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Reverse redistribution: Revisited with myocardial contrast echocardiography

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The aim of this study is to better understand the pattern and nature of reverse redistribution (RR) in myocardial perfusion imaging. In 20 consecutive acute myocardial infarction (MI) patients, frequency of RR was correlated with that of subendocardial MI that was detected by myocardial contrast echocardiography (MCE). RR was judged to be present when there was more than one grade of worsening in perfusion on 24 hr delayed images compared with the initial rest images. MCE evaluated no opacification in the subendocardial myocardium to suggest subendocardial MI.

Kendall's nonparametric correlation coefficiency was calculated. Concordant cases were 15 of 20 (75%) and correlation was statistically significant ($p = 0.0285$). Our results suggested that RR was correlated with MCE-detected nontransmural MI.

Key words: reverse redistribution, myocardial perfusion imaging, myocardial contrast echocardiography, subendocardial MI

INTRODUCTION

REVERSE REDISTRIBUTION (RR) was defined as the appearance of a defect on the redistribution image in a region with normal or near-normal initial uptake of thallium in myocardial perfusion imaging.[1] This finding was first reported by Tanasescu et al. in 1979 on exercise planar imaging with worsening defects during redistribution.[2] Since then there have been many explanations of this puzzling phenomenon, one of which was that it is a sign of nontransmural myocardial infarction with patency of the infarct-related coronary artery suggested by Weiss et al. in 1986.[3] In their paper they quoted the wavefront phenomenon, the finding from an animal experiment by Reimer et al.[4] indicating that myocardial necrosis almost always starts from the subendocardium, and that after early reperfusion, the subepicardial layers of the myocardium are the regions with most extensive salvage.

Visualization of the nontransmural involvement has become possible by the advent of a relatively new diagnostic method, myocardial contrast echocardiography (MCE).[5] MCE is unique in that by injecting microbubbles into the coronary artery it can visualize the microvascularity of the myocardium, and the microvascularity throughout the whole thickness of the myocardium, from the subendocardium to the subepicardium, is visible in the same imaging plane so that the nontransmural presence of hypoperfusion or no perfusion can be evaluated.

To better understand the nature of RR, this current study correlates the subendocardial myocardial infarction detected by MCE with the RR by myocardial SPECT imaging.

PATIENTS AND METHODS

We selected 20 consecutive acute MI patients. They had clinical symptoms of acute MI, increase in cardiac isoenzymes, or ischemic EKG findings (either Q waves or ischemic ST changes), and their maximum CPKs were 2196.9 ± 1955. Table 1 shows the patients' demographic data. There were 13 men and 7 women. Their ages were between 44 and 79 (mean age of 57.5 ± 17.6). Their infarct-related arteries (IRA) were revascularized with either primary or delayed PTCAs and we confirmed that

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Table 1 Patients' demographic data, days of PTCAs and SPECT, PTCA arteries, locations and grades of perfusion defects on the initial and delayed images, and MCE scores

No.	Age/Sex	Days from onset		Location		Grade		MCE
		PTCA	SPECT	PTCA	Defect on SPECT	Initial	Delayed	
1	F/51	7	7	d-RCA	basal inferior	mild	mod	SE
2	M/64	5	16	m-LAD	mid-anteroseptal	mild	mod	SE
3	M/48	5	5	p-LCX	lateral & inferolateral	normal	mild	SE
4	M/67	6	6	d-LCX	mid-inferolateral	mild	mod	SE
5	M/76	1	5	p-RCA	basal inferior	mild	sev	SE
6	F/66	4	6	p-LAD	mid-anterior	mod	sev	SE
7	F/45	3	4	p-LAD	mid-anterior	mild	mod	SE
8	M/44	6	6	d-RCA	apical & inferolateral	mild	mod	SE
9	M/49	3	5	m-RCA	mid-inferior	mild	mod	1
				m-LCX				
10	F/79	3	3	m-LAD	apical & anteroseptal	mild	mod	0.5
11	M/45	4	5	d-LCX	inferior apical	mild	sev	0.5
12	F/78	6	6	m&d-RCA	inferior	abs	abs	SE
13	M/56	3	8	m-RCA	inferior	abs	abs	SE
14	M/42	1	5	m-LAD	mid-anteroseptal & apical	mod	mild	0.5
15	M/72	3	6	m&d-LAD	anteroseptal & apical	sev	sev	0.5
				p-LCX	septal	mod	mod	
					inferior	sev	sev	
16	F/76	10	11	m-LAD	anteroseptal	sev	sev	0.5
					inferior	mod	mod	
17	F/59	1	5	m-LAD	anterior & apical	sev	sev	0
				d-LAD				
18	M/73	1	7	m-RCA	basal inferior	sev	sev	1
19	M/48	5	5	m-LAD	anterior & apical	abs	abs	0.5
20	M/52	8	9	m-LAD	anteroseptal & apical	sev	sev	0.5
					inferior	mod	mod	

