Multimodality Imaging of Anatomy and Function in Coronary Artery Disease

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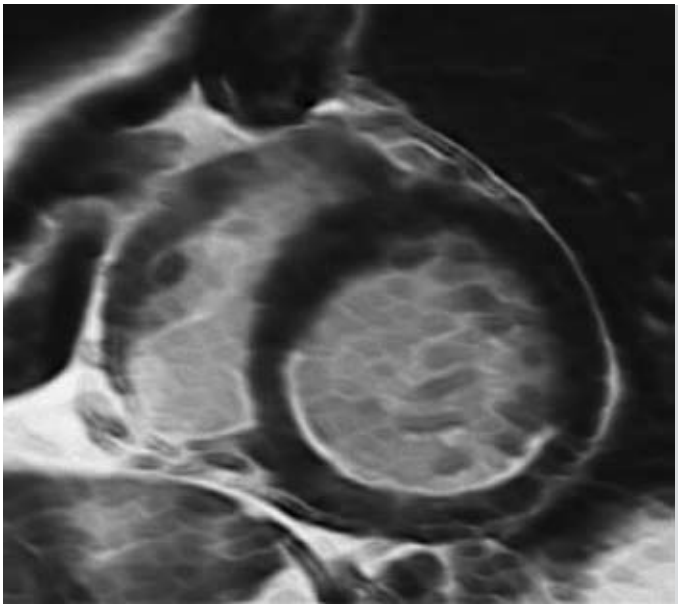

Part V

Non-Coronary Imaging

Chapter 21

Quantification of Myocardial Infarct Size and Transmurality by Contrast-enhanced Magnetic Resonance Imaging in Men

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Abstract

Background

Contrast-enhanced Magnetic Resonance Imaging (ce-MRI) allows precise delineation of infarct transmurality. An issue of debate is whether data analysis should be performed visually or quantitatively. Accordingly, a head-to-head comparison was performed between visual and quantitative analysis of infarct transmurality on ce-MRI. In addition, infarct transmurality was related to the severity of resting wall motion abnormalities.

Methods

In 27 patients with chronic ischemic left ventricular (LV) dysfunction (LV ejection fraction 33 ± 8%) and previous infarction, cine MRI (to assess regional wall motion) and ce-MRI were performed. Using a 17-segment model, each segment was assigned a wall motion score (from normokinesia to dyskinesia) and segmental infarct transmurality was visually assessed on a 5-point scale (0=no infarction, 1=transmurality ≤25% of LV wall thickness, 2=transmurality 26-50%, 3=transmurality 51-75%, and 4=transmurality 76-100%). Quantification of transmurality was performed using threshold analysis; myocardium showing signal intensity above the threshold was considered scar tissue and the percentage of transmurality qwas calculated automatically.

Results

Wall motion was abnormal in 56% of the 459 segments and 55% of segments revealed hyperenhancement (indicating scar tissue). The agreement between visual and quantitative analysis was excellent: 90% (kappa 0.86) of segments were categorized similarly by visual and quantitative analysis. Infarct transmurality paralleled the severity of contractile dysfunction; 96% of normal or mildly hypokinetic segments had infarct transmurality ≤25%, whereas 93% of a- and dyskinetic segments had transmurality >50% on visual analysis.

Conclusion

Visual analysis of ce-MRI studies may be sufficient for assessment of transmurality of infarction.

Introduction

Assessment of viability and scar tissue is important to guide treatment of patients with ischemic cardiomyopathy [1-3]. Recently, contrast-enhanced magnetic resonance imaging (ce-MRI) has emerged as a non-invasive technique that allows imaging of scar tissue with a high spatial resolution. A close correlation has been shown between irreversible myocardial injury and hyperenhancement following administration of a gadolinium-based contrast agent [4;5]. Furthermore, ce-MRI allows precise delineation of the transmurality of infarction. A current issue of debate is whether the analysis of the ce-MRI studies should be performed visually or quantitatively. Quantitative analysis may be time-consuming while on the other hand visual assessment of transmurality may be less accurate. Accordingly, the purpose of this study was 2-fold: (1) to demonstrate the feasibility of quantitative assessment of transmurality, and (2) to perform a head-to-head comparison between visual and quantitative analysis. In addition, the results of both techniques were related to the severity of resting wall motion abnormalities.

