ORIGINAL ARTICLES

Perfusion and Contrast Agents

Mechanism and Clinical Significance of Precordial ST Depression in Inferior Myocardial Infarction: Evaluation by Contrast-Enhanced Dynamic Myocardial Perfusion Magnetic Resonance Imaging

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ABSTRACT

We elucidated the mechanism and clinical significance of precordial ST depression in patients with an inferior myocardial infarction using first-pass, contrast-enhanced, myocardial perfusion magnetic resonance imaging (MRI). Forty-seven patients with acute inferior myocardial infarction underwent first-pass contrast-enhanced MR studies within 2–6 days postinfarction. Patients were followed-up for a minimum of 1 year after infarct (range, 12–32 months). Total perfusion deficit scores derived qualitatively from MRIs were compared in patients with (group 1, n = 30) and without (group 2, n = 17) ST depression precordially. Perfusion remote from the infarct zone was also compared. The combined end points of adverse clinical events and/or the need for further intervention were assessed for each group. Total perfusion deficit scores were significantly higher in group 1 than group 2 (medians 9.7 versus 4.5, $p < 0.005$). Posterolateral basal extension of hypoperfusion was greater in group 1 versus group 2 (1.23 versus 0.42, $p < 0.02$), with no evidence of remote anterior perfusion abnormalities. There were more patients with an adverse clinical end point in group 1 versus group 2 (18 versus 1, $p < 0.01$). Furthermore, in patients with ST depression (group 1), there was a significant increase in number of adverse clinical end points in patients with a global deficit score > 15 versus 0–5 (7/7 versus 1/7, $p < 0.01$). MRI shows that precordial ST depression in inferior myocardial infarction is a marker for a larger global perfusion abnormality with posterolateral basal extension and an increase in adverse clinical end points. Furthermore, the magnitude of the perfusion deficit

121

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correlates with an increase in the number of adverse clinical end points, highlighting the potential of MRI perfusion studies as a research and clinical tool in myocardial infarction.
KEY WORDS: *Magnetic resonance imaging; Myocardial infarction; Precordial ST depression; Clinical outcome.*

INTRODUCTION

Precordial ST depression is frequently observed in patients with acute inferior wall myocardial infarction. Early clinicopathologic studies suggested that the mechanism was due to a larger infarct with extension to the posterolateral wall of the left ventricle (1). However, subsequent studies using a variety of imaging techniques to determine the significance of this finding have yielded conflicting results. Left ventricular angiography (2), radionuclide wall motion studies (3), thallium perfusion imaging (4,5), and echocardiography (6) performed within hours or days of the infarction show more extensive infarction in patients with precordial ST depression, particularly posterolateral, septal, and inferoposterior extension of the inferior infarct. In addition, the presence of precordial ST depression is associated with more extensive left ventricular dysfunction and higher peak serum creatine kinase levels and an adverse prognosis (7–11). However, other reports ascribe these findings to a benign electrical phenomenon due to "reciprocal" changes, reflecting the degree of inferior wall ST elevation (12–14) without the concomitant group differences in left ventricular function and cardiac enzyme rise. There is conflicting evidence regarding the benefit of reperfusion therapy in inferior myocardial infarction (15,16); therefore, it would be useful to identify whether the electrocardiographic sign of precordial ST depression in inferior infarction identifies a larger area of myocardium at risk with an adverse outcome because these patients are more likely to benefit from thrombolysis (17).

Some studies have also reported that remote *anterior* ischemia (18) is responsible for precordial ST depression due to either a larger arterial supply of the infarct artery (19) or concomitant left anterior descending artery disease, which is unmasked by interruption of the right coronary or circumflex artery that may have been enhancing remote regional perfusion by collaterals, so-called ischemia at a distance (20). Nevertheless, attempts to correlate the extent of coronary disease or disease of the left anterior descending coronary have produced conflicting results (2,21–24).

