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Quantitative Analysis of Late Gadolinium Enhancement in Hypertrophic Cardiomyopathy: Comparison of diagnostic performance in myocardial fibrosis between Gadobutrol and Gadopentetate Dimeglumine

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Abstract

Purpose The purpose of this study was to compare different semi-automated late gadolinium enhancement (LGE) quantification techniques using gadobutrol and gadopentetate dimeglumine contrast agents with regard to the diagnosis of fibrotic myocardium in patients with hypertrophic cardiomyopathy (HCM).

Methods Thirty patients with HCM underwent two cardiac MRI protocols with use of gadobutrol and gadopentetate dimeglumine. Contrast-to-noise ratio (CNR) between LGE area and remote myocardium (CNRremote), between LGE area and left ventricular blood pool (CNRpool), and signal-to-noise ratio (SNR) in LGE were compared . The presence and quantity of LGE were determined by visual assessment. With Signal Threshold versus Reference Mean (STRM) based thresholds of 2 SD, 5 SD, and 6 SD above the mean signal intensity (SI) of reference myocardium, the Full-Width at Half-Maximum (FWHM) technique was used. The volume and segments of the LGE area were compared between the two types of contrast agents.

Results LGE was present in 26 of 30 (86.6%) patients in both protocols. The CNRremote of fibrotic myocardium in gadobutrol and gadopentetate dimeglumine agents was 26.82 ± 14.24 and 21.46 ± 10.59, respectively ($P < 0.05$). The CNRpool was significantly higher in gadobutrol (9.32 ± 7.64 vs. 6.39 ± 6.11, $P < 0.05$). The SNR was higher in gadobutrol (33.36 ± 14.35 vs. 27.53 ± 10.91, $P < 0.05$). The volume of scar size in MR images acquired with gadobutrol were significantly higher than those with gadopentetate dimeglumine($P < 0.05$), and the STRM of 5 SD technique showed the greatest agreement with visual assessment (ICC = 0.99) in both examinations. There was no significant difference in fibrotic segments of the fibrotic myocardium in the LGE area ($P < 0.05$).

Conclusions This study shows that Gadobutrol is an effective contrast agent for LGE imaging with superior delineation

of fibrotic myocardium as compared to gadopentetate dimeglumine. The 5 SD technique yields the closest approximation of the extent of LGE identified by visual assessment.

Keywords: contrast agent; gadobutrol; gadopentetate dimeglumine; hypertrophic cardiomyopathy; late gadolinium enhancement; magnetic resonance imaging

Introduction

In the diagnosis of hypertrophic cardiomyopathy (HCM), myocardial fibrosis may occur before morphological changes, and it is closely related to arrhythmia and sudden cardiac death [1]. Cardiac magnetic resonance (CMR) is an effective imaging technology to evaluate myocardial fibrosis, because it has high spatial resolution and tissue contrast resolution for differentiating myocardial necrosis from fibrotic changes [2,3]. Late gadolinium enhancement (LGE) via intravenous injection of contrast agent is widely used in clinical CMR as it can enhance depiction of myocardial reinforcement signal[4]. Accurate assessment of -scar size and morphology is important for clinical decision making according to numerous clinical settings [5]. Several semi-automated gray-scale thresholding techniques have been developed based on the signal intensity (SI) of the normal remote myocardium [6,7] and Full-Width at Half-Maximum (FWHM) [8] for improving precision and reproducibility in the detection and quantification of myocardial fibrosis [9,10].

Linear non-ionic gadolinium chelate with contrast enhancement to detect myocardial viability is commonly used in traditional CMR. However, the recently marketed gadobutrol is a macrocyclic non-ionic gadolinium chelate [11]. It possesses low dosage, high concentration and high relaxivity, showing no evident decrease with increase of field intensity. The shortening of T1 is strong, and it can obtain better contrast enhancement, which is more appropriate in MRI with high field intensity [12]. Currently, gadobutrol is not widely applied in HCM cardiac MRI, and there is no report comparing its application with traditional linear chelate. Therefore, the purpose of this study was to investigate the effectiveness of LGE MRI between gadobutrol and gadopentetate dimeglumine contrast agents. In particular, the aim of this study was to compare five methods for quantifying LGE in patients with HCM, namely, 2 SD, 5 SD, 6 SD, FWHM, and manual contouring techniques with the aim of determining the value of gadobutrol in diagnosing HCM .

Materials and Methods

Patients' enrollment

This study was approved by the Institutional Review Board of Beijing Anzhen Hospital. Informed consents were obtained from all participants. Between Dec 2014 and May 2015, a total of 36 patients with a history of HCM confirmed by transthoracic echocardiography were considered for enrollment, and then 6 patients who refused to participate in a second

study-related CMR scan were excluded. Finally, 30 patients were included. Inclusion criteria included patients with diagnostic findings consisting of left ventricular hypertrophy, left ventricular wall thickness ≥ 15 mm or ≥ 13 mm but with genetic family history. Exclusion criteria were history of moderate or severe impairment of renal function (GFR < 60 ml/min), contrast agent allergy history, general contraindications for CMR, as well as refused consent or disability to give appropriate informed consent. The study was supported by the Natural Science Foundation of China (81671647), Capital Health Research and Devvelopment of Special (2016-4-2063). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the International Conference on Harmonization Guideline E6: Good Clinical Practice.