Methods

Patients and study protocol

The study group consisted of 27 consecutive patients with chronic coronary artery disease and a previous infarction (>1 month before the study). The inclusion criteria were: 1) sinus rhythm, 2) angiographically proven coronary artery disease, 3) myocardial infarction >1 month before the study.
Exclusion criteria included: 1) recent myocardial infarction (≤1 month) or episode of unstable angina and/or heart failure requiring hospitalization (≤1 month), 2) cardiac pacemakers or intracranial aneurysm clips, 3) (supra-)ventricular arrhythmias.
The study protocol included a resting cine MRI-study to analyze regional and global LV function, followed by ce-MRI to determine infarct size. All patients gave written informed consent to the study protocol, which was approved by the local ethics committee.

Data acquisition

Patients were positioned supine in a clinical 1.5-T scanner (Gyroscan NT Intera, Philips Medical Systems, Best, The Netherlands). All images were acquired using a five elements synergy coil during breath-holds and were gated to the electrocardiogram. To determine the final short-axis imaging plane, transverse, oblique sagittal, and double-oblique left ventricular long-axis scout images were obtained as previously described [6]. Depending on the heart size, the heart was imaged from apex to base with 10 to 12 imaging levels in the short-axis orientation using a sensitivity encoding imaging technique balanced fast field echo sequence. Typical parameters were field of view 400 x 400 mm^2, matrix size 256 x 256, slice thickness 10.00 mm, slice gap 0.00 mm, flip angle 50°, time to echo 1.82 ms and time

to repeat 3.65 ms. The number of cardiac phases depended on the heart rate. Prior to the acquisition of the delayed enhancement images, optimization of inversion time was performed for each patient individually starting at 15 minutes after a bolus injection of Gd-DTPA (Magnevist; Schering/Berlex, Berlin, Germany, 0.15 mmol/kg). In order to achieve maximum contrast between viable and non-viable myocardial tissue, a series of real-time planscan images with decreasing inversion time, starting at approximately 300 ms were obtained. Real-time planscanning allows immediate adjustment of inversion time by instant acquisition of short-axis test slices, without the need for breath holding. In 50-70 seconds a series of images with different inversion times in steps of 5 ms can be acquired to obtain the optimum inversion time with nulled (black) myocardium and high signal intensity of infarcted tissue. The following parameters were applied: field of view 400 x 400 mm^2, matrix size 256 x 256, slice thickness 6.00 mm, flip angle 15°, time to echo 1.44 ms and time to repeat 4.3 ms.
Contrast-enhanced images were acquired at 17-19 minutes after contrast administration, with an inversion-recovery gradient echo sequence, in the same views as those used for cine MR. Depending on the patient's heart rate and heart size, 20 to 24 slices were obtained in two breath-hold acquisitions of approximately 15 seconds. Typical parameters were the following: field of view 400 x 400 mm^2, matrix size 256 x 256, slice thickness 5.00 mm, slice gap – 5 mm, flip angle 15°, time to echo 1.36 ms and time to repeat 4.53 ms.

Data analysis

Regional and global function

For the assessment of regional wall motion, cine MR images were visually interpreted by two experienced observers (blinded to other MR and clinical data) using a previously described 17-segment model [7]. Each segment was assigned a wall motion score using a 5-point scale: 0: normokinesia, 1: mild hypokinesia, 2: severe hypokinesia, 3: akinesia, and 4: dyskinesia.
To determine global function, endocardial borders were outlined manually on the short-axis cine images using previously validated software (MR Analytical Software System [MASS], version 5.0, Leiden, The Netherlands). Papillary muscles were regarded as being part of the ventricular cavity. LV end-systolic and LV end-diastolic volumes were calculated. Subsequently the related LV ejection fraction was derived by subtracting the end-systolic volume from the volume at end-diastole and dividing the result by the end-diastolic volume.

