Late Gadolinium Enhancement from Cardiac Magnetic Resonance in Ischemic and Non-Ischemic Cardiomyopathy

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Background: *Diagnosis of coronary artery disease in patients with heart failure with systolic dysfunction usually requires coronary angiography. Cardiac magnetic resonance (CMR) is an accurate tool for the assessment of myocardial scar which may be the major cause of left ventricular systolic dysfunction.*
Objective: *This study was to determine the prevalence and the difference in pattern of late gadolinium enhancement (LGE) between patients with ischemic (ICM) and non-ischemic cardiomyopathy (NICM).*
Material and Method: *We enrolled 98 patients with heart failure and left ventricular systolic dysfunction with left ventricular ejection fraction less than 50%. All patients underwent CMR. CMR protocol included functional study and assessment of LGE. Left ventricular volume and ejection fraction was measured. The presence and extent of LGE including its pattern were assessed.*
Results: *There were 58 patients with ICM and 40 patients with NICM. Patients with NICM had a lower left ventricular ejection fraction than those with ICM with a similar left ventricular wall thickness. LGE was detected in 53 patients with ICM (91.5%) and 10 patients with NICM (25%). LGE pattern was transmural or subendocardial pattern in patients with ICM and midwall scar in those with NICM.*
Conclusion: *The presence and pattern of LGE can differentiate systolic heart failure from ICM and NICM.*

Keywords: *Late gadolinium enhancement, Cardiomyopathy*

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Heart failure due to left ventricular systolic dysfunction can be classified in to 2 major categories: ischemic (ICM) and non-ischemic cardiomyopathy (NICM)[1] . Cardiac magnetic resonance has its unique characteristic in the visualization of myocardial scar [2,3]; thereby, it is an excellent tool for the differentiation between the 2 conditions. It has been shown by cardiac magnetic resonance (CMR) that almost all of patients with ICM had evidence of previous myocardial infarction as shown by late gadolinium enhancement (LGE)[4,5]. A significant proportion of myocardial infarctions are unrecognized[6]. There have been some studies showing the difference in LGE pattern in patients with ICM and NICM[4]. They showed that LGE had a high sensitivity for the diagnosis of ICM. NICM can have many patterns of LGE. The most common form is the midwall scar at interventricular septum[4], despite the diffused involvement of myocardium. CMR can also provide an excellent image spatial resolution for the accurate assessment of ventricular volume and function[2,7].

The objectives of this study were 1) to determine the prevalence of LGE in patients with ICM and NICM and 2) to determine the difference in LGE patterns in patients with heart failure from ICM and NICM.

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Material and Method

Study population

The inclusion criteria for this study were 1) men or women above 30 years of age 2) history of heart failure within 6 months 3) left ventricular systolic dysfunction defined as left ventricular ejection fraction < 50% on echocardiogram, CMR, or left ventriculogram and 4) scheduled for coronary angiogram or underwent

coronary angiogram within 1 year. Exclusion criteria were 1) contraindication for CMR which included claustrophobia, metallic implantation such as intracranial clip, pacemaker or internal defibrillator implantation, 2) allergy to gadolinium 3) pregnancy 4) clinically unstable 5) history of revascularization and 6) heart failure from valvular or pericardial causes. Patients were classified as ICM or NICM by the presence or absence of at least 50% diameter stenosis in 1 or more major coronary arteries on coronary angiography[4].

Study procedures

This study was approved by the Ethic Committee. All patients provided written informed consent prior to participation. Clinical data and an ECG were obtained prior to the MRI procedure. Pathological Q-wave from ECG was defined by standard criteria[8].