Equipment and contrast agents

MR scans were performed on a 1.5 T scanner (Siemens Sonata 1.5T) with chest ECG gating and breath-hold techniques. True fast imaging with steady procession(True FISP) was applied with TR 43.5 ms and TE 1.45 ms. The matrix of 134×192 and layer thickness of 8 mm were chosen to perform cine cardiac MR at long and short axis views. Contrast agent was injected via ulnar vein under high pressure, and the late imaging was performed at 15 min after the injection. The direction was cardiac short axis view and vertical, parallel interventricular septum long axis view. IR-turbo FLASH sequence with TR 900, TE 3.5 and FA 25° was applied and matrix 205×256 was chosen to perform perfusion imaging in delayed phase. The scanning layer thickness was 8 mm with FOV between 320 mm × 320 mm and 340 mm × 340 mm. Gadobutrol and gadopentetate dimeglumine have different molecular structures and T1 relaxations (r1) [13]. Under 1.5 T field intensity, gadobutrol has a higher T1 relaxation (r1 = 5.2 $mmol^{-1}s^{-1}$ vs. r1 = 4.1$mmol^{-1}s^{-1}$). The dosage of gadobutrol was calculated as follows: dosage (gadobutrol) = 4.1 $mmol^{-1}s^{-1}$/5.2 $mmol^{-1}s^{-1}$x 0.20 mmol/kg. Therefore, in the two examinations, contrast agents gadopentetate dimeglumine (0.20 mmol/kg, Magnevist, Bayer Schering Pharma, Germany) and gadobutrol (0.15 mmol/kg, Gadovist, Bayer Schering Pharma, Germany) were randomly used. The interval time between the two examinations was 24-72 h, which avoided any residue of the first examination due to short time, and also prevented the influence of long interval time on any change in the lesion. Knopp et al [14] found almost no residual enhancement 24 h after injection of contrast agent. The same scanning sequence and parameters were used in the two scans, and the location of examination layer was chosen by an experienced technician to ensure the similarity of the location.

Image post-processing

All images were analyzed for assessment of LV function and volumes, the endocardial and epicardial contours were manually drawn in systole and diastole using dedicated workstation(Viewing and Argus, Siemens Healthcare, Erlangen,

Germany), with papillary muscles excluded. The ejection fraction (EF) value, cardiac index (CI) and stroke volume (SV) were measured. The presence of LV LGE was visually assessed by two observers (with 10 and 8 years of experience in CMR, respectively) in an independent blinded fashion. Any disagreement was adjudicated by the third observer who had 20 years of cardiovascular MRI experience. For late enhancement evaluation, the myocardium was segmented based on the 17-segment classification recommended by the American Heart Association [15]. Presence or absence of late enhancement was used as evaluation basis for the cardiac MRI. Quantitative assessment of image quality was conducted by measuring signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR). The CNR included CNRremote and CNRpool as detailed below:

$$SNR = SIMLE/SD \quad (1)$$

$$CNRremote = (SIMLE - SINM)/SD \quad (2)$$

$$CNRpool = (SIMLE - SILVC)/SD \quad (3)$$

SIMLE indicates fibrosis myocardial signal intensity, and SD implies air signal intensity outside of the patient. CNRremote indicates the CNR between fibrotic myocardium and normal myocardium. CNRpool indicates the CNR between fibrotic myocardium and left ventricular cavity. SINM was normal myocardial signal intensity, and SILVC was left ventricular heart cavity signal intensity. Regions of interest (ROIs) included: 1) fibrotic myocardium, 2) left ventricular heart cavity, 3) normal myocardium, 4) image background (Figs 1A , B). Cine cardiac MR vertical long axis view could show myocardial hypertrophy.

Scar size was quantified on LGE images using the cardiac analysis software package Q-mass (QMassMR, version 8.1; Medis, Leiden, the Netherlands). The short axis late enhancement images, encompassing the entire left ventricle from the base to the apex, the endo- and epicardial contours were traced semiautomatically on the short-axis slices. An ROI was traced by an operator on a region of unenhanced myocardium (remote area), and total LGE volume was quantified using four semi-automated techniques and compared to an expert manual adjustment of the SI threshold (Fig 2 and Fig 3). Techniques tested included Signal Threshold versus Reference Mean (STRM)-based thresholds of 2 SD, 5 SD, and 6 SD above the mean SI of reference myocardium, according to previous studies [6,16,17]. For FWHM-based assessments, the reference region for each slice was defined as an area inclusive of the maximum signal intensity of visually apparent LGE.

Statistical analysis

Statistical analysis was performed using SPSS (SPSS, V 20.0A IBM, Armonk, NY, USA Continuous variables were expressed as mean ± SD. The normal distribution data was analyzed by Kolmogorov-Smirnov method, and paired t - test

was used to evaluate the difference of SNR, CNR and LGE volume between the two contrast agents. $P < 0.05$ was considered to be statistically significant. For fibrotic myocardial volume, Bland Altman analysis and intraclass correlation coefficients (ICC) were reported for each semi-automated technique versus visual assessment for the two contrast agents.

Results

General characteristics of the study population

Cardiac MRI was successfully performed on 30 patients(17 males and 13 females with a mean age of 46.1 ± 9.02 years, range: 33 - 62 years), of which 26 showed late enhancement (86.6%). A total of 26 patients with 442 myocardial segments were included, of which four did not show myocardial enhancement signal and were excluded in the following analysis. One patient experienced symptoms such as nausea and rash within 15 min after examination, which disappeared after 1 h, and was a transient response. Table 1 shows the characteristics of our study population.

Comparison of myocardial late enhancement

After late enhancement, results showed that CNRpool measured with gadobutrol was significantly higher than that with gadopentetate dimeglumine (10.28 ± 8.74 vs. 7.64 ± 6.27, $P < 0.05$). The CNRremote between fibrotic myocardium and normal myocardium was 27.38 ± 14.83 and 20.94 ± 10.70, respectively, corresponding to the MR scans performed with gadobutrol and gadopentetate dimeglumine agents ($P < 0.05$). SNR was also higher in the MR scan with use of gadobutrol than that with gadopentetate dimeglumine (34.16 ± 14.3 vs. 25.94 ± 10.14, $P < 0.05$) (Table 2). The volume of scar size of four semi-automated techniques and visual assessment were statistically significant difference ($P < 0.01$) between the two contrast agents (Table 3). The volume of scarsize in MR images acquired with gadobutrol were significantly higher than those with gadopentetate dimeglumine. There was no significant difference in fibrotic segments of the fibrotic myocardium between the scans using gadobutrol (5.89 ± 2.73) and gadopentetate dimeglumine (5.50 ± 2.37), $P > 0.05$ (Fig 4).

Comparison of consistency between the two contrast agents on LGE MR

Bland-Altman plots showed good consistency on the late enhancement areas in images acquired with gadopentetate dimeglumine (Fig 5) and gadobutrol contrast agents (Fig 6).The STRM of 5 SD technique showed the highest agreement with visual assessment (ICC = 0.99) as compared to the 2 SD (ICC = 0.84), 6 SD (ICC = 0.95), and FWHM (ICC = 0.58) methods in gadopentetate dimeglumine examinations. Similarly, the 5 SD technique showed the highest agreement with visual assessment (ICC = 0.99) as compared to the 2 SD (ICC = 0.80), 6 SD (ICC = 0.97), and FWHM (ICC = 0.60) in the use of gadobutrol examination. Overall, the STRM of 5 SD technique showed the highest agreement with visual assessment. The STRM of 2 SD overestimated the total LGE volume, while FWHM underestimated it.