p = proximal, m = mid, d = distal, mod = moderate, sev = severe, abs = absent, SE = subendocardial MI by MCE

there was no significant residual stenosis after the PTCA. Table 1 shows the arteries of the PTCAs. After the revascularization, MCE by intracoronary injection of the microbubbles into the IRA was performed; sonicated Hexabrix 3 m*l* were injected. Within 24 hours of the MCE, myocardial SPECT imaging was performed. The time from the onset to the PTCAs and the SPECT imaging is shown in days in Table 1. Rest images within 15 min of intravenous injection of 111 MBq (3 mCi) of thallium and 24-hour delayed images were obtained. A Butterworth filter was used with an order of 5 and a cutoff value of 0.38 to process the images.

The MCE was evaluated as to whether or not it showed subendocardial MI. There were three grades of opacification for microvascularity of the myocardium: 1 for normal opacification, 0.5 for partial opacification, and 0 for no opacification. Subendocardial MI was diagnosed when there was no opacification in the subendocardial myocardium with the opacification confined to the epicardium.

The perfusion defects on myocardial perfusion images were semiquantitatively graded to be mild, moderate, severe, or absent by visual analysis. Percent uptake was not used for grading. RR was judged to be present if there was more than one grade of worsening in myocardial perfusion on the 24 hour delayed images.

Table 2 2 × 2 table of myocardial contrast echocardiography that detected nontransmural MI and myocardial perfusion SPECT imaging that observed reverse redistribution. Correlation was significant (p = 0.0285)

SPECT \ MCE	+	−	
+	8	3	11
−	2	7	9
	10	10	20

Nonparametric Kendall correlation coefficiency was calculated with a SAS statistical package, and a p value less than 0.05 was considered to be significant.

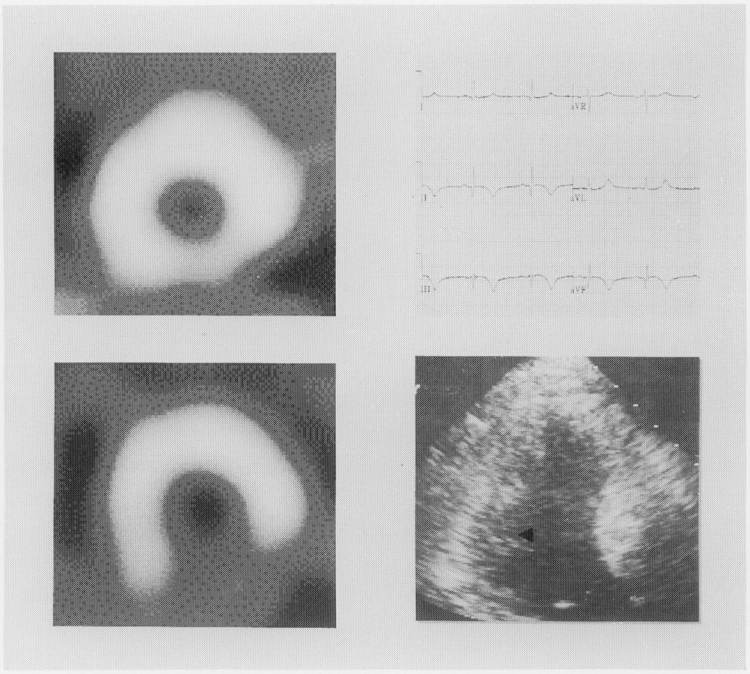

Fig. 1 These SPECT images show the RR and concordant nontransmural MI detected by MCE. There is a large moderate perfusion defect in the inferior wall on the rest images (left top) that is worsened to become a larger severe defect on the delayed images (left bottom). The MCE (right bottom) demonstrates no opacification of the subendocardium in the inferior wall (arrow) with intact microvascularity of the overlying subepicardial myocardium, representing a nontransmural MI. The ECG (right top) taken at this time shows the presence of Q-waves.