It has recently become possible to obtain qualitative and semiquantitative estimates of myocardial perfusion using contrast-enhanced, ultrafast, cardiac-gated mag-

netic resonance imaging (MRI) (25). The high temporal and spatial resolution allows regions of infarcted myocardium to be delineated as areas showing reduced enhancement (26). The noninvasive and nontoxic nature of MRI make it a potentially attractive technique. However, no studies to date have demonstrated whether MRI can elucidate the perfusion correlates of precordial ST depression in acute inferior myocardial infarction and whether such measurements can predict clinical outcome. Therefore, we prospectively studied a group of patients with acute inferior myocardial infarction using MRI.

METHODS

Patients

From November 1993 to October 1996, 103 patients admitted to our coronary care unit with a first myocardial infarction were enrolled into a study assessing myocardial-perfusion MRI using a new contrast agent, gadobenate dimeglumine (MultiHance®, Bracco, S.p.A, Milan, Italy), and compared with electrocardiogram (ECG) for the detection of myocardial infarction. Forty-seven patients satisfied the following criteria for inferior myocardial infarction: typical history of prolonged ischemic pain; serial ECG changes of both ST elevation greater or equal to 0.1 mV and new pathologic Q waves in two or more in limb leads II, III, or aVF; and a twofold or greater rise in creatine kinase, creatine kinase-MB isoenzyme, and lactic dehydrogenase. Patients with intraventricular conduction blocks or who had left ventricular hypertrophy were excluded. No patients were included who were being treated with cardiac glycosides. Forty-five of 47 patients (96%) underwent thrombolysis with streptokinase within 6 hr of onset of chest pain. The study was approved by the locally appointed ethics committee, and informed consent was gained from all study patients.

Electrocardiography

All patients had a 12-lead ECG within a mean time of 3.8 ± 2.2 hr after the onset of chest pain before thrombolysis. ECGs were reviewed by a cardiologist blinded to the remaining data. Significant precordial ST depression was defined as greater or equal to 0.1 mV downslop-

ing ST depression measured 80 msec after the J point in two or more of ECG leads V_1 to V_4. These patients were assigned to group 1, and patients without significant precordial ST depression were assigned to group 2.

Clinical Follow-Up

After discharge each patient was followed by contacting the general practitioner by letter or phone. The clinical status of each patient was assessed at a minimum of 1 yr postinfarction (range, 12–32 months; mean, 17 months) for end points, including adverse clinical events, and/or the need for further intervention. Adverse clinical events were classified as death or reinfarction. The need for further intervention was classified as angina necessitating coronary angiography and also whether the patient went on to have percutaneous coronary angioplasty or coronary artery bypass surgery.

Magnetic Resonance Imaging

All patients underwent MRI within 2–6 days of the infarct, using a 1.0-T Siemens Magnetom Impact (Siemens, Erlangen, Germany) scanner. The patients had precordial ECG electrodes applied for cardiac gating of the images before being placed in the isocenter of the magnet. Three double-oblique short-axis planes through the left ventricle were acquired sequentially—basal, mid-left ventricular (through the papillary muscles), and apical—using a snapshot-fast low-angle shot (FLASH) sequence (27). This sequence used a 180° inversion pulse to provide T1 contrast, followed by a FLASH acquisition with a very short echo time (2 msec) and repetition time (4.7 msec). The flip angle of the excitation pulses was 8°, with a 64 × 64 data matrix, a 250-mm field of view, and slice thickness of 10 mm. Image acquisition commenced 300 msec after the inversion pulse and was gated to the ECG so that image acquisition occurred during late diastole, thus minimizing motion artifacts. An image at each anatomic position was acquired approximately every six heartbeats, with a total of 20 images at each of the three levels.