Discussion

The potential importance of LGE quantification in patients with HCM has been highlighted by numerous recent studies [18-21], but differences in the LGE assessment methods have made clinical interpretations confusing. The lack of standardization for the assessment of LGE in HCM is probably due to certain features of the disease and inherent challenges related to LGE imaging. In this study, we investigated several semi-automated LGE quantification techniques and two gadolinium agents for the diagnostic accuracy and reproducibility in patients with HCM. Our findings showed that 5 SD above the mean signal intensity for visually normal remote myocardium yielded the closest approximation of the extent of LGE identified by visual assessment, and it was a highly reproducible method for LGE quantification in patients with HCM. The high relaxivity of gadobutrol could decrease its dosage without losing image quality or diagnosis information, and achieve high quality cardiovascular imaging with comparable effectiveness of gadopentetate dimeglumine in the clinic.

When chronic myocardial injury occurs, the normal myocardial cells are replaced by collagenous cicatrix leading to myocardial fibrosis. Protein invasion or degraded myocardial fibrosis filling can show irregular arrangement of myocardial cells, leading to expanded extracellular space [22,23]. The concentration of contrast agent outside the cells will increase, also resulting in myocardial late enhancement. In HCM, the characteristics of late enhancement is patchy and multifocal enhancement in the combination site of interventricular septum and left ventricular free wall or the thickest region in interventricular septum. Generally, late enhancement can reflect myocardial fibrosis accurately, which is an effective method for HCM diagnosis and identification [24]. The range and size of myocardial fibrosis are important indicators of HCM patients' prognosis, and can guide revascularization treatment [25]. This has been confirmed by this study as our results showed focal fibrosis with unclear boundary, accurate quantification is difficult.

Gadopentetate dimeglumine is a widely used contrast agent in cardiac imaging, and the common dose is 0.20 mmol/kg. Recently, the second generation of macrocyclic non-ionic contrast agent gadobutrol has been widely applied in clinics. While the application of gadobutrol in cardiac late imaging is limited, there are still some published studies about use of gadobutrol in other DCE CMRI studies [26-29]. In our study, the usage of gadobutrol with corrected relaxation dosage and gadopentetate dimeglumine with standard dosage was more advantageous in cardiac delayed imaging. Gadobutrol with higher T1 relaxation could decrease the dosage of contrast agent in delayed imaging. In a recent study, Fenchel et al [30] were the first to examine gadobutrol for multislice first-pass magnetic myocardial perfusion imaging. They conducted a phantom study in which the SNR and CNR values of gadobutrol were

compared with those of gadopentetate. Interestingly, they found that the determination of T1 relaxation times at the various concentrations of gadobutroldoped phantoms yielded a significant decrease in T1 relaxation time compared with identical concentrations of gadopentetate - that is, the effect of gadobutrol on T1 was more pronounced. Therefore, it seems to suggest that gadobutrol is a favorable contrast medium for evaluation of stress myocardial perfusion because of its high concentration and that it seems to help to overcome the well known shortcomings of lower-concentration gadolinium-based contrast agents, that is, low SNR and CNR, this is confirmed by our study. The results showed that after late enhancement, CNRpool, CNRremote and SNR of gadobutrol were higher than those of gadopentetate dimeglumine. In this study, the two agents had significant differences in delayed imaging fibrotic myocardium volumes. The scarsize volumes in gadobutrol were higher than gadopentetate dimeglumine ($P < 0.01$) in five different measurement methods. As compared to visual assessment, our results identified the STRM of 5 SD technique to provide the closest estimate of LGE burden among the population. The 2 SD technique systematically over-estimated the LGE burden volume as compared to the reference standard, while thresholds of 6 SD and FWHM systematically under-estimated the LGE burden, as illustrated in Figures 2-3. Previous studies demonstrated that FWHM[8,31] might be the appropriate method for LGE quantification in MI. Other studies suggested 5 SD [17], 6 SD [32], or manual contouring [17] as suitable methods. However, none of these studies included test - retest repeatability. In our study, two contrast agents were used for two tests to verify the accuracy of different measurement methods. Fibrotic myocardium area shown to have good consistency in evaluating late enhancement analyzed by Bland - Altman and ICC. Whether gadolinium concentration was higher in gadobutrol, different electrovalences of contrast agent (non - ionic gadobutrol and ionic gadopentetate dimeglumine) or different molecular structures of the contrast agents (macrocyclic gadobutrol and linear gadopentetate dimeglumine) needs further investigation.

A recent study by Rudolph et al [28] reported that applying 0.2 mmol/kg Gd-DTPA as the reference, the delineation of scar size was similar with 0.15 mmol/kg gadobutrol, whereas the use 0.10 mmol/kg gadobutrol led to reduced tissue contrast. Our data are different to these results. There may be several possible explanations for this discrepancy between both studies. First, could be the different patient population. Rudolph et al study was composed of patients with CAD only included men while our study was patients with HCM including both sexes. The second, Rudolph defined areas of LGE as a signal intensity of more than 6 SD above the mean of remote myocardium while our study used a variety of methods to calculate the scar size and found that 5SD is better, and Rudolph noted the dose of 0.10 mmol/kg gadobutrol was associated with lower signal

intensity, therefore, the measurement of scar size needs to be further studied. And the third may be two studies using different machine, one is 1.5T and the other is 3.0T. Wagner et al. [29] compared the late enhancement of gadobutrol (0.15 mmol/kg) and gadopentetate dimeglumine (0.22 mmol/kg) in chronic myocardial infarction, and showed no significant difference in evaluating infarction area, and the difference of CNRremote between infarction myocardium and normal myocardium was minor. However, the CNRpool between infarction myocardium and left ventricular heart cavity of gadobutrol was higher than that of gadopentetate dimeglumine which is consistent with our study. As discussed above, there are some studies on gadobutrol application on myocardial infarction coronary heart disease. However, as compared to fibrosis caused by myocardial infarction, the characteristics of late enhancement caused by myocardial disease possessed unclear boundary, unfixed location and insignificant signal. In this study, the imaging effect of 0.15 mmol/kg gadobutrol was an effective contrast agent for LGE imaging with superior delineation of scar size to that of 0.20 mmol/kg gadopentetate dimeglumine. In fact, the two contrast agents showed a very similar pattern from the late enhancement way, location and distribution region, whereas the application of 0.1 mmol/kg gadobutrol led to lower signal intensity and higher discrepancy regarding scar size.

