 3.82	0.833 (0.712, 0.906)
	2 SD	14.99 ± 7.19	15.46 ± 6.14	0.620 (0.395, 0.774)
	3 SD	9.70 ± 4.75	10.11 ± 4.25	0.659 (0.450, 0.800)
	4 SD	4.07 ± 2.68	4.37 ± 2.70	0.810 (0.675, 0.892)

Data are mean ± standard deviation.
MDE = myocardial delayed enhancement, ICC = intraclass correlation coefficient, CI = confidence interval, SD = standard deviation

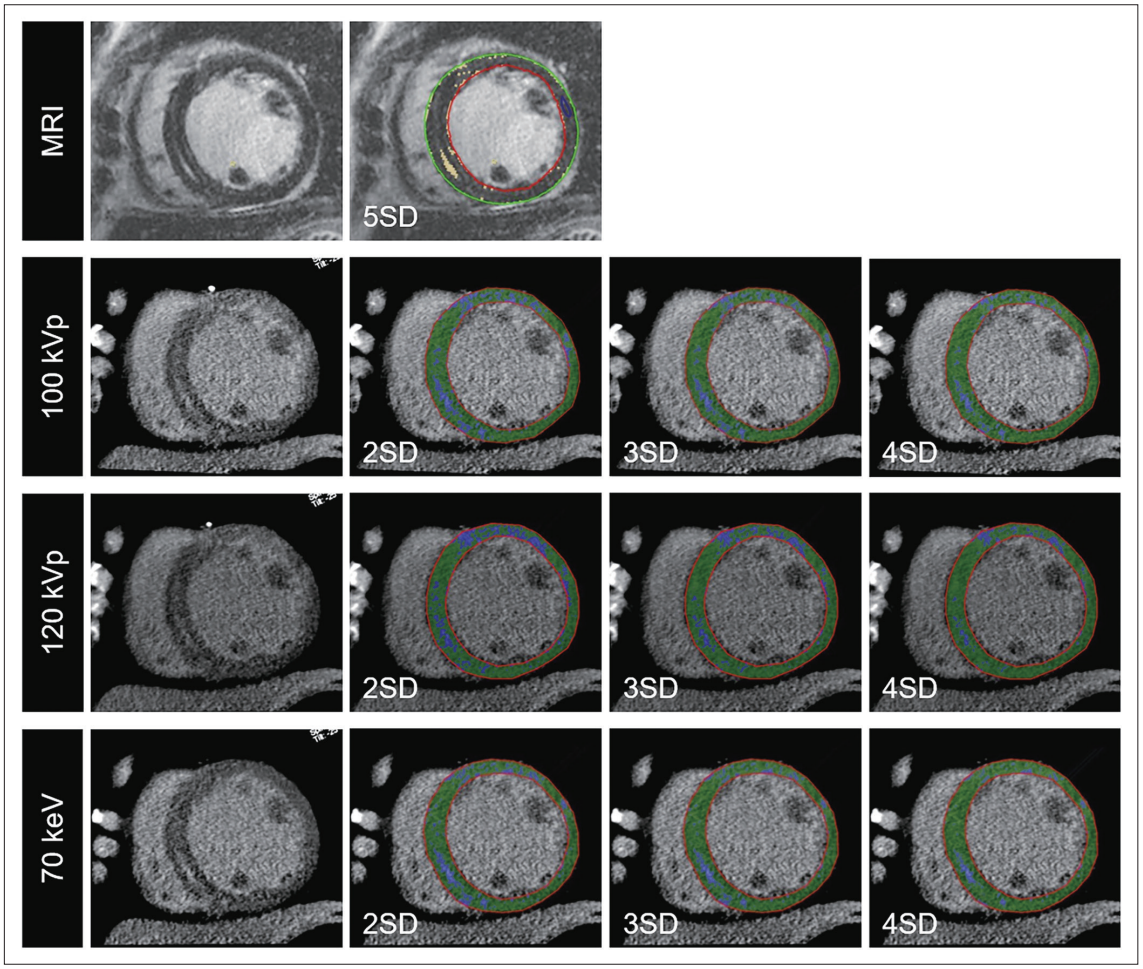

Fig. 2. An example case of LGE and MDE quantification in a 61-year-old female with nonischemic dilated cardiomyopathy. The first row presents mid-wall