Perfusion was assessed by injecting the contrast agent gadobenate dimeglumine (0.05 mmol/kg body weight) via the antecubital vein after the fifth image. Before contrast injection, the sequence gave low signal intensity throughout the myocardium. As the contrast reached the heart, "normal" myocardium enhanced homogeneously, whereas hypoenhancing regions were interpreted as a perfusion defect. An MRI radiologist with good experience in the interpretation of cardiac MRIs and blinded to

the rest of the data divided each short-axis oblique slice into 10 regions of interest (ROI) equally spaced circumferentially to allow a systematic grading scheme. A perfusion score using a four-point ordinal scale from 0 to 3 (0, normally enhancing myocardium; 1, mild hypoenhancement; 2, moderate hypoenhancement; 3, marked hypoenhancement) was used for each ROI. The reference standard for the degree of hypoenhancement was the enhancement pattern and peak seen in apparently normal ROIs remote from the involved area. The given score indicated the maximum level of hypoenhancement seen over the whole series of images. No attempt was made to account for the pattern of hypoenhancement within the ROI (e.g., the lateral extent or the extension through the thickness of myocardium). The ROIs were assigned to conventional anatomic locations as shown in Fig 1.
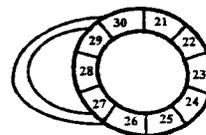
BASAL
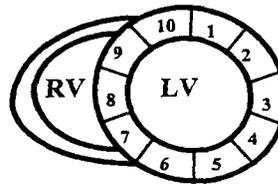
ROI Basal slice	Anatomical location
1,2	Anterior
3	Anterolateral
4	Posterolateral
5,6	Posterior
7	Posteroseptal
8	Septal
9,10	Anteroseptal

MID LV
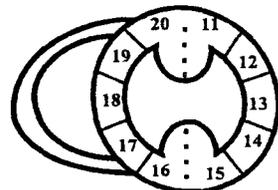
ROI Mid-LV slice	Anatomical location
11,12	Anterior
13	Anterolateral
14	Posterolateral
15,16	Posterior
17	Posteroseptal
18	Septal
19,20	Anteroseptal

APICAL

ROI Apical slice	Anatomical location
21,22	Anterior
23	Anterolateral
24	Posterolateral
25,26	Posterior
27	Posteroseptal
28	Septal
29,30	Anteroseptal

Figure 1. Schematic of the three anatomic slice locations acquired by MRI. Each slice is radially divided into 10 regions of interest that are then allocated to anatomic regions as indicated. LV, left ventricle; MID LV, mid left ventricle slice; ROI, regions of interest; RV right ventricle.

Assignment of Regional Score

Where two segments represent one anatomic area, such as the basal anterior region of the heart constituted by ROI 1 and 2, a regional perfusion score was derived by taking the mean perfusion scores for each segment, increasing the four-point ordinal scale to a seven-point scale with the following possible grades: 0, 0.5, 1, 1.5, 2, 2.5, and 3 for each anatomic segment. For example, if ROI 1 scored 1 and ROI 2 scored 2, the score for the anterior segment would be 2 plus 1 divided by 2, i.e., 1.5. A perfusion index for each anatomic region was calculated by averaging the scores for the relevant segment in all patients.

Assignment of Total Perfusion Deficit Score

A total perfusion deficit score for MRI was assigned to each patient by summing the perfusion scores in all 21 anatomic regions to gain a global impression of perfusion abnormality in each patient.

Statistical Analysis

The nonparametric Mann-Whitney U test was used to compare ranked regional perfusion scores in groups 1 and 2 and total perfusion deficit scores for all regions. Because the perfusion deficit index is a categoric scale, standard deviations are not given in Table 2. The two-tailed Student's t-test was used to compare interval data such as cardiac enzyme differences, and results are expressed as means ± SD. Fisher's exact test was used to compare the frequency of a particular characteristic or adverse clinical event in group 1 versus group 2. A $p < 0.05$ was considered significant.