Scar tissue; Visual analysis

Delayed enhancement images were scored visually by two experienced observers (blinded to other MR and clinical data) using the same 17-segment model as used for function analysis (see Figure 21.1). Each segment was graded on a 5-point scale: 0: absence of hyperenhancement, 1: hyperenhancement 1-25% of LV wall thickness, 2: hyperenhancement extending to 26-50%, 3: hyperenhancement extending to 51-75%, and 4: hyperenhancement extending to 76-100% of LV wall thickness 8. To assess intra- and interobserver agreements, 10 patients were re-analyzed. The resulting intra- and interobserver agreement were 97% and 94%, respectively.

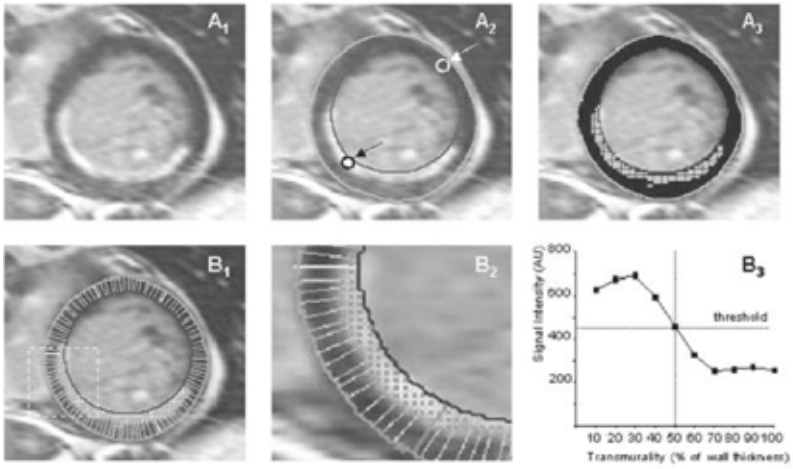

Figure 1. Subsequent steps of quantitative analysis of transmurality of infarction.
A1: Representative contrast enhanced, short-axis slice. A2: Two manually drawn regions of intereset; 1 in the center of infarction (black arrow) and another in normal myocardium (white arrow). A3: Contrast-enhanced slice after application of the threshold value. B1: Application of the modified centerline method, resulting in 100 equidistant chords along the LV wall. B2: Enlargement of the dashed box in Panel B1.
B3: A signal intensity curve of one of these centerline chords, showing the signal intensity in 10 points along this particular centerline chord, revealing infarction of 50% of LV wall thickness.

Scar tissue; Quantitative analysis

The transmural extent of infarction was also determined using threshold analysis (see Figure 1). In one representative slice of each delayed enhancement set, 2 regions of interest were manually drawn; one in a region showing the highest signal intensity (center of infarction) and another equally sized region of interest in normal myocardium (with normal wall motion). A threshold value was calculated by dividing the sum of the signal intensities in both regions of interest by 2. Myocardial tissue showing a signal intensity ≥ the threshold value was considered scar tissue.

The extent of transmurality was subsequently determined by the use of the modified centerline method [9]. Using 10 points along each centerline chord, percentage of LV wall thickness with increased signal intensity was determined and expressed as an average per segment to allow comparison with the visual analysis. Signal intensity of the 10 equidistant points was determined by bipolar interpolation. No zoom was used. To assess inter- and intraobserver variability of quantitative analysis (to assess extent of infarcted tissue), 10 patients were re-analyzed. The inter- and intraobserver variability were 4.2 ± 6.6% and 3.0 ± 5.1%, respectively.

Statistical analysis

Continuous data were expressed as mean ± SD and compared using the 2-tailed Student's t test for paired and unpaired data when appropriate. Simultaneous comparison of >2 mean values was performed using 1-way analysis of variance (ANOVA). Relations were determined by linear regression analysis. The agreement for segmental wall motion and scar score, and visual and quantitative

analysis of scar tissue, was assessed from 5 x 5 tables using weighted kappa statistics. Kappa values of <0.4, between 0.4 and 0.75 and >0.75 were considered to represent poor, fair to good and excellent agreement, respectively, based on Fleiss' classification [10]. The kappa values are reported with their standard errors (SE). A P-value <0.05 was considered statistically significant.