LGE (yellow) in the inferior septal wall of the left ventricle, using the 5-SD threshold. In the second, third, and fourth rows, a raw image and threshold-based quantification of MDE at 100 kVp, 120 kVp, and 70 keV, respectively, are displayed. In each CT image, the blue area represents MDE, and the green area represents the non-MDE myocardium. LGE = late gadolinium enhancement, MDE = myocardial delayed enhancement, SD = standard deviation

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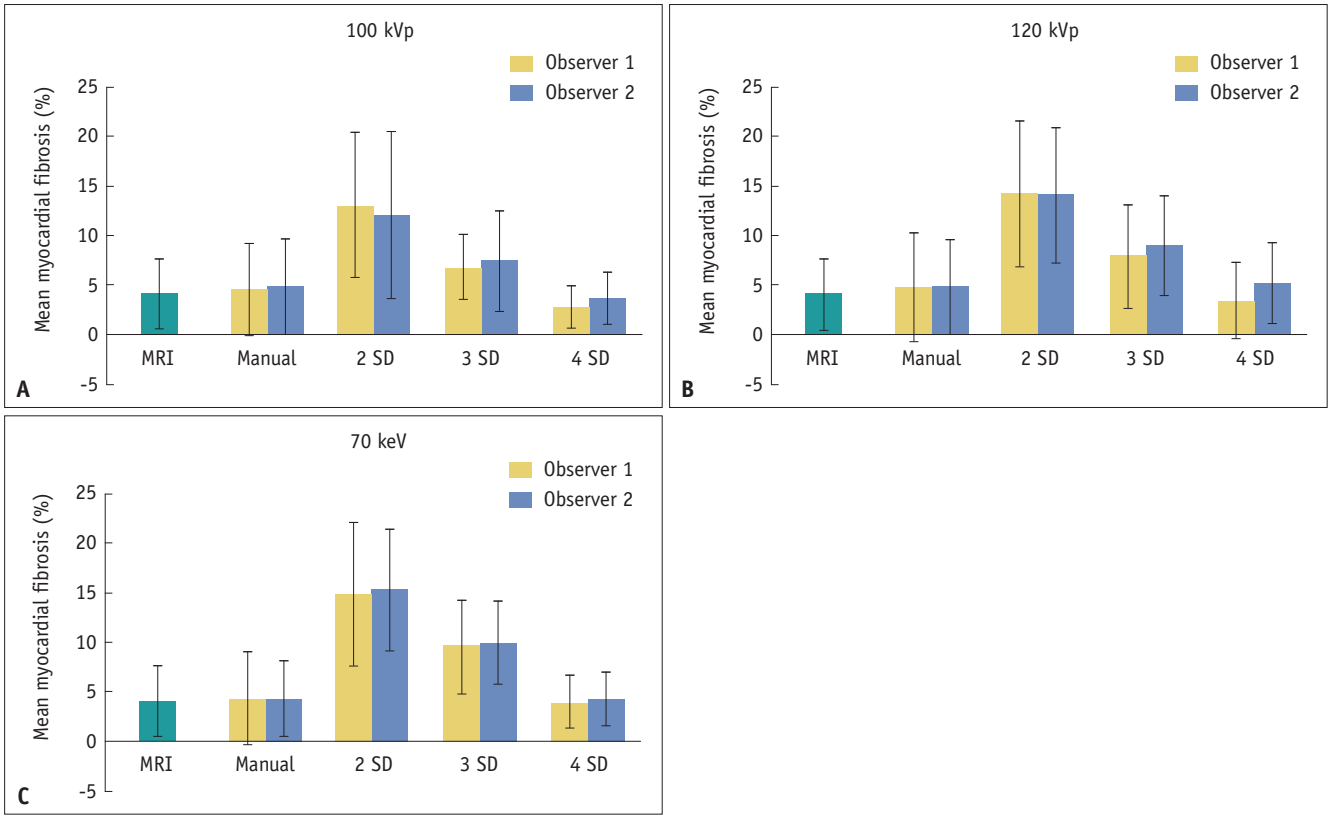