RESULTS

Electrocardiographic and Enzymatic Findings

Thirty patients (64%) demonstrated ST depression in precordial leads V_1 to V_4 (group 1), and in 17 patients (36%) this finding was absent (group 2). Group 1 showed a larger peak creatine kinase-MB and lactate dehydrogenase level than group 2, although this did not reach statistical significance. The clinical characteristics of the two groups are described in Table 1.

MRI Findings

There was a significantly larger total median perfusion deficit score in group 1 compared with group 2 (9.7 versus 4.5, $p < 0.005$) (Fig. 2). The MRI perfusion deficit index for 21 anatomic regions is shown in Table 2. As expected from the presence of inferior infarction on the ECG, the maximum deficit with MRI was seen in the posterior segments (ROI 5 and 6) of the basal and mid-left ventricular slices. In these segments, there was no significant difference between groups 1 and 2. However, group 1 patients had significantly greater regional deficit in the posterolateral segment of the basal slice (1.23 versus 0.41, $p < 0.02$). Figure 3 illustrates the posterolateral extension of the infarct demonstrated in actual images from patients. The adjacent anterolateral segment also showed significantly greater deficit in group 1 versus 2 ($p < 0.05$). The anteriorly located segments (anterior and anteroseptal) showed no significant deficit in either group.

Clinical Follow-Up

The clinical outcomes of patients in both groups 1 and 2 are shown in Table 3. There was a significantly higher

Table 1

Clinical and Electrocardiographic Characteristics of Patients

	Entire Study Group	Group 1	Group 2	p
No. of patients	47	30	17	
Age (yr)	58.0 ± 11.2	58.3 ± 11.5	57.3 ± 11.0	NS
Male (%)	87 (41/47)	100 (30/30)	65 (11/17)	<0.01
Pain to ECG (hr)	3.8 ± 2.2	3.8 ± 1.9	3.8 ± 2.7	NS
CK-MB*	197 ± 93	209 ± 95	176 ± 90	NS
LDH*	2096 ± 895	2170 ± 977	1981 ± 761	NS

Values are means ± SD. CK-MB, myocardial creatine kinase.
*Measured peak.
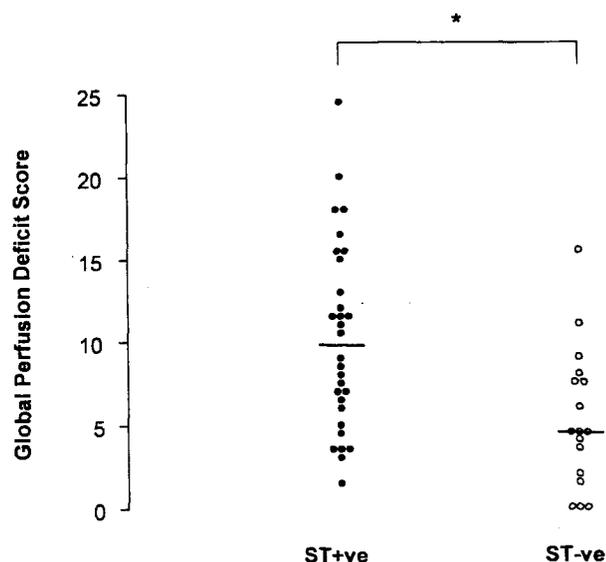
Figure 2. Total summed perfusion deficit scores for all regions of interest as measured with MRI for patients both with and without precordial ST depression. ST + ve, patients with inferior infarction and additional ST depression greater than or equal to 0.1 mV in two or more ECG leads V_1 to V_4. ST-ve, patients with inferior infarction and no ST depression. Bars indicate median value. $*p < 0.005$.

number of adverse clinical end points in patients in group 1 compared with group 2 (18 versus 1, $p < 0.01$). When the 30 patients with precordial ST depression (group 1) were ranked according to their global perfusion deficit score, there was a progressive increase in the number of

end points as the severity score increased, with a significant difference in patients with a score >15 versus 0–5 (7/7 versus 1/7, $p < 0.01$) (Fig. 4).

