

Comparison Of Cardiac MR And 99m^{Tc} Sestamibi Spect In The Evaluation Of Myocardial Perfusion And Viability In Coronary Artery Disease

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Abstract

Objective- The present study was designed to compare the role of 99mTc sestamibi scintigraphy (SPECT) and cardiac MR (CMR) in the detection of viable myocardium and to delineate myocardial scar tissue in patients with established chronic ischemic heart disease.

Methods- Thirty six patients with established chronic ischemic heart disease on coronary angiograms which was the gold standard underwent both stress CMR and 99mTc sestamibi studies. Out of these 11 patients who had reduced end diastolic thickness <5.5mm alongwith wall motion abnormalities also underwent dobutamine MR (DMR) for determining the contractile myocardial reserve.

Results- Both CMR and SPECT showed a good correlation in the detection of perfusion defects ($r=0.89$) with the diagnostic region of operating characteristics being 0.97. The sensitivity and specificity of SPECT to detect perfusion defects were 82.6% and 90.4% respectively. In comparison CMR had a sensitivity, specificity of 92.8% and 98.2% respectively in identifying such defects. It was also superior in defining transmural infarcts(TMI) with sensitivity being 100% vs 79.3% of SPECT ($p<0.0001$) and all the 10 segments with TMI showed irreversible myocardial dysfunction on DMR. This was the only imaging parameter that indicated myocardial non viability with a specificity of 100%.

Conclusions- CMR is a useful diagnostic tool in the evaluation of patients with chronic myocardial ischemia and is superior to SPECT in the detection and quantification of myocardial infarctions. Demonstration of a TMI on CMR is a finding strongly associated with non viability of the myocardium and may preclude the need for doing a DMR in such cases.

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INTRODUCTION

Ischemic heart disease is one of the leading cause of death world wide. Currently, thallium or 99mTc sestamibi SPECT scans are the most common noninvasive method of evaluating patients with suspected myocardial ischemia. However, these studies have pitfalls due to limited spatial resolution, difficulty in evaluating the inferior wall of the left ventricle adjacent to the diaphragm, and also lack penetration in obese patients (1). With routine MR imaging acquisition techniques, a robust CMR examination was inconceivable because of unacceptably long examination time and motion artifacts. Recent developments in MRI hardware and software have resulted in improved gradient performance, faster imaging and

improved image quality(2). CMR imaging protocols in both resting state and with pharmacological stress are now being advocated in coronary artery disease patients for combined evaluation of cardiac function, myocardial perfusion and viability(3). The technique of first-pass contrast imaging on CMR can not only help assess myocardial perfusion with accuracy similar to that of conventional nuclear techniques but with higher spatial resolution and freedom from attenuation artifacts (2,3). Similarly the late enhancement seen on CMR after the injection of contrast agent is also being suggested as a sensitive marker of myocardial viability as it depicts the transmural extent and also allows quantification of nonviable myocardial tissue (4,5,6). With this background the present study was designed to compare the results

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of both the CMR and SPECT in patients with clinically established chronic ischemic heart disease for a) Detection of myocardial ischemia b) Extent of myocardial infarcts c) Assessment of myocardial viability.

MATERIAL AND METHODS

Thirty six patients with clinical diagnosis of chronic ischemic heart disease who had any of the following: >70% stenosis on coronary angiogram (the gold standard), positive stress test, class II to III angina with EKG ST-T changes, clinical evidence of previous myocardial infarction; were taken up for stress myocardial perfusion studies using 99mTc Sestamibi and contrast enhanced CMR

All patients underwent the examination in the presence of a cardiologist Akh * and cardiac radiologists Ak #, GM** in the MR suite.

The CMR examination was performed on a 1.5 Tesla MRI (Symphony Maestro class, Siemens, Erlangen, Germany AG) with 30mT/m Sprint class gradient system.

The patient was made to lie supine and two 20 G IV access lines were obtained in both the cubital veins. 4 electrodes leads were applied on the chest followed by a 4 channel phased array torso coil.

The study protocol involved the following steps

1. Multilocalisers:

True FISP(fast imaging in steady precession) three slice multilocalizer views were taken in axial, coronal and sagittal planes followed by 2 chamber, 4 chamber and short axis localisers.