According to the classification of gadolinium contrast agents by EMEA [33], gadobutrol is a low-risk and safe contrast agent for patients with renal insufficiency [34]. NSF is a rare, potentially fatal disease, leading to fibrosis of skin, musculoskeletal system and inner organs of patients with severe kidney disease. There is no effective therapy for NSF, but only effective prevention [35, 36]. Patients with coronary artery disease are more frequently affected by renal impairment than the normal population [37]. In the spring of 2008, the EMA classified GBCAs as high-, medium- or low-risk agents related to causing NSF [38]. gadopentetate dimeglumine was defined as high risk, and gadobutrol as low risk. Having been established in controlled clinical trials, this safety profile of gadobutrol was confirmed by postmarketing surveillance data. With more than 5.7 million estimated administrations of gadobutrol, a total of 1175 (0.02%) suspected adverse drug reactions and 0% incidence of NSF have been reported [39]. And Edwards B J et al [40] had reported a total of 692 NSF cases in the USA and Europe, of these, 23% (162/692) of cases involved gadopentetate dimeglumine. Based on the previous reports on high combination of gadobutrol in heart infusion and our study on its effects in late enhancement, we believe that gadobutrol is a good choice for cardiac MRI.

The limitation of this study was that the sample size was small and it was based on a single center experience. Further studies based on analysis of more cases are required. Another limitation is lack of correlating findings with clinical follow-up. It would be desirable to include patient's outcome in the diagnostic assessment, thus further strengthening the clinical

value of the study findings.

In conclusion, in the delayed imaging of HCM, the high relaxivity of gadobutrol could decrease the dosage of contrast agent without losing image quality or diagnosis information, which could achieve high quality cardiovascular imaging with comparable effectiveness of gadopentetate dimeglumine in the clinic. The STRM of 5 SD LGE segmentation technique provided the highest accuracy and acceptable reproducibility for total scar size volume quantification versus the expert reference standard.

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Compliance with Ethical Standards:

Conflict of Interest:

Dongting Liu declares that she has no conflict of interest.

Jiayi Liu declares that he has no conflict of interest.

Xiaohai Ma declares that he has no conflict of interest.

Lei Zhao declares that she has no conflict of interest.

Hui Chen declares that she has no conflict of interest.

Zhonghua Sun declares that he has no conflict of interest.

Zhanming Fan declares that he has no conflict of interest.

Research involving human participants 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 obtained from all individual participants included in the study.

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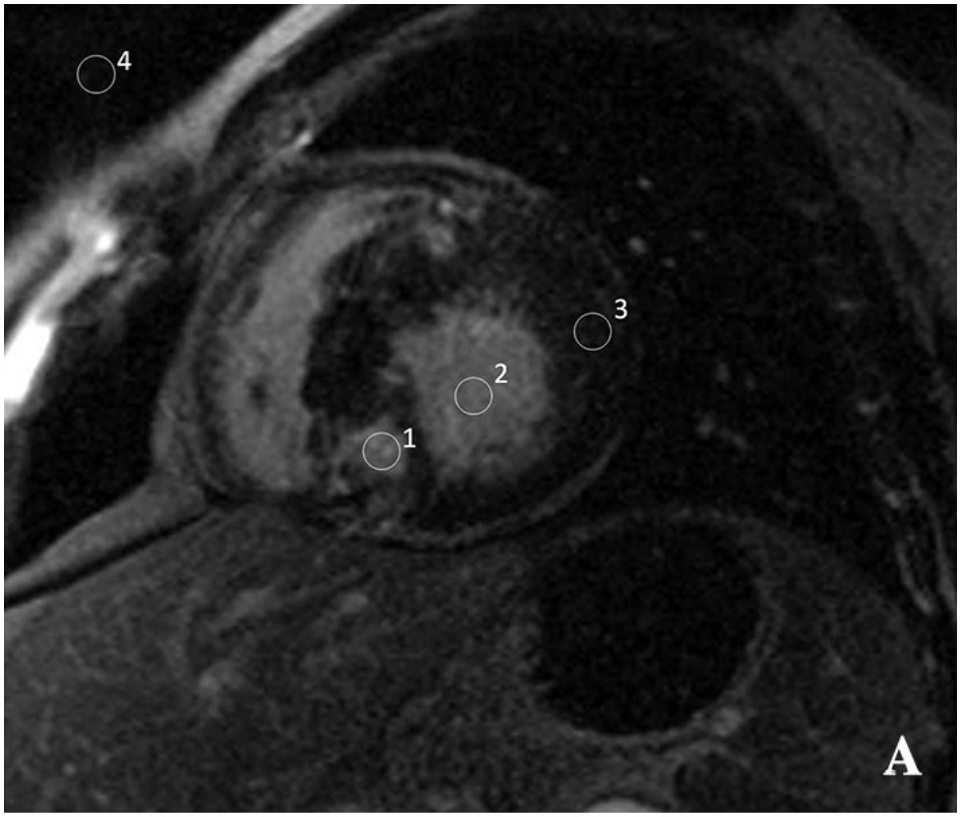
Supporting Information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3
2
1
A