DISCUSSION

This is the first study of its kind by using an MRI perfusion technique to assess the mechanism of precordial ST depression in inferior myocardial infarction and correlate it with clinical follow-up. The snapshot-FLASH technique tracks a bolus of contrast in its first pass through the myocardium. The gadolinium compound is largely intravascular in its first pass through the myocardium and rapidly equilibrates to the extravascular space; thus, low signal intensity for the infarcted regions is due to the fact that no gadolinium has reached this part of the tissue during the initial enhancement phase, and therefore the images give an indication of regional tissue perfusion (25). Moreover, the area of perfusion deficit in infarcted regions demonstrated with MRI correlates well with fixed defects that are seen with thallium-201 single-photon emission tomography (26). In view of this correlation, the perfusion deficit scores used in our study may be regarded as an index of infarct size.

The main finding in our study was that MRI showed a larger global perfusion abnormality in the group with precordial ST depression, and on regional analysis this proved to be due to extension of the inferior perfusion deficit to the posterolateral wall. Furthermore, patients with precordial ST depression had a significantly higher number of adverse clinical end points and the event rate correlated with the degree of total perfusion abnormality.

Table 2

Regional Myocardial Perfusion Deficit Scores as Measured with Contrast-Enhanced MRI in Patients With and Without Precordial ST Depression in Inferior Myocardial Infarction

|	Regional MRI Perfusion Scores at Each Level								
	Basal			Mid-LV			Apical		
	ST+ve	ST-ve	p	ST+ve	ST-ve	p	ST+ve	ST-ve	p
Anterior	0.17	0.00	nc	0.00	0.00	nc	0.03	0.00	nc
Anterolateral	0.57	0.06	0.04	0.23	0.00	nc	0.10	0.00	nc
Posterolateral	1.23	0.41	0.01	0.87	0.30	0.07	0.27	0.06	0.40
Posterior	1.32	0.98	0.26	1.03	0.62	0.19	0.45	0.41	0.62
Posteroseptal	1.00	0.76	0.57	0.87	0.70	0.59	0.60	0.29	0.09
Septal	0.33	0.00	nc	0.50	0.35	0.51	0.37	0.12	0.51
Anteroseptal	0.05	0.00	nc	0.18	0.09	0.62	0.10	0.09	0.91