CMR protocol

CMR was performed with the 1.5 Tesla Gyroscan NT Intera Philips scanner (Philips Medical Systems, Best, the Netherlands). The CMR protocol included the assessment of cardiac function and LGE. Functional study was performed with the steady state free precession technique and cardiac gated sequence in the long axis view, the multiple slice short axis view covering the whole left ventricle and the 4 chamber view. Parameters for functional study were as follows: repetition time/echo time/number of excitations (TR/TE/NEX) = 3.7/1.8/2, 390 x 312 mm field of view, 256 x 240 matrix, 1.52 x 1.3 reconstruction pixel, 8 mm slice thickness and 70 degree flip angle.

LGE was performed with the use of 3D segmented-gradient-echo inversion-recovery sequence after 10 minutes after the intravenous injection of 0.2 mmol/kg of gadolinium (Magnevist, Schering AG, Berlin, Germany). The images were acquired in short axis view, long axis view and 4 chamber view. The short axis images of LGE were obtained with the same number of slices and same positions as the cine functional images. Parameters for LGE were as follows: TR/TE = 4.1/1.25 ms, 303 x 384 mm field of view, 240 x 256 matrix, 1.26 x 1.5 mm reconstruction pixel, 8 mm slice thickness, 15 degree flip angle and 1.5 SENSitivity Encoding (SENSE) factor.

Analysis of CMR images

CMR images were analyzed on an independent ViewForum workstation (Philips Medical Systems, Best, the Netherlands) by an experienced cardiologist unaware of the results of the coronary angiography. Left ventricular myocardium was divided into 17 segments according to the standard segmentation method (9) with the exclusion of segment 17. Wall motion of each segment was graded into 5 grades as follows: 1 = normal, 2 = hypokinesia, 3 = akinesia and 4 = dyskinesia or aneurysm. Summation of wall motion score was calculated. Endocardial and epicardial borders of the short axis images were semi-automatically detected followed by a manual adjustment. Measurement of left ventricular end-diastolic and end-systolic volume (LVEDV and LVESV) and left ventricular mass (LVMASS) was performed. Left ventricular ejection fraction (LVEF) was calculated from (LVEDV-LVESV)/LVEDV and adjusted to the proportion of 100%. Left ventricular volumes and mass were indexed by the adjustment of the body surface area. Average wall thickness of each of the 16 standard myocardial segments was measured. Average wall thickness of all segments was calculated.

The presence or absence of LGE was recorded. LGE was divided by visual assessment into 5 grades: 0%, 1-25%, 26-50%, 51-75% and 76-100% according to the extent of LGE as a percentage to the myocardial area of each segment. Total size of LGE was calculated from the sum of LGE extent of all segments divided by 4 times the total number of segments[10].

Intra- and inter-observer variability of the extent of myocardial scarring in our center was 1.9 $\pm$ 5.1% and 2.8 $\pm$ 9.2% respectively. Our previous data showed a good correlation between visual assessment and the quantitative analysis of LGE (kappa = 0.952, $p < 0.001$) and for evaluation of the extent of the LGE (Spearman rank correlation coefficient = 0.934, $p < 0.001$)[11].

Statistical analysis

Continuous variables were described as mean and standard deviation (SD). Categorical variables were described as number of cases and percentages. Unpaired t-test was used to compare means of continuous data between ICM and NICM groups. Chi-square test was used to assess the differences of proportion of categorical variables between ICM and NICM groups. A p-value of < 0.05 was considered statistically significant. SPSS for windows (SPSS Inc., an IBM, Chicago, Illinois, USA) was used to perform the statistical analysis.