Fig. 3. Mean myocardial delayed enhancement (%) measured by each quantification method, with the first bar representing late gadolinium enhancement as the reference, at **(A)** 100 kVp, **(B)** 120 kVp, and **(C)** 70 keV. Error bars represent SDs. SD = standard deviation

interobserver agreement. In all CT sets, the results of the 2-SD threshold showed the largest values, whereas the 4-SD threshold yielded the smallest values, which were closest to the results of manual quantification (Fig. 3).

The agreements between the LGE% on MRI and the MDE% measured in each CT set are shown in Table 3. The highest degree of agreement was obtained with the 70-keV CT using the 4-SD threshold (CCC = 0.803), followed by manual quantification, which showed good agreement (CCC = 0.781). Manual quantification showed good agreement for both 100- and 120-kVp CTs (CCC = 0.718 and 0.705, respectively), whereas threshold-based quantification yielded modest agreement. From the Bland–Altman analysis, manual quantification of all CT sets showed a small bias with an acceptable range for 95% limits of agreement compared to MRI (-0.599% with -8.101% to 6.903%, -0.738% with -8.847% to 7.371%, and -0.319% with -6.994% to 6.356% for 100 kVp, 120 kVp, and 70 keV, respectively). Among the 2-, 3-, and 4-SD thresholds, the 4-SD threshold for conventional CTs demonstrated a small bias with an acceptable range for 95% limits of agreement (0.835% with -5.693% to 7.364% and -0.243% with -7.102% to 6.615% for 100 kVp and 120 kVp, respectively). The smallest bias with the narrowest range of 95% limits of agreement was achieved with the 4-SD threshold on 70-keV CT (-0.119% with -4.216% to 3.978%). Figure 4 illustrates representative plots from the Bland–Altman analysis.

Table 3. Agreements between LGE% and MDE%

CT	Methods	CCC (95% CI)	Bland-Altman analysis (%)*
100 kVp	Manual	0.718 (0.597, 0.806)	-0.599 (-8.101, 6.903)
	2 SD	0.410 (0.217, 0.571)	-8.474 (-21.807, 4.858)
	3 SD	0.439 (0.252, 0.595)	-3.057 (-11.276, 5.162)
	4 SD	0.583 (0.424, 0.707)	0.835 (-5.693, 7.364)
120 kVp	Manual	0.705 (0.580, 0.797)	-0.738 (-8.847, 7.371)
	2 SD	0.492 (0.313, 0.636)	-10.101 (-21.240, 1.038)
	3 SD	0.496 (0.319, 0.640)	-4.422 (-13.141, 4.297)
	4 SD	0.587 (0.429, 0.710)	-0.243 (-7.102, 6.615)
70 keV	Manual	0.781 (0.683, 0.852)	-0.319 (-6.994, 6.356)
	2 SD	0.488 (0.309, 0.634)	-11.128 (-21.714, -0.541)
	3 SD	0.567 (0.405, 0.695)	-5.801 (-12.248, 0.645)
	4 SD	0.803 (0.711, 0.867)	-0.119 (-4.216, 3.978)

*Bland-Altman bias with 95% limits of agreement in parentheses. LGE = late gadolinium enhancement, MDE = myocardial delayed enhancement, CCC = concordant correlation coefficient, CI = confidence interval, SD = standard deviation