ST+ve, ST depression ≥ 0.1 mV in two or more ECG leads V_1 to V_4; ST-ve, no significant ST depression; nc, not computable by Mann-Whitney test as one of the data sets contains a null value.
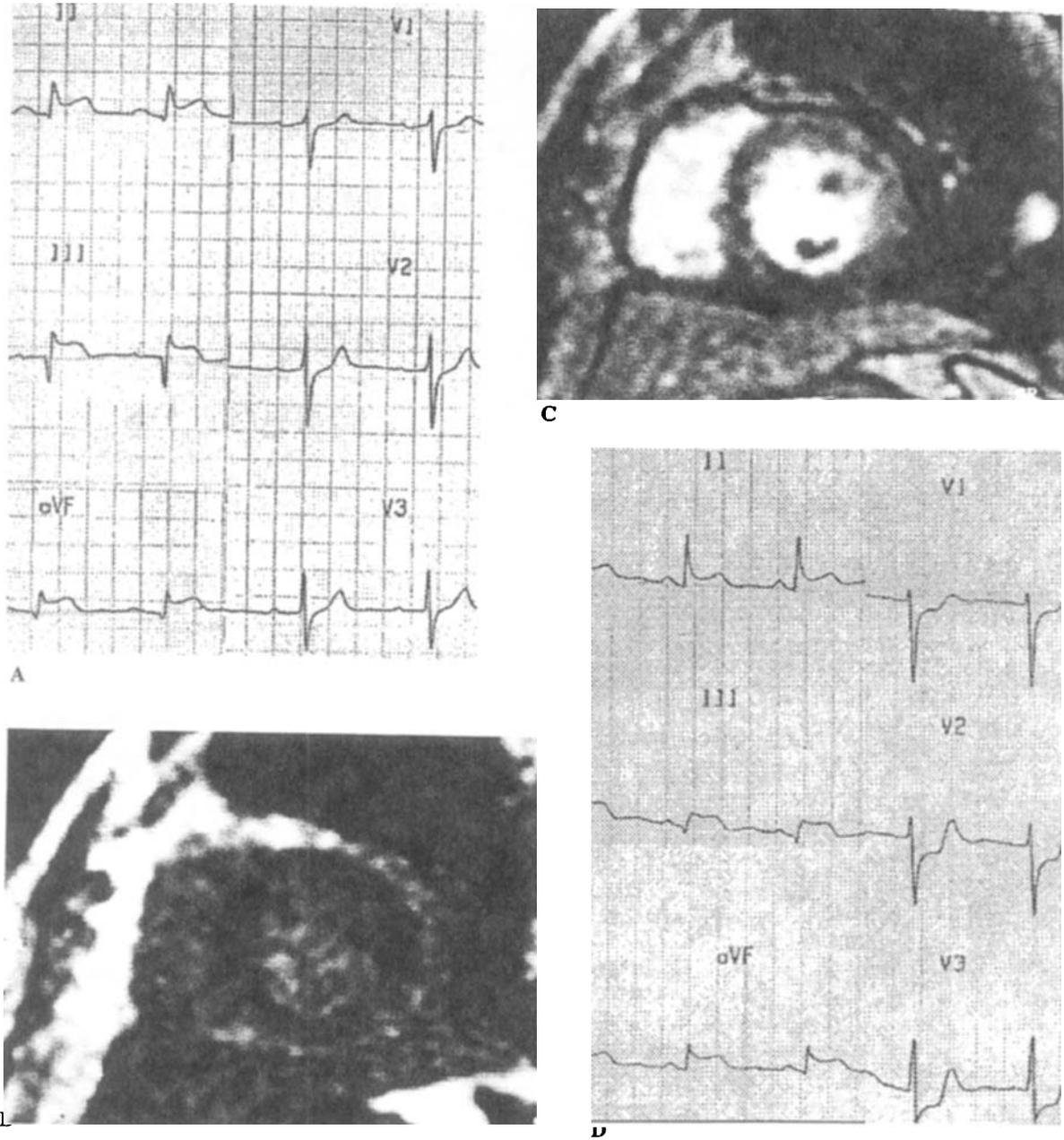
Figure 3. (A) ECG of patient with acute inferior infarction alone (ST elevation in limb leads II, III, and aVF) with (B) MRI image to show precontrast image at the basal level, where the myocardium is nulled. (C) Postcontrast image with area of low signal intensity confined to the posterior segments (ROIs 5 and 6) and no lateral extension. (D) ECG of patient with acute inferior infarction (ST elevation in limb leads II, III, and aVF) and additional ST depression in precordial leads V_1 to V_3 with (E) corresponding precontrast MRI image at the basal level and (F) postcontrast image with area of low signal intensity extending laterally to ROI 4 and 3.
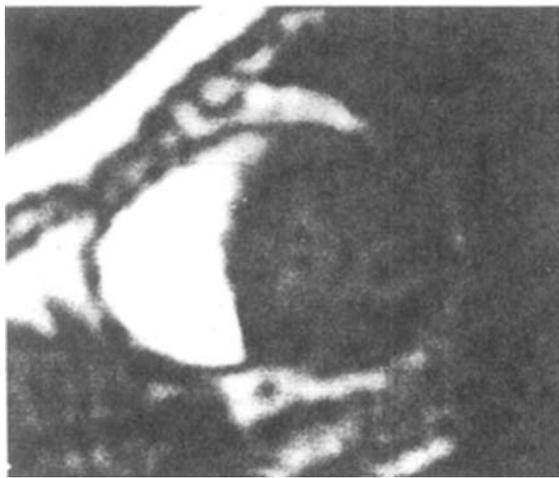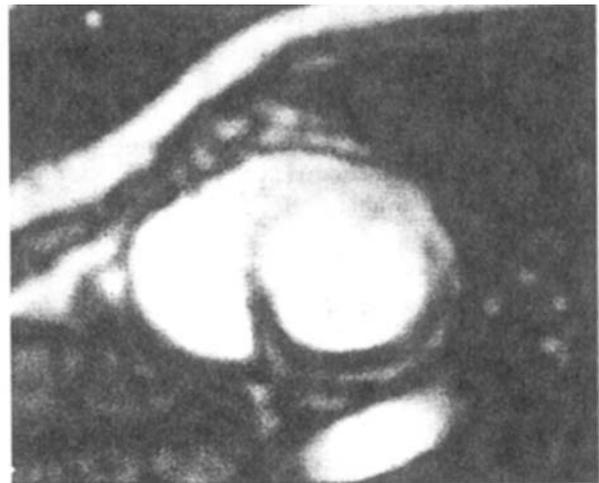
E   F