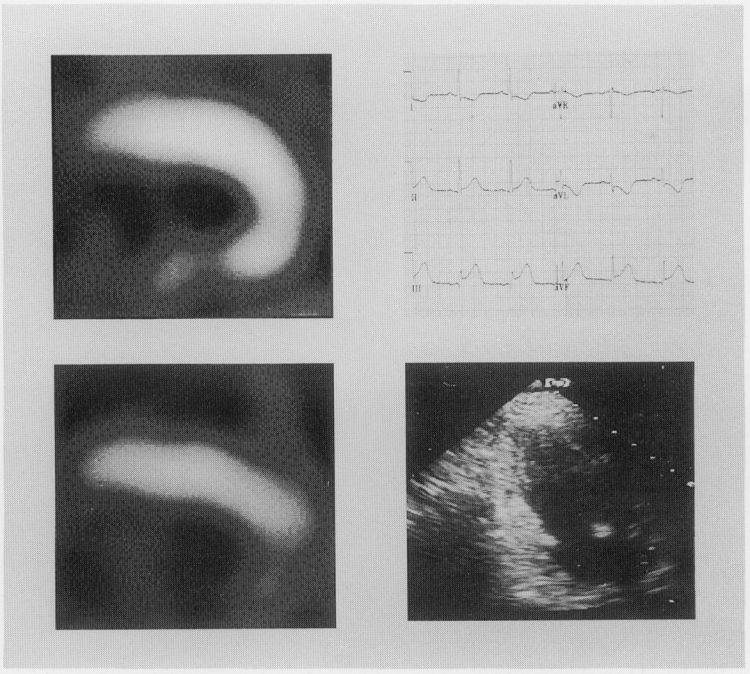

Fig. 2 This shows discordant findings. Whereas there is RR in the inferior wall, the MCE shows patchy microvascularity of 0.5 grade opacification throughout the entire myocardium. The ECG shows no Q-waves but ischemic ST changes.

RESULTS

The detailed locations and grades of the perfusion defects on the initial and delayed images are shown in Table 1. There was no case with normal perfusion detected by SPECT. If a case was not of subendocardial MI by MCE, it was of transmural MI with various opacifications. As shown in Table 2, concordant cases were 15 of 20 (75%); 8 were positive and 7 negative in both tests. Statistical analysis proved that the correlation between the MCE-positive (subendocardial MI) cases and the SPECT-positive (cases with RR) cases was significant (Kendall correlation coefficiency of 0.5025 with a p value of 0.0285).

Figure 1 shows a case of the MCE-positive and SPECT-positive cases. All eight such cases had Q-waves in the ECG. Figure 2 shows one example of the three MCE-negative and SPECT-positive cases. All three such cases had no Q-waves but ischemic ST changes.

DISCUSSION

Although the pattern of RR was first observed on exercise planar imaging with worsening defects during redistribution,[2] a similar pattern has been reported in various imaging protocols: either exercise or pharmacologic stress[6] and rest images, rest and redistribution images,[7,8] with[6,9] or without reinjection, or with 24 hour further delayed images.[10,11] It is therefore considered appropriate to define the RR as the appearance of a defect on the redistribution or delayed image in a region with normal or near normal initial uptake of thallium in myocardial perfusion imaging.[1] Pace et al. further typed the RR into an RR-A (normal rest and abnormal redistribution) or an RR-B (abnormal rest and worsened redistribution) with a suggestion of a difference in viability between them.[12] The RR has also been observed in the myocardial perfusion imaging with MIBI.[8,13,14]

The RR is observed in a mixture of viable and nonviable myocardium and implies preserved regional blood flow.[1] The IRAs of all our cases were successfully revascularized by PTCA and their reperfusion was confirmed. Being nontransmural is a form of a mixture of viable and nonviable myocardium and is observed almost always in the form of subendocardial MI, not of subepicardial MI.[3]

Inherently, myocardial SPECT imaging cannot evaluate the nontransmural characteristic, because it can only measure a total radioactivity through the whole thickness of the myocardium to judge its degree of perfusion. On the other hand, MCE is able to evaluate with considerable certainty whether any perfusion defects are nontransmural or transmural.

It is noteworthy that the transmural involvement does not always coincide with the presence of Q-waves in the ECG. According to a study that investigated autopsy findings, not all (67%) of the transmural MIs had Q-waves and a good proportion (30%) of the nontransmural (or subendocardial) MIs had Q-waves.[15] This discrepancy was also observed in our cases.

Interestingly, all three cases that had positive RR and negative MCE had no Q-waves but ischemic ST changes, findings of so-called ST MIs. Those cases had been followed up to show improved wall motion in later studies. This raises the question whether myocardial SPECT imaging, by observing RR, performs better than MCE in detecting the mild nontransmural, i.e. subendocardial MI, that provides a better prognosis than transmural MI.

We are not entirely convinced that the MCE can detect all the nontransmural MIs without any problems. The MCE uses semiquantitative visual analysis with three-tiered grades, and the intermediate 0.5 is sometimes not easy to grade. Taking the limitations of the two tests into consideration, we did not consider it appropriate to analyze the sensitivity and specificity, because neither of the tests was a gold standard test in evaluating the true nontransmural involvement and perfusion. Nonetheless, there was a significant correlation between the findings in the two tests that surely warrants confirmation with a large-scaled study.

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