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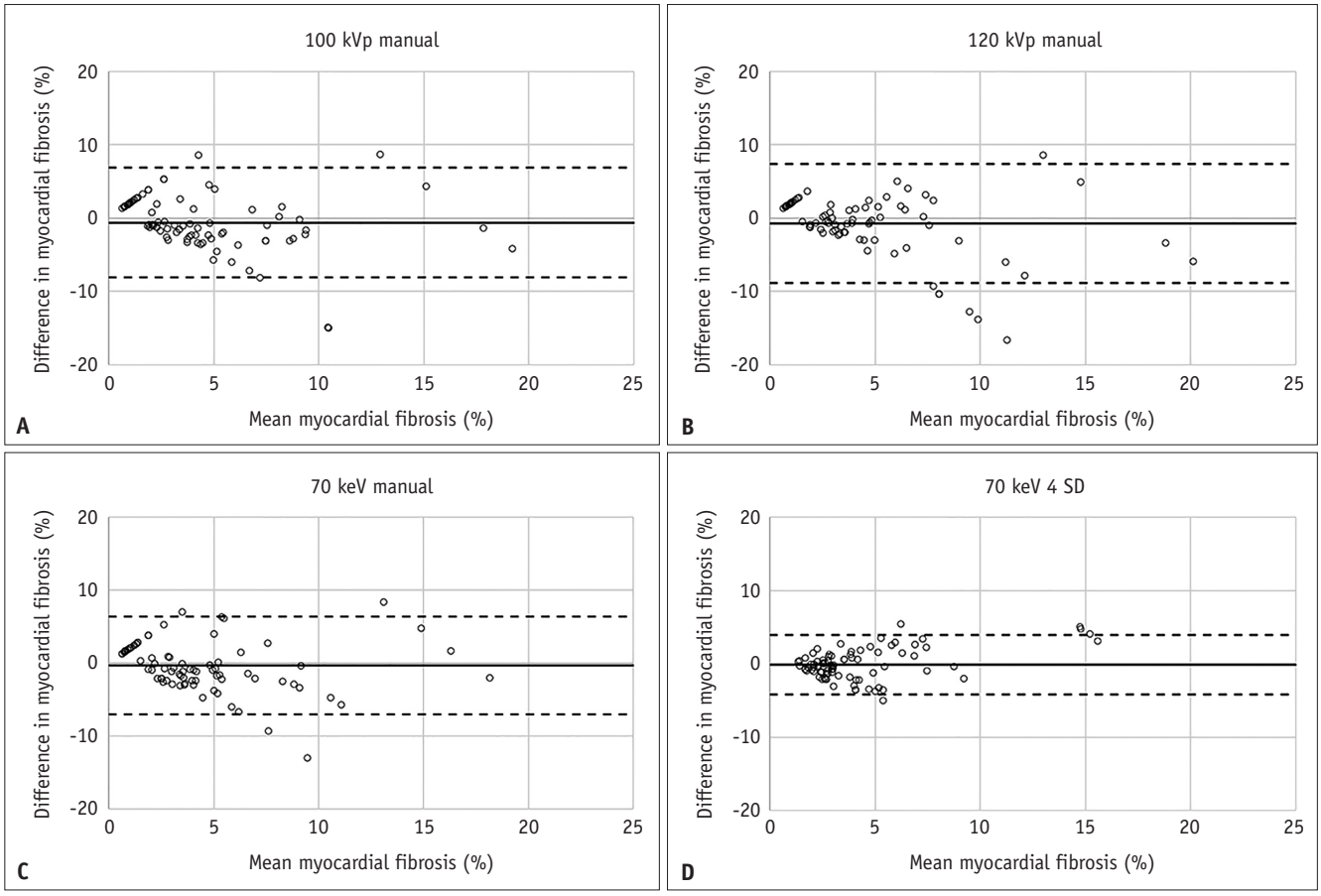