Figure 3. Continued

Precordial ST depression in patients with inferior myocardial infarction has been the subject of investigation for nearly half a century, starting initially with postmortem correlations with ECGs in patients who had died of their infarction in the acute phase (1). These studies suggested that the patients with inferior infarction and additional ST depression had more extensive infarction with posterobasal and posterolateral extension of the infarct, and the ST depression represented cross-cavity vectoral representation of the inferior ECG. However, an assortment of studies performed within hours to weeks after the infarct have reached a variety of conclusions about the mechanism of precordial ST depression in inferior wall infarction. In the prethrombolytic era, a number of studies provided evidence that patients with precordial changes had sustained larger infarcts, including signifi-

cantly higher cardiac enzyme rises (3,23). Other investigators disputed this, arguing that it simply represents a reciprocal electrical phenomenon with no difference in infarct size between patients with and without additional ST depression (12,13,28). However, a recent 16,521 patient study where all patients underwent thrombolysis added further weight to the argument that precordial ST depression is associated with a larger infarct (10). In addition to revealing a larger perfusion abnormality in pa-

Table 3

Follow-up Clinical Data on Patients at Minimum of 1 yr

	ST−ve (n = 17)	ST+ve (n = 30)
Deaths	0	1
Further MI	0	3
Angina requiring angiography	1	9
PTCA	0	3
CABG	0	2
Total events	1	18*

MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting.
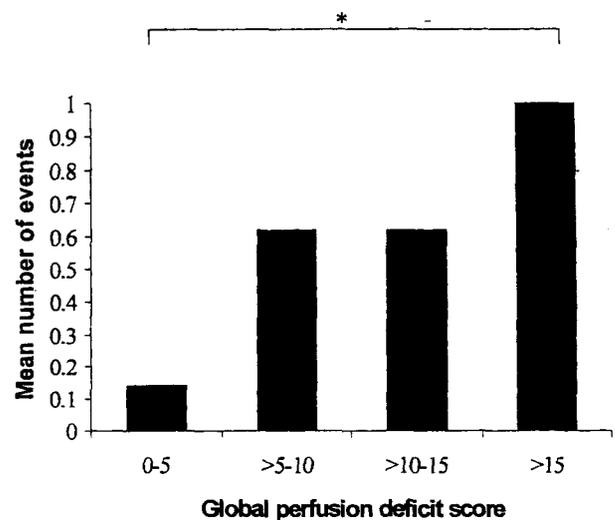* $p < 0.01$.

Figure 4. Mean number of clinical end points according to grade of perfusion deficit index in patients with precordial ST depression. *$p < 0.01$.

tients with additional precordial ST depression, our study also showed a higher measured peak cardiac enzyme level in this group, although this did not reach statistical significance. This may be due to the confounding effect of reperfusion in most of our patients, which makes the interpretation based on measured peak enzyme levels unreliable because of washout (29).