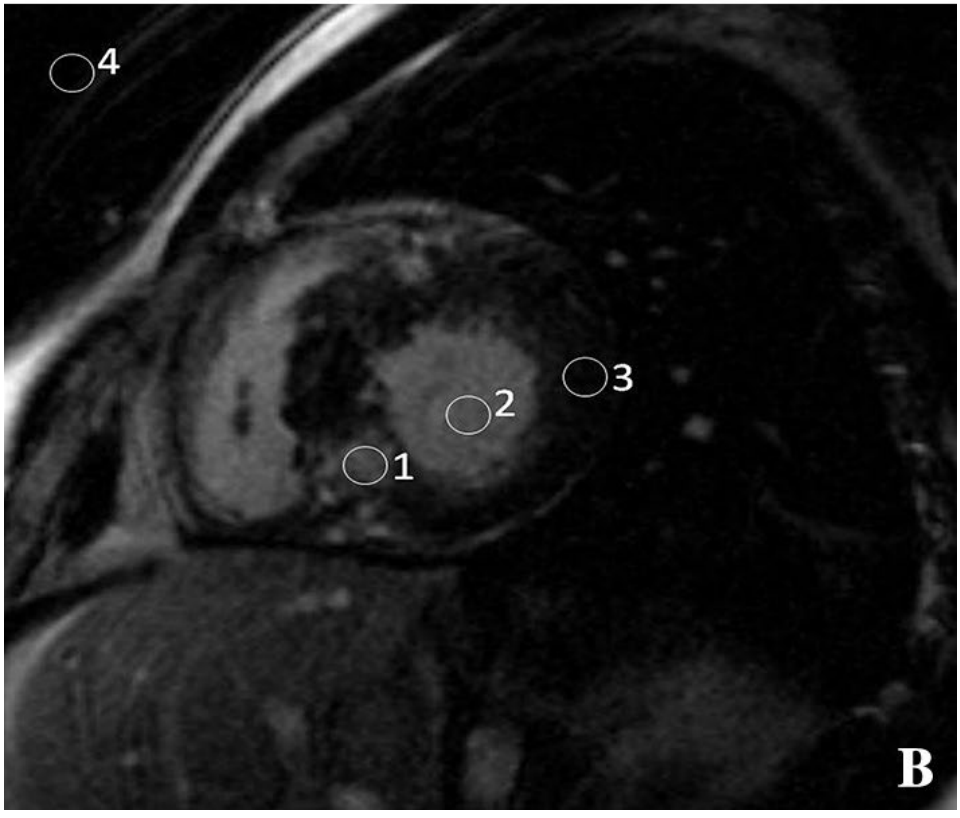

4
3
2
1
B

Figure 1. Assessment of signal intensities (SI) on IR-GRE images in a patient with transmural infarction for calculation of CNR. SIs were determined in circular ROIs placed in the scarred myocardium (1), left ventricular lumen (2), and remote myocardium (3) on representative gadopentetate dimeglumine (A) and gadobutrol (B) enhanced MR images.

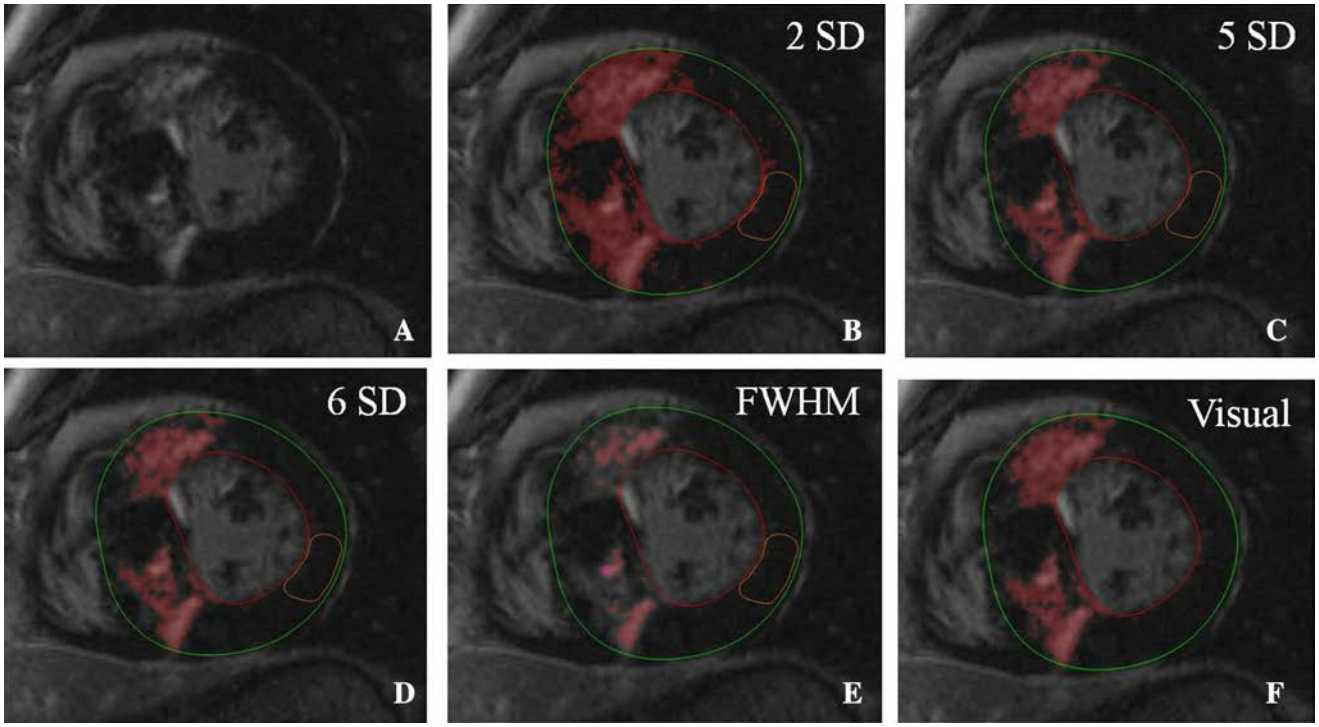


Figure 2. Example of raw late gadopentetate dimeglumine-enhanced image (A) of a patient, the Signal Threshold versus Reference Mean (STRM)–based segmentation at 2 SD (B), 5 SD (C) and 6 SD thresholds (D), full-width at half-maximum (FWHM)-based segmentation (E) and manual contouring (F).