Results

Patients

The patient characteristics are summarized in Table 1. The study group consisted of 27 males, with a mean age of 65 ± 7 years. All patients had a history of previous myocardial infarction (>3 months before the study) and showed Q waves on the electrocardiogram (11 inferior, 16 anterior). The patients had on average 2.7 ± 0.6 stenosed coronary arteries. Cardiac medication was continued during the study period and consisted of β-blockers (n = 12), angiotensin-converting enzyme-inhibitors (n =16), diuretics (n = 16), statins (n = 15), calcium antagonists (n = 10), nitrates (n = 9) and oral anti-coagulation or aspirin (n = 27).

Table 1. Clinical characteristics of the study population (n=27).

	n (%)
Age (years)	65 ± 7
Previous infarction	27 (100%)
Q wave on electrocardiogram	27 (100%)
Multi-vessel disease	24 (89%)
Angina Pectoris	
CCS class 1/2	23 (85%)
CCS class 3/4	4 (15%)
Heart Failure (NYHA class)	
1/2	15 (56%)
3/4	12 (44%)

CCS: Canadian Cardiovascular Society;
NYHA: New York Heart Association.

Regional function, Global function

Systolic wall thickening was normal in 200 (44%) of 459 segments. End-diastolic volumes measured from the short-axis cine images ranged from 187 to 407 ml (mean 269 ± 70 ml). End-systolic volumes ranged from 99 tot 313 ml (mean 184 ± 68 ml). Accordingly, LV ejection fraction ranged from 21% to 52% (mean 33 ± 8%). Since assessment of viability is most important in patients with severely depressed LV ejection fraction, separate analysis was performed in 15 patients with a LV ejection fraction ≤35%. In these patients end-diastolic and end-systolic volumes ranged from 218 to 407 ml (mean 311 ± 66 ml) and 155 to 313 ml (mean 229 ± 58 ml), respectively. Mean LV ejection fraction

was 27 ± 4% (range 21 to 35%). Linear regression revealed good correlations (y = -0.37 x + 22.0, r = 0.79, P <0.01 and y = -0.37 x + 17.8, r = 0.79, P <0.01) between LV ejection fraction and the number of dysfunctional segments and between LV ejection fraction and the number of severe dysfunctional segments, respectively.

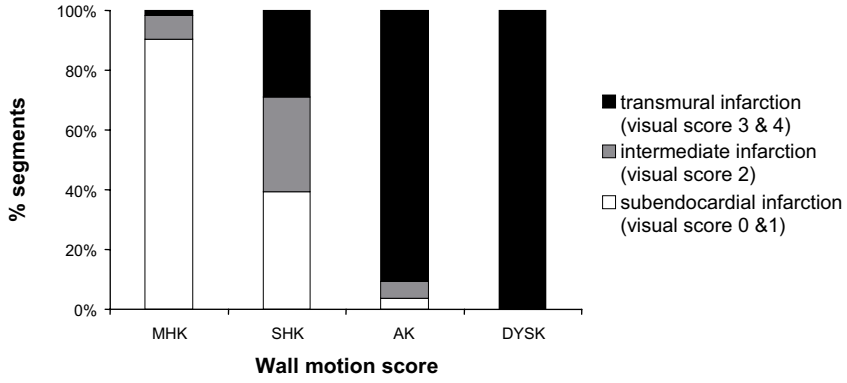

Figure 2. Percentag segments with different scores of transmurality of delayed enhancement in relation to regional wall motion score. The extent of hyperenhancement paralleled the severity of contractile dysfunction. *ak = akinesia, dysk = dyskinesia, mhk = mild hypokinesia, and shk = severe hypokinesia.*

Visual analysis of scar tissue

Of the 459 segments evaluated, 253 (55%) segments revealed hyperenhancement. The extent of hyperenhancement paralleled the severity of contractile dysfunction (Figure 2) and the likelihood of hyperenhancement >50% of LV wall thickness, was significantly higher in a- or dyskinetic segments than in mildly hypokinetic or normal segments (93% vs. 2% vs. 0%, P <0.05). Precise data are shown in Table 2. Percentages of visual scar scores in relation to the segmental wall motion score are depicted in Figure 2.