Our study suggests that the anatomic location of the larger perfusion deficit in the patients with additional ST depression is due to extension of the inferior infarct to the posterolateral wall, which is in keeping with clinico-pathologic studies (1) using other imaging modalities, including radionuclide ventriculography (3), x-ray ventriculography (30), qualitative (4) and quantitative (5) thallium planar scintigraphy, echocardiography (6), and technetium SPECT (31). Furthermore, the perfusion of the anterior and anteroseptal regions was normal, implying remote ischemia in the territory of the left anterior descending artery was not a mechanism for ST depression, which again agrees with previous studies (4,23, 32,33). However, the anterolateral segment also showed significantly greater hypoperfusion in group 1 patients. This is almost certainly due to extension from the posterolateral segment and does not imply remote ischemia but extensive posterolateral involvement with some overlap into the anterolateral territory, as previously observed (23).

Even in the posterior segments (ROI 5 and 6) that showed the maximum deficit, the mean scores for the regional perfusion deficit were perhaps lower than one might expect given the recent infarction in this territory. Figure 2 shows that 17 patients (36%) had total perfusion deficit scores between 0 and 5, indicating virtually normal perfusion, which may be a reflection of reperfusion after thrombolysis in these subjects. This is consistent with angiographic studies after streptokinase that have shown a fully patent artery in 35% of patients. The effect of reperfusion would have diluted the overall scores and reduced the mean.

The clinical significance of precordial ST depression in inferior myocardial infarction has been disputed in previous studies, some of which support the notion that this sign is associated with an increase in adverse clinical end points (7–11), whereas others refute this (12–14). In our study we observed an increase in the number of adverse clinical end points at 1 yr in the group with precordial ST depression. Furthermore, in those with ST depression there was a concomitant increase in the mean number of adverse clinical end points as perfusion deficit score increased. The precise reason for this striking correlation remains to be elucidated but probably reflects either the

infarct size or extent of coronary disease. Our findings suggest future potential in this noninvasive imaging modality to assist therapeutic decision making and give prognostic information in patients with acute myocardial infarction.

Limitations of This Study

The MRI sequence only gives three short axis levels through the left ventricle and so the evaluation is not comprehensive. The apex is particularly difficult to assess because of the thick slices, where partial volume effects of overlapping myocardium and contrast in the ventricle give rise to difficulty in interpretation of the apical perfusion. This may be why the apical perfusion deficit scores were consistently lower than the other levels. It would be desirable to have a long-axis apical view similar to standard tomographic reconstruction using SPECT. Our particular study was more concerned with observing changes in the basal slice, which was not hampered by this limitation, but conclusions about apical involvement have to be tentative. Our technique only provided one slice every six heart beats, but rapid advances in MRI scanners and sequences now make it possible to image the entire heart in a single beat, which will allow a more comprehensive evaluation of the ventricle in future (34).

Qualitative evaluation has been shown to be an acceptable method in the analysis of planar and SPECT thallium scans, but there is as yet limited knowledge with MRI. Methods for assessing myocardial perfusion quantitatively are under development and show early promise (35,36).

CONCLUSIONS

We have shown that first-pass contrast-enhanced MRI can demonstrate perfusion abnormalities in patients with inferior myocardial infarction, adding further evidence that patients with additional precordial ST depression have a significantly larger total perfusion deficit score and higher degree of posterolateral basal wall involvement. Furthermore, this translates to a larger number of adverse clinical end points.

Finally, there is a progressive increase in the mean number of adverse clinical end points as the perfusion deficit measured with MRI worsens. In view of the noninvasive and potentially quantitative nature of MRI, it may have a clinical role in assessing eligibility and success rate for the most effective reperfusion strategy and prognosis in myocardial infarction.

ACKNOWLEDGMENTS

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