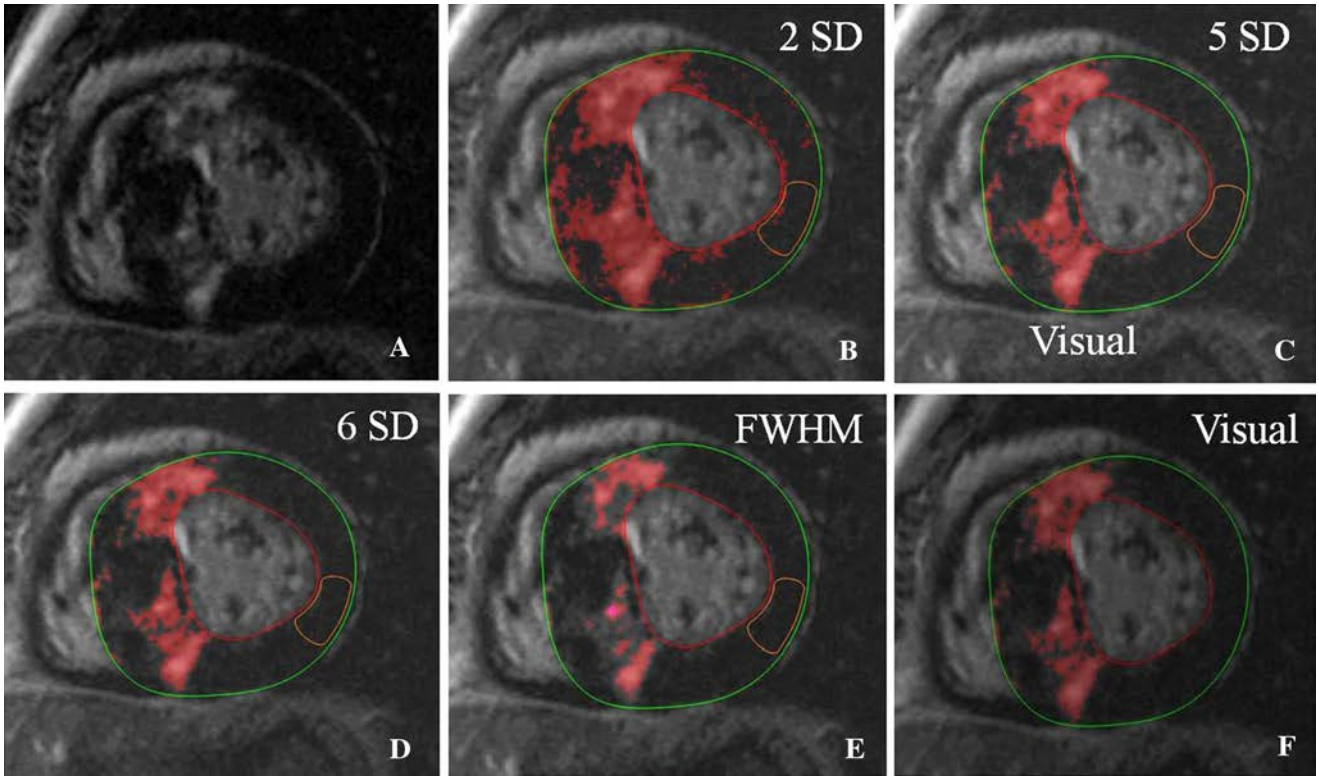
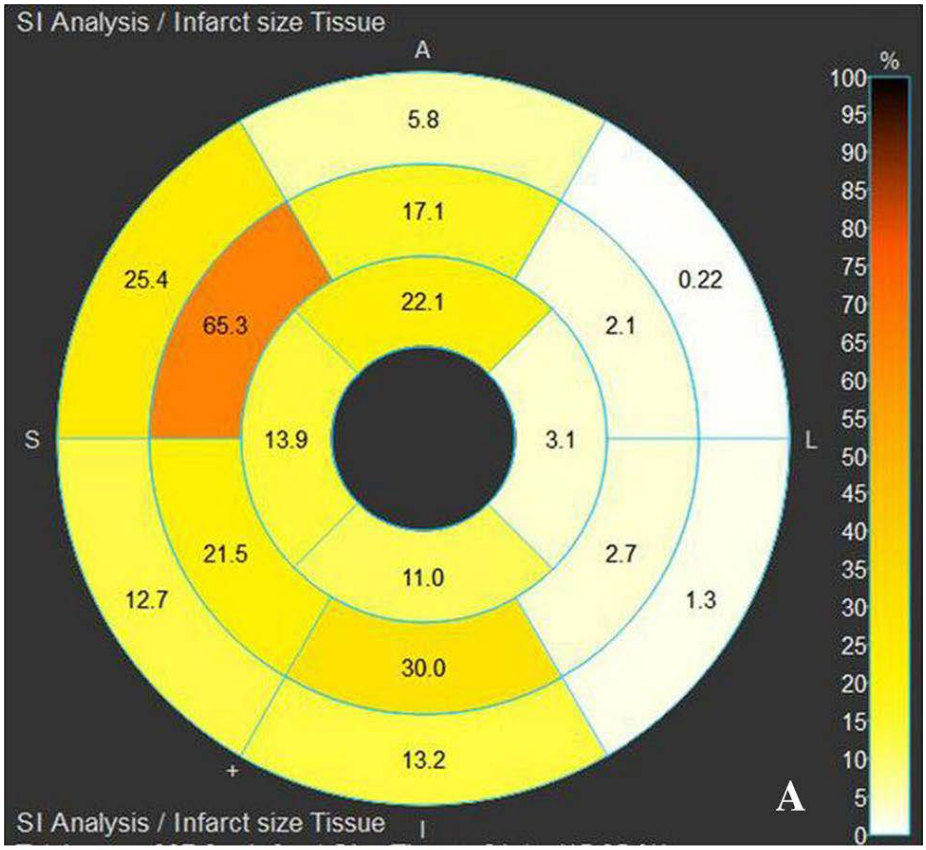


Figure 3. Example of late gadobutrol-enhanced images of the same patient. (A) raw image, (B) 2 SD, (C) 5 SD, (D) 6 SD, (E) FWHM and (F) manual contouring.