Table 2. Relation between visual hyperenhancement score and severity of contractile dysfunction (expressed as wall motion score) (65%, kappa 0.51).

	Hyperenhancement score (visual analysis)					
Wall motion score	**0**	**1**	**2**	**3**	**4**	**Total**
0	172	28	0	0	0	200
1	31	70	9	2	0	112
2	3	28	25	23	0	79
3	0	2	3	21	28	54
4	0	0	0	3	11	14
Total	206	128	37	49	39	459

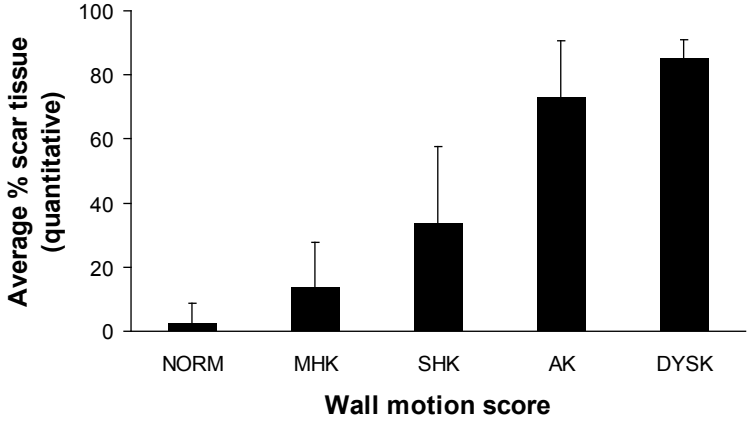

Figure 3. Relation between the severity of contractile dysfunction (expressed as wall motion score) and the average quantitative percentage of hyperenhancement through the left ventricular wall. Average quantitative percentage of hyperenhancement increased from 14% in mild hypokinetic segments to an average of 85% in dyskinetic segments (P <0.05).
ak = akinesia, dysk = dyskinesia, mhk = mild hypokinesia, norm = normokinesia, and shk = severe hypokinesia.

Table 3. Agreement between quantitative and visual scoring of scar tissue (90%, kappa 0.86).

	Quantitative analysis					
Visual analysis	**0**	**1-25%**	**26-50%**	**51-75%**	**76-100%**	**Total**
0	188	18	0	0	0	206
1	5	117	4	2	0	128
2	0	3	33	1	0	37
3	0	0	0	42	7	49
4	0	0	0	5	34	39
Total	193	138	37	50	41	459

Quantitative analysis of scar tissue

The quantitative percentage of transmurality on delayed enhancement images also paralleled the severity of resting wall motion abnormalities and increased from an average of 14% in mild hypokinetic segments to an average of 85% in dyskinetic segments (P <0.05). Average percentages of transmurality for each wall motion score are shown in Figure 3. An excellent agreement was found between the visual and quantitative analysis: 90% of 459 segments were scored identically (with a kappa statistics of 0.86, SE 0.02). Quantitative assessment of scar tissue yielded a different result in 45 (10%) segments, and shifted 13 (29%) of these discrepant segments to a lower transmurality score and 32 (71%) to a higher transmurality score (Table 3). Average quantitative scores for the different visual scores are presented in Figure 4.