Results

A total of 98 patients were enrolled. There

were 58 patients with ICM (59.2%) and 40 patients with NICM (40.8%). Baseline characteristics of both groups are shown in Table 1. As expected patients with ICM had more cardiovascular risk factors and are on more antiplatelet medications and statins. Coronary angiography of patients with ICM showed single vessel disease in 7 (12.1%), double vessel disease in 17 (29.3%) and triple vessel disease in 34 (58.6%). CMR variables are shown in Table 2. Patients with NICM had a larger left ventricular volume, lower LVEF but a

Table 1. Baseline characteristics of patients with ICM and NICM

Variables		ICM (n = 58)	NICM (n = 40)	p-value
Age (years)		61.5 ± 8.2	59.4 ± 11.3	0.212
Male gender (%)		47 (81)	19 (47.5)	0.001
Body surface area (m^2)		1.70 ± 0.18	1.64 ± 0.17	0.093
Body mass index (kg/m^2)		24.0 ± 3.9	24.1 ± 3.8	0.862
Diabetes mellitus		29 (50)	13 (32.5)	0.085
Systemic hypertension		36 (62.1)	16 (40)	0.031
Hypercholesterolemia		42 (72.4)	13 (32.5)	< 0.001
Current smoker		21 (36.2)	4 (10)	0.003
History of chest pain		37 (63.8)	5 (12.5)	< 0.001
History of myocardial infarction		35 (60.3)	0 (0)	< 0.001
Medications	- beta blockers	35 (60.3)	17 (42.5)	0.082
	- calcium antagonists	4 (6.9)	3 (7.5)	0.909
	- nitrates	40 (69)	22 (55)	0.159
	- antiplatelet agents	54 (93.1)	27 (67.5)	0.001
	- ACE inhibitors or angiotensin blockers	41 (70.7)	32 (80)	0.299
	- statins	45 (77.6)	18 (45)	0.001
Systolic blood pressure (mmHg)		133.1 ± 21.8	125.2 ± 25.2	0.101
Diastolic blood pressure (mmHg)		79.2 ± 9.8	76.7 ± 12.8	0.263
Heart rate (bpm)		79.6 ± 10.5	78.2 ± 19.7	0.676
Q-wave from ECG		23 (42.6)	7 (22.6)	0.063

Data are presented as mean ± SD or number (%)
ICM = ischemic cardiomyopathy, NICM = non-ischemic cardiomyopathy, ACE = angiotensin converting enzyme

Table 2. Comparisons of CMR data between patients with ICM and NICM

Variables	ICM (n = 58)	NICM (n = 40)	p-value
LVDD (mm)	63.5 ± 8.2	66.7 ± 9.6	0.056
LVDS (mm)	53.5 ± 9.7	58.9 ± 11.0	0.006
LVEDVI (ml/m^2)	119.3 ± 44.2	131.0 ± 45.2	0.206
LVESVI (ml/m^2)	83.8 ± 41.9	97.1 ± 40.0	0.119
LVMASSI (gm/m^2)	69.2 ± 18.0	71.4 ± 23.4	0.601
LVSV (ml)	62.1 ± 14.2	55.6 ± 23.3	0.162
LVEF (%)	32.8 ± 9,4	27.1 ± 9.4	0.004
Wall motion score	31.8 ± 5.8	31.6 ± 5.0	0.794
Average wall thickness (mm)	4.8 ± 0.9	4.9 ± 0.9	0.682
Presence of myocardial scar	53 (91.4)	10 (25)	< 0.001
Presence of midwall scar	0 (0)	10 (25)	< 0.001
Percentages of myocardial scar (%)	30.1 ± 18.7	11.5 ± 24.1	< 0.001

Data are presented as mean ± SD or number (%)
ICM = ischemic cardiomyopathy, NICM = non-ischemic cardiomyopathy, LVDD = left ventricular diastolic dimension, LVDS = left ventricular systolic dimension, LVEDVI = left ventricular end-diastolic volume index, LVESVI = left ventricular end-systolic volume index, LVMASSI = left ventricular mass index, LVSV = left ventricular stroke volume, LVEF = left ventricular ejection fraction

similar average wall thickness. LGE was detected in 53 patients with ICM (91.5%) and 10 patients (25%) of patients with NICM. Among patients with ICM, patterns of LGE were transmural scar defined by at least 1 segment with LGE extent more than 50% in 39 patients (73.6%) and subendocardial scar in 14 patients (26.4%) (Fig. 1). Among patients with NICM who had scar, LGE was midwall location of interventricular septum in all of them (Fig. 2). Midwall scar was not detected in any patients with ICM. There were 5 patients with ICM who had no LGE from CMR. All of them had LVEF more than 40%. All ICM patients with LVEF < 40% had LGE.