SI Analysis / Infarct size Tissue
A
5.8
17.1
22.1
25.4
65.3
0.22
2.1
S
13.9
3.1
L
21.5
11.0
2.7
12.7
1.3
30.0
13.2
+
I
%
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
A
SI Analysis / Infarct size Tissue

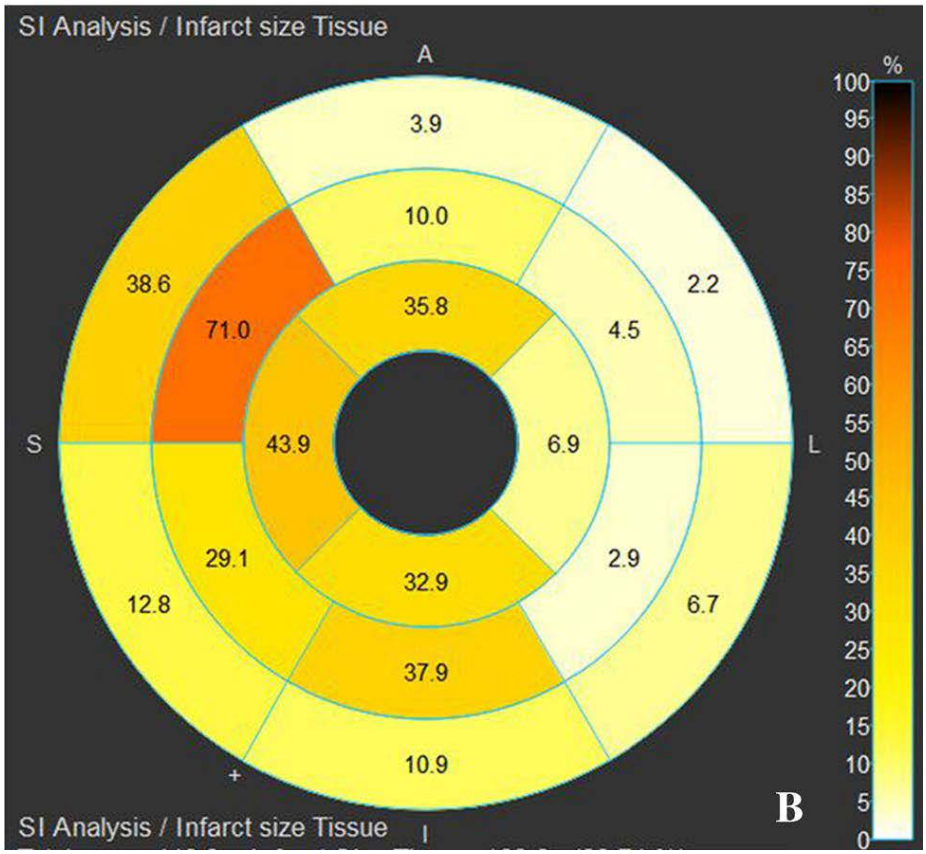

SI Analysis / Infarct size Tissue
A
3.9
10.0
35.8
38.6
71.0
2.2
4.5
S
43.9
6.9
L
29.1
32.9
2.9
12.8
6.7
37.9
10.9
+
I
%
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
B
SI Analysis / Infarct size Tissue

Figure 4. The scartransmurality was calculated for each segment by dividing the area of late gadolinium enhancement by the total area of myocardium. Imaging of the same patient in MR scans with use of gadopentetate dimeglumine (A) and gadobutrol agents (B).

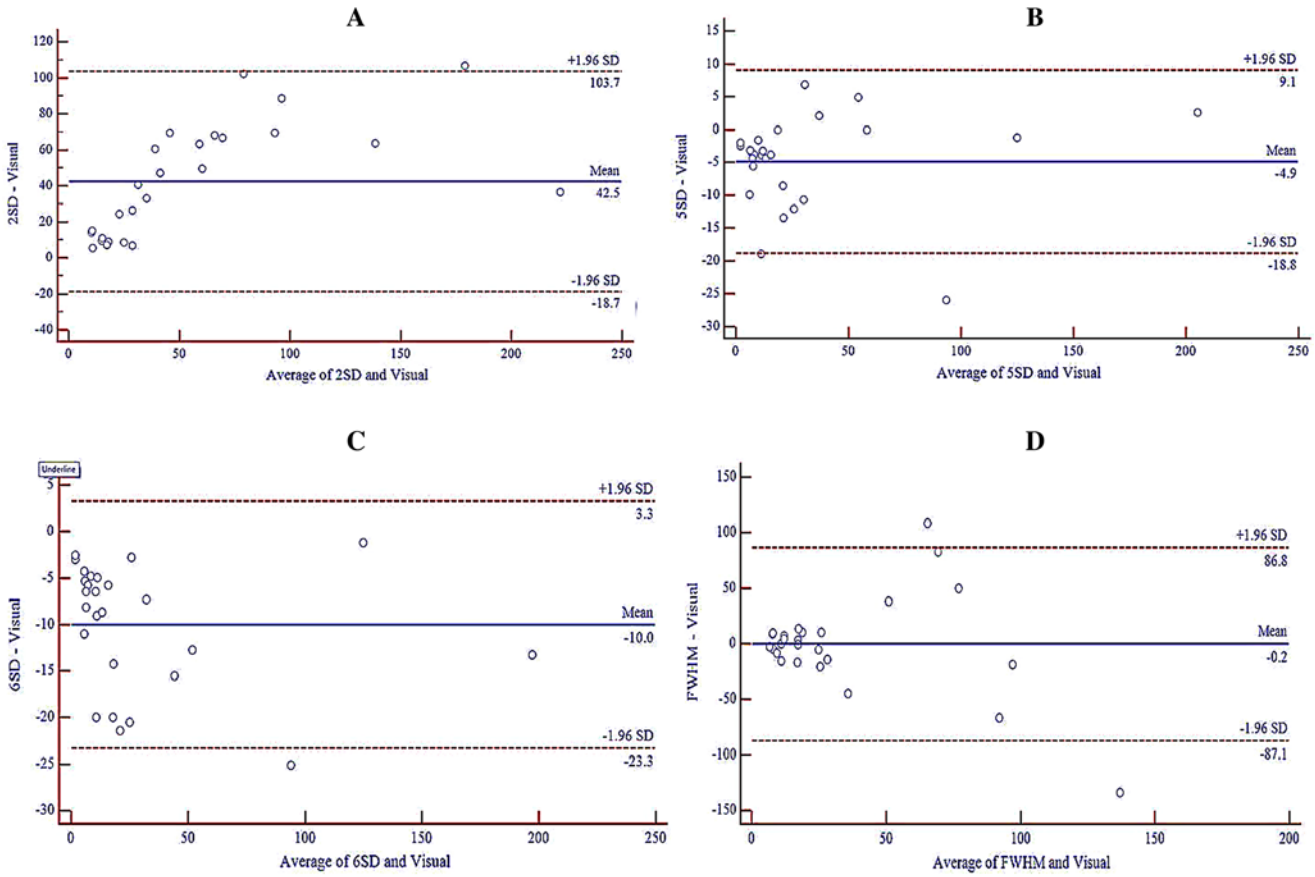


Figure 5. Bland-Altman plots showed good consistency on the late enhancement areas in gadopentetate dimeglumine.