Fig. 4. Bland–Altman plots show agreement between MRI and CT for myocardial fibrosis quantification. **A-D:** The quantification methods with the least bias for each CT are **(A)** manual quantification at 100 kVp, **(B)** manual quantification at 120 kVp, **(C)** manual quantification at 70 keV, and **(D)** the 4-SD threshold at 70 keV. Late gadolinium enhancement on MRI was measured using the 5-SD threshold. On each plot, the solid line represents the mean difference (bias), and the dotted lines represent the 95% limits of agreement. Empty circles denote data points. SD = standard deviation

Prognostic Value of MDE as a Marker for Myocardial Fibrosis on Cardiac CT

During a median follow-up of 1625 days (interquartile range, 712–1430 days), 10 patients (23%, 10/43) experienced a primary composite outcome: two (5%, 2/43) cardiac deaths, three (7%, 3/43) heart transplantation, seven (16%, 7/43) heart failure hospitalizations, and five (11%, 5/43) ICD therapies. All seven patients hospitalized for heart failure experienced other events: two ICD therapies, two cardiac deaths, and three heart transplantations.

The 4-SD threshold on 70-keV CT was chosen for the Kaplan–Meier analysis owing to its highest interobserver agreement and results comparable to MRI. The optimal cutoff value of the MDE% from the 4-SD threshold on 70-keV CT for adverse events was 4.3%. When patients were divided into three groups according to 1) absence of MDE (n = 14), 2) MDE ≤ 4.3% (n = 14), and 3) MDE > 4.3% (n = 15), Kaplan–Meier analysis showed a significant difference between the risk subgroups (log-rank P = 0.005) (Fig. 5).

DISCUSSION

Our study's significant finding was that MDE quantified using the 4-SD threshold showed the highest concordance with LGE in patients with NIDCM and demonstrated excellent interobserver agreement on 70-keV monochromatic CT. In addition, quantification of the MDE showed prognostic value, as evidenced by the significant divergence in survival curves between risk subgroups based on the MDE quantified using the 4-SD threshold on 70-keV monochromatic CT.

NIDCM is defined as ventricular dilatation and systolic dysfunction without abnormal loading conditions or significant coronary artery disease [22]. The importance of assessing myocardial fibrosis in NIDCM through LGE

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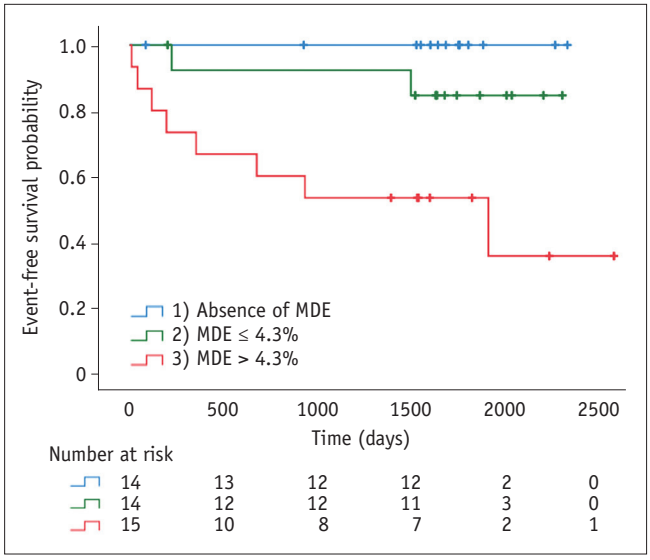

Fig. 5. Kaplan–Meier analysis illustrates event-free survival probability according to MDE quantification. Patients were divided into three groups according to 1) absence of MDE, 2) MDE ≤ 4.3%, and 3) MDE > 4.3%. Significant differences between these risk subgroups were observed in the survival curves (log-rank $P = 0.005$). MDE = myocardial delayed enhancement

imaging has been emphasized in past publications, with LGE being strongly linked to contractile dysfunction and ventricular arrhythmia [22,23]. Although studies use different quantification methods and provide a wide range of cutoff values (4.4%–17.0% of LV mass) to discriminate the risk for adverse cardiac events [24-27], the 5-SD threshold on cardiac MRI is widely used for NIDCM based on histopathologic evidence and clinical relevance [27-29]. While research involving cardiac CT for evaluating myocardial fibrosis is ongoing, most earlier studies have relied on manual quantification. This is primarily because there is still no consensus on CT thresholds for MDE and no commercially available software for MDE quantification with cardiac CT [10].