Discussion

The results of this study showed that LGE was detected in 91.5% of patients with ICM and 25% of patients with NICM. The patterns of LGE were transmural or subendocardial scar in patients with ICM and midwall location in those with NICM.

Previous studies showed that CMR had a high sensitivity for the diagnosis of ICM by using LGE technique[4,5] with the sensitivity up to 100%[4]. LGE in patients with ICM may be transmural scar or subendocardial scar[3,12]. LGE was also detected in 16-65% of patients with NICM[4,5,13-15]. Patterns of LGE in patients with NICM may be midwall scar, patchy scar or subendocardial scar. Midwall scar is the most common pattern[4,13]. Our study showed that sensitivity of LGE for the detection of ICM was 91.5%. However, all ICM patients with LVEF < 40% had LGE. LVEF criteria to be included in previous studies varied from < 40% (5) to < 50%[15]. In our study LGE had the greatest value to exclude ICM among patients with LVEF < 40%. We found LGE in only 25% of patients with NICM. All LGEs in patients with NICM were midwall scar which is similar to a previous report[13]. Subendocardial scar in patients with NICM that has been reported in a previous study[4] may be related to subendocardial myocardial infarction in patients who had non-significant coronary artery disease.

Coronary angiography is the gold standard for the diagnosis of coronary artery disease. However, the procedure is considered invasive study and not without risk. Besides, it requires hospital admission and exposes patients to adverse effects of the contrast agent. There are other CMR techniques for the detection of coronary artery disease such as stress perfusion CMR[16] or coronary magnetic resonance angiography (MRA)[17]. However, coronary MRA takes a long scan time and image resolution is not as good as multi-detector computerized tomography (MDCT)[18].

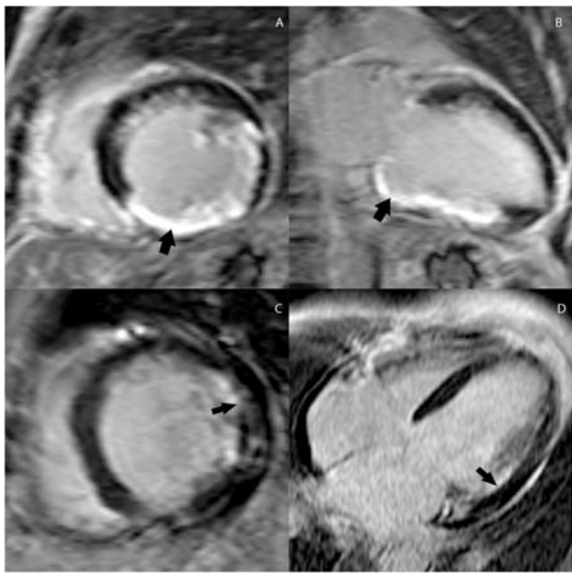

Fig. 1 LGE patterns in patients with ICM showing transmural scar (arrow) of inferior wall in short axis (A) and long axis (B) view and subendocardial scar (small arrow) of lateral wall in short axis (C) and 4-chamber view (D) in another patient

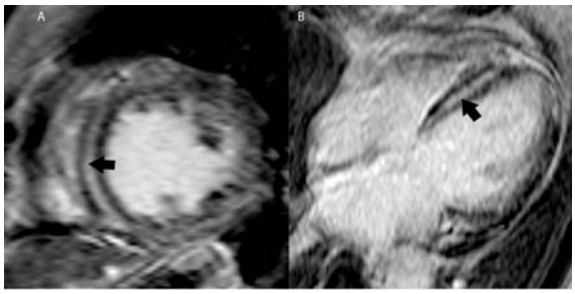

Fig. 2 LGE patterns in a patient with NICM showing midwall scar at interventricular septum in short axis (A) and 4-chamber view (B)