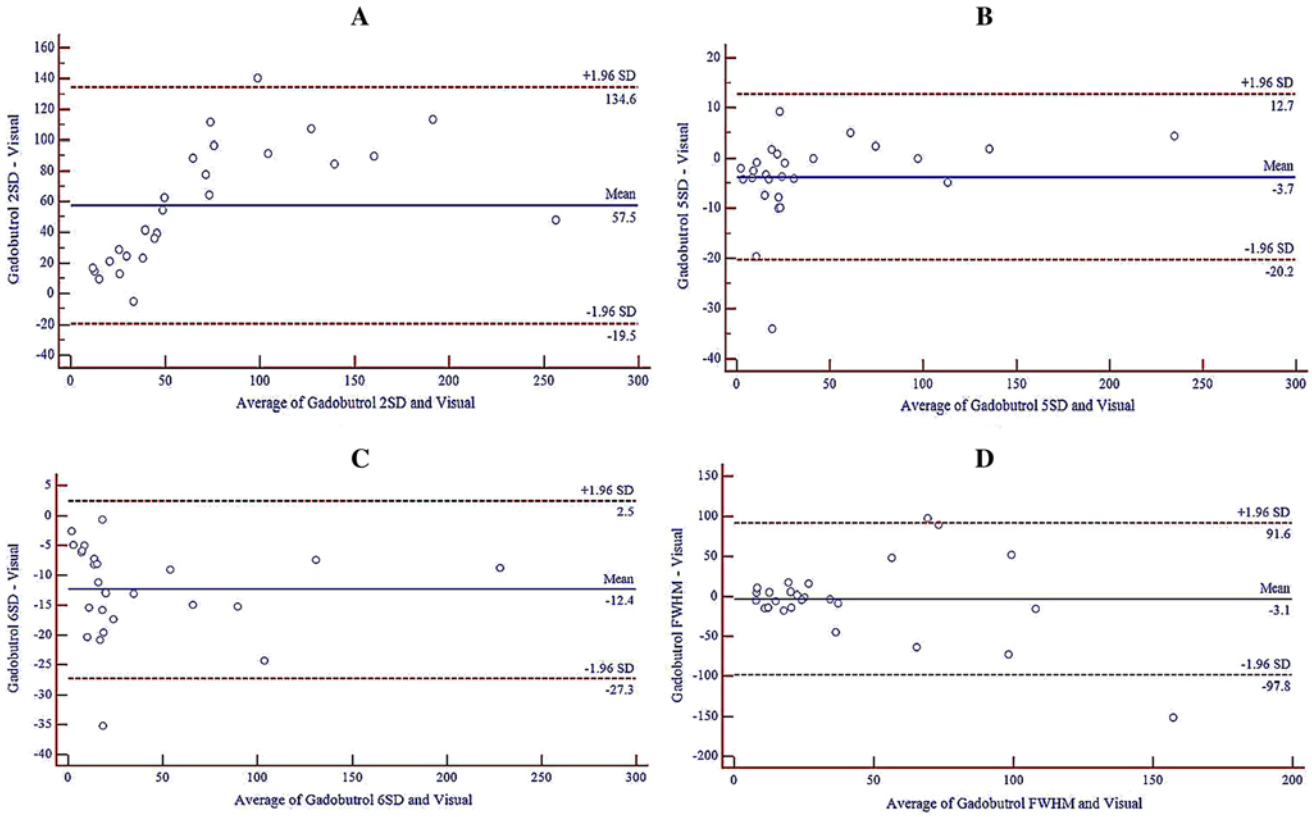


Figure 6. Bland-Altman plots showed good consistency on the late enhancement areas in the use of gadobutrol agent.

Table 1 Characteristics of the study population

	Frequency (%)	Mean ± SD[b]
Gender		
Male	17[a] (56.7)	–
Female	13 (43.3)	–
Age	–	46.1 ± 9.02
HCM type		
Asymmetric with LVOT obstruction	3 (10.0)	–
Asymmetric without LVOT obstruction	14 (46.7)	–
Apical HCM	5 (16.6)	–
Symmetric HCM	8 (26.7)	–
Chest pain		
Exertional	19 (63.3)	–
Atypical	11 (36.7)	–
EF value (%)	–	57.9 ± 17.23
SV (ml)	–	49.7 ± 18.82
CO (l/min)	–	3.36 ± 1.27

[a]Indicates the number of patients, and data in parentheses are percentages

[b]Represents mean ± standard deviation

Table 2 Comparison of CNR and SNR between the two groups

Contrast agent	CNRpool	CNRremote	SNR
Gadobutrol	10.28 ± 8.74	27.38 ± 14.83	34.16 ± 14.3
Gadopentetate dimeglumine	7.64 ± 6.27	20.94 ± 10.70	25.94 ± 10.14
T value	2.89	3.40	−5.31
P value	<0.05	<0.05	<0.05

Values are presented as mean ± SD, P < 0.05 was considered to be statistically significant

Table 3 Comparison of infarct size volumes between the two groups

Volume of infarct size	Gadobutrol	Gadopentetate dimeglumine	*T* value	*P* value
2 SD	100.91 ± 73.64	77.27 ± 64.15	−7.37	0.0001
5 SD	39.64 ± 53.78	29.90 ± 40.06	−4.48	0.0001
6 SD	30.98 ± 50.81	24.75 ± 43.92	−3.06	0.005
FWHM	40.24 ± 38.69	34.58 ± 35.75	−3.53	0.002
Visual	43.37 ± 51.12	34.75 ± 45.32	−4.25	0.0002

Volume of infarct size (ml)