In this study, the results of threshold-based quantification on conventional CT did not show good interobserver agreement or notable benefits over MRI, in contrast to the 4-SD threshold at 70 keV. These results may be attributed to the enhanced contrast-to-noise ratio in monochromatic CT, as there is currently no practical way to separate true enhancement from noise. This is particularly pronounced in polychromatic CT images at 100 and 120 kVp, which inherently exhibit more noise than monochromatic images.

In the present study, we chose 70 keV among the various monochromatic energy levels based on a previous study that identified it as the most accurate for detecting MDE in cardiomyopathies [11]. Previous studies comparing monochromatic images at different energy levels have supported that 70–80 keV provides the best contrast-to-noise ratio with reduced beam-hardening artifacts [11,15,30,31]. However, further studies must explore other energy levels before establishing this approach as a standard protocol for quantifying myocardial fibrosis. We chose thresholds of 2, 3, and 4 SDs because the attenuation difference between hyperenhanced areas and the remote myocardium on CT images might result in underestimating the MDE with larger SDs. While threshold-based quantification yielded modest agreement in the 100- and 120-kVp CT scans, the 4-SD threshold yielded the best results among the 2-, 3-, and 4-SD thresholds. Therefore, 4-SD will yield good results even at other energy levels. Furthermore, we excluded the full-width-at-half-maximum technique from this analysis because of its potential inappropriateness in cases without MDE or inaccuracy in cases with mid-wall fibrosis, a typical pattern in NIDCM [32].

This study had several limitations. First, this was a single-center study with a relatively small cohort of patients. Consequently, we could not perform Cox regression analysis, which was used to build predictive models for time-to-event data, owing to the limited sample size and number of events. A study with a larger sample size is necessary for further validation. Second, this study incorporated two cohorts distinct from earlier studies, enrolling patients over consecutive periods. Despite this, identical inclusion and exclusion criteria were applied, and the contrast per body weight was uniform across both cohorts. Third, we used an area histogram to quantify the MDE on cardiac CT, as there is currently no commercially available software for this purpose. Future development of dedicated software for MDE quantification will require additional validation of our results using such tools.

In conclusion, applying the 4-SD threshold on 70-keV monochromatic CT demonstrated the capability of quantifying MDE as a marker for myocardial fibrosis, with a performance comparable to that of cardiac MRI. This approach can be used to strategize the risk of patients with NIDCM. Future research is required to refine semi-automated quantification methods, potentially leveraging pixel intensity maps to enhance the accuracy of MDE assessments.

Supplement

The Supplement is available with this article at https://doi.org/10.3348/kjr.2023.1271.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

Hye-Jeong Lee, who holds the respective position of Section Editor of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. The remaining author has declared no conflicts of interest.

Author Contributions

Conceptualization: Jong-Chan Youn, Hye-Jeong Lee. Data curation: Jong-Chan Youn. Formal analysis: Na Young Kim, Hye-Jeong Lee. Funding acquisition: Hye-Jeong Lee. Investigation: Dong Jin Im, Yoo Jin Hong, Hye-Jeong Lee. Methodology: Na Young Kim, Hye-Jeong Lee. Project administration: Jong-Chan Youn, Hye-Jeong Lee. Resources: Jong-Chan Youn, Hye-Jeong Lee. Supervision: Byoung Wook Choi, Seok-Min Kang. Writing—original draft: Na Young Kim, Hye-Jeong Lee. Writing—review & editing: Na Young Kim, Jong-Chan Youn, Hye-Jeong Lee.

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