2. Resting Cardiac Function:

Multiple 8 mm thickness sections with interslice gap of 4 mm from base to the apex of the heart in short axis views were obtained using Cine True Fisp sequence with following parameters: TR/TE 29.7/1.32, FOV 280mm phase resolution 84% bandwidth 977 Hz segmentation 20; 25 phases/cardiac cycle . The quantitative analysis of the data collected was done on Argus soft ware (Siemens, Erlangen Germany AG).

3. Stress myocardial perfusion :

IV adenosine infusion was started using 140microgram/Kg/mt for 6 minutes and 0.1 mmol/Kg body weight intravenous gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) was injected in the other vein at 3 minutes followed by 10cc flush of saline. Breathold three short axis views at the base mid and distal left ventricle level were taken using dynamic segmented k-space gradient-echo pulse Turboflash sequence- TR/TE /FA 285/1.27/8 with non selective saturation recovery

with inversion time of 280-300 msec using a band width 780 hz.

4. Injection of 99mTc Sestamibi

30 seconds following the gadolinium injection ,10 mci 99mTc -sestamibi (Cardiolite; Bristol-Meyers Squibb, North Billerica, MA, USA) was injected through the first cannula while the patient was still in the MR suite.

5. Tissue Characterisation.

Delayed 5-15 minute multiple short axis views from base to the apex and the 2 chamber and 4 chamber views were also taken for any late myocardial enhancement using Turboflash sequence TR/TE/FA 700/4.3/30 with non selective inversion recovery with inversion time(TI) of 440-550 with phase segmentation of 25 bandwidth 247 Mhz. The TI in each patient was optimized by using a TI determining sequence and the TI of the image which showed most appropriate nulling of myocardium was selected.

6. SPECT Study

Patients were shifted to the nuclear medicine suite for 99mTc Sestamibi SPECT scan. The imaging was done on a SPECT gamma camera (DICAM Siemens, Erlangen, Germany AG) after 30 minutes of injection. A gated SPECT study was performed with 16 frames acquired per cardiac cycle followed by data reconstructions in short axis, vertical and horizontal long axis.

Resting images of the heart were taken after 3 hours following a second injection of the 30mci 99mTc Sestamibi and reconstructed images were obtained in the axial, vertical and horizontal long axis.

7. Cine DMR .

All patients with reduced end diastolic thickness of less than 5.5 mm with regional wall motion abnormalities and or late myocardial enhancement more than 50% of the myocardial thickness were called again the next day for a low dose DMR study. Intravenous dobutamine infusion was given using a dose of 5-10 microg/Kg/minute for three minutes each and after the completion of each dose the cine study of the heart was done using the same protocol as in step 2.

DMR was done to assess the contractile reserve which was taken as a) Positive ionotropic response with improved systolic thickness and contractility b)No response as no change in the systolic thickness or contractility.c) Negative/monophasic response as deterioration in the contractility.

8.Image Analysis.

All the cardiac examinations were studied independently by Ak, Akp and Gm for the following:

- The myocardial perfusion defects in the first pass study were seen as hypointense areas in the short axis views

with the myocardium being divided into a sixteen segment model of heart.

- Any late enhancement of the myocardium seen as hyperintense area in the late 5-15 minute images and also to see the exact location and the thickness of the myocardium involved i.e. subendocardial, intramural - less than 25 %, 25-50 % and transmural (more than 50%) were determined.
- Regional wall motion abnormalities were categorized on an ordinal scale from 2 to -1 with score of 2 as normal systolic wall thickening, score 1 as hypokinetic, score 0 akinetic and score -1 as dyskinetic.

Myocardial viability: was defined as any of the following

- An area of myocardial perfusion defect on CMR with no late enhancement, or showing late enhancement with scar thickness of less than 50% of total myocardial thickness and with a wall motion score of 1 or 2.
- An area of reversible perfusion defect on the scintiscan.
- All other segments not falling into the above criteria were then assessed with DMR to look for any

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improvement in the systolic thickening of the myocardium which if increased by more than 2.5 mm as compared to the resting wall thickness was then taken as viable.

SPECT scans were observed for the presence of perfusion defects in the stress and resting short axis views from the base to the apex also on the same pattern of 16 segment model and were classified as fixed, if present on both the resting and stress views and as reversible if there was any change /reperfusion on the resting scan. Regional wall motion was assessed by means of subjective evaluation of endocardial excursion and regional wall thickening and was graded on the same score of 2 to -1 as on the CMR.