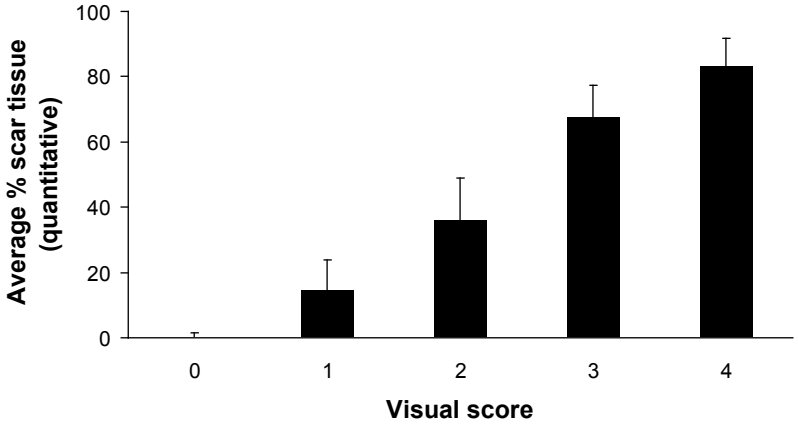

Figure 4. Average percentage hyperenhancement (quantitative) in relation to segmental visual scar score.

Discussion

Recently, gadolinium-based contrast agents have been used extensively in combination with MRI to identify infarcted myocardium [8;11]. The accuracy of ce-MRI in the assessment of infarcted myocardium has been evaluated by Kim and colleagues [11]. The authors demonstrated in animal-model of occlusion and reperfusion, an excellent agreement between the transmural and circumferential extent of infarction assessed by ce-MRI as compared to histology. In addition, in patients after acute myocardial infarction, the extent of scar tissue on ce-MRI correlated well with the enzymatically assessed damage [8].

In patients with chronic ischemic cardiomyopathy, direct comparisons with positron emission tomography and F18-fluorodeoxyglucose demonstrated a good agreement between the 2 techniques for assessing viability [12]. Moreover, Kim and colleagues demonstrated that the extent of scar tissue on ce-MRI was predictive of improvement of function after revascularization [13]: patients with small subendocardial necrosis had a high likelihood of functional recovery post-revascularization, as compared to a low likelihood of recovery in patients with transmural infarction.

The major advantage of MRI over other imaging techniques is the extremely high resolution, allowing assessment of minimal infarction. Recently, Wagner et al [14] performed a head-to-head comparison between ce-MRI and SPECT imaging, and demonstrated that 47% of segments with small subendocardial infarctions on ce-MRI were not detected by SPECT.

Currently, the ce-MRI studies are analyzed visually, and the transmurality of infarction is divided into quintiles based on visual inspection [8;13]. However, the high resolution of MRI makes the technique extremely suited for quantitative analysis. At present, various MRI-derived parameters have been evaluated quantitatively, including LV volumes, LV ejection fraction, segmental systolic thickening and end-systolic wall thickness [15-17], providing extreme precision to assess these parameters. Similarly, quantitative evaluation of transmurality of infarcted tissue on ce-MRI would allow a higher precision to define the exact percentage infarcted tissue of the LV wall. All previous studies however

have relied on visual analysis; in the current study, the feasibility of a more objective, quantitative approach was demonstrated. Using threshold analysis for signal intensity, precise delineation of the transmural extent of infarcted tissue was possible (although animal experiments are still needed to validate the technique). However, when the quantitative approach was compared directly to visual analysis, an excellent agreement with 90% of segments classified in the same quintiles of transmurality (Table 3), and only 10% of segments was shifted to a lower or higher quintile when quantitative analysis was compared to visual analysis. Based on these findings, one may conclude that visual analysis may be sufficient for clinical assessment of the extent and transmurality on ce-MRI. Eventually, a head-to-head comparison between visual and quantitative analysis is needed in patients undergoing revascularization, in order to determine whether precise quantification results in superior prediction of improvement of function after revascularization.

Besides the comparison between visual and quantitative analysis, the transmurality on ce-MRI was compared to the severity of contractile dysfunction. Comparable to the findings by Mahrholdt et al [18], the extent of transmurality paralleled the severity of wall motion abnormalities: segments with normal function had no or minimal infarction, whereas segments with a- or dyskinesia had extensive scar tissue.

In conclusion, excellent agreement between visual and quantitative analysis of ce-MRI for assessment of scar tissue was demonstrated, suggesting that visual analysis is sufficient in the assessment of transmurality of infarction on ce-MRI.

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