Sensitivity, specificity and accuracy are not as good as MDCT[19]. However, MDCT has some disadvantages. It exposes patients to a relatively high radiation dose[20] and a potentially nephrotoxic contrast agent. Besides, CMR detects myocardial scar better than MDCT[21]. Stress CMR can be performed by perfusion study with adenosine infusion or wall motion study with dobutamine stress[22]. Both of them, however, are less accurate in patients with severe left ventricular dysfunction[23,24] which is related to a difficulty in the interpretation in changes in wall motion grade with dobutamine and a false positive perfusion defect at subendocardial region with perfusion CMR due to an increase in left ventricular end-diastolic pressure.

Therefore, CMR for the assessment of cardiac function and LGE are the preferred methods for the differentiation between ICM and NICM.

In conclusion, more than 90% of patients with ICM had LGE. In fact, 100% of patients with ICM and severe left ventricular dysfunction had LGE. Midwall scar was detected in 25% of patients with NICM.

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Potential conflicts of interest

None.

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การตรวจเอ็มอาร์ไอเพื่อประเมินแผลเป็นที่หัวใจในการแยกโรคผู้ป่วยที่มีการบีบตัวของหัวใจผิดปกติ

รุ่งโรจน์ กฤตยพงษ์, ธนัญญา บุณยศิรินันท์, ไพรัช สายวิรุณพร, สุทธิพล อุดมพันธุรักษ์

ภูมิหลัง*: การวินิจฉัยโรคหลอดเลือดหัวใจตีบในผู้ป่วยที่มีภาวะหัวใจล้มเหลว จากการบีบตัวของกล้ามเนื้อ หัวใจผิดปกติมักต้องใช้วิธีการฉีดสีตรวจหลอดเลือดหัวใจ*

วัตถุประสงค์*: เพื่อศึกษาความชุกและลักษณะของรอยแผลเป็นที่กล้ามเนื้อหัวใจในผู้ป่วยที่มีสาเหตุจากโรคของหลอดเลือดหัวใจตีบ (ICM) และโรคของกล้ามเนื้อหัวใจ (NICM)*

วัสดุและวิธีการ*: คณะผู้นิพนธ์ทำการศึกษาผู้ป่วย 98 คน ที่เป็นหัวใจล้มเหลวและการบีบตัวของหัวใจผิดปกติคือค่าการบีบตัวของหัวใจห้องล่างซ้าย (left ventricular ejection fraction) น้อยกว่า 50% ผู้ป่วยทุกรายได้รับการตรวจ CMR เพื่อประเมินการทำงานของหัวใจและรอยแผลเป็นที่หัวใจ*

ผลการศึกษา*: ผู้ป่วย 58 รายเป็น ICM 40 รายเป็น NICM ผู้ป่วย NICM มีการทำงานหัวใจผิดปกติมากกว่า ICM ตรวจพบรอยแผลเป็น 91.5% ของผู้ป่วย ICM และ 25% ของผู้ป่วย NICM ลักษณะของรอยแผลเป็นของผู้ป่วย ICM เป็นแบบตลอดทั้งผนังหัวใจบริเวณที่เป็น (transmural scar) หรือเฉพาะบริเวณใกล้พื้นผิวด้านใน (subendocardial scar) ลักษณะรอยแผลเป็นของผู้ป่วย NICM เป็นเฉพาะบริเวณส่วนกลางของผนังหัวใจ (midwall)*

สรุป*: การตรวจพบรอยแผลเป็นและลักษณะของรอยแผลเป็นบนกล้ามเนื้อหัวใจช่วยแยกผู้ป่วย ICM และ NICM ได้*