The results of both the studies were then compared and analysed using statistical analysis software (Analyse-It Software Ltd, Leeds UK) and the sensitivity, specificity, positive and negative predictive values calculated. Results of both the modalities were compared using Pearsons correlation coefficient and the diagnostic accuracy of SPECT and CMR assessed by Receiver operator

TABLE 1 - Comparison data of Fixed Perfusion Defects seen on SPECT and CMR.

	SPECT	CMR
Fixed Defects		
Segments	81	58
Sensitivity	79.30%	100%
Specificity	93.20%	100%
Positive Predictive Value	56.80%	100%
Negative Predictive Value	97.60%	100%
Accuracy	91.80%	100%

TABLE 2 - Comparison data of Reversible Defects seen on SPECT and CMR

	SPECT	CMR
Reversible defects		
Segments	156	136
False Positive	26.90%	7%
False Negatives	15.30%	5%
Sensitivity	82.60%	92.80%
Specificity	90.40%	98.20%
Positive Predictive Value	73.10%	94.10%
Negative Predictive Value	94.30%	98.20%
Accuracy	88.50%	96.90%

characteristic (ROC) analysis.

RESULTS

Out of the 36 patients examined there were 28 male and 8 female patients in the age group of 35-58 years with mean age 43 ± 3 years. All the 36 patients had a positive stress test with $> 2\text{mm}$ ST depression; 30 patients had positive coronary angiograms of which 14 patients had significant stenosis ($> 70\%$) on coronary angiography with 9 of these patients had a past history of myocardial infarction, 16 patients had 50-70 % stenosis ; 6 patients had a normal angiogram out of which 4 patients had past history of myocardial infarctions and 2 patients had dilated cardiomyopathy. A total of 576 myocardial segments were examined for perfusion on both SPECT and CMR which clearly revealed perfusion defects (Fig 1). The SPECT showed perfusion defects in 156 segments while 420 had homogenous myocardial perfusion; there were 42(26.9%) false positive and 24(15.3%) false negative with a sensitivity of 82.6% and specificity of 90.4% (Table 1). The positive and negative predictive values were 73.1% and 94.3% respectively with an overall accuracy of 88.5%. Fixed myocardial perfusion defects were seen in 81 segments on SPECT out of which 35 (43.2%) were false positive and 12(14%) false negative; SPECT thus showed a 79.3% sensitivity and a specificity of 93.2% with positive and negative predictive values of 56.8% and a 97.6% respectively with an accuracy of 91.8% to detect fixed perfusion defects (Table 2).

Compared to SPECT the CMR showed myocardial perfusion defects in 136 segments with normal perfusion in 440; out of these 10(7%) segments were false positive and 8(5%) were false negative and had sensitivity of 92.8% and specificity of 98.2% with a positive and a negative predictive values of 94.1% of 98.2% respectively with an accuracy of 96.9% (Table 1). CMR revealed late enhancements consistent with infarcts in 58 myocardial segments with no false positive or negative - a sensitivity and specificity of 100% (Table 2).

The data of the SPECT was reassessed with a corrected algorithm i.e. the perfusion defects with the absence of the regional wall motion abnormality which were earlier taken to be falsely positive were corrected as viable ; 21 myocardial segments which had no wall motion abnormality were thus found as normal; this correction further improved the specificity of gated SPECT study for the detection of myocardial to 96.3%, positive predictive value to 87.7% with overall accuracy of 93.1%. Similar effect of the corrected algorithm was seen in the analysis of the fixed defects with specificity improving to 96.5% and positive predictive value to 71.9% from 56.8% and overall accuracy to 94.8%.

Eleven patients underwent DMR for the evaluation of In

myocardial contractility in 55 ischemic segments on CMR and SPECT. The results of DMR (Figure 2) showed improved systolic thickening consistent with myocardial viability in 29 segments (7 patients), monophasic response in 1 patient (16 segments) and no response in 10 segments (3 patients). The patients with monophasic response had perfusion defects on CMR in 10 segments along with transmural infarcts (TMI) in 6 (Figure 3 a-b) and showed fixed defects on SPECT in 10 with reversible defects in 6 while the patients with no change comprised of dysfunction in 6 and TMI in 4 on CMR and fixed defects in 4 and viable segments in 4 on SPECT. The patients which showed a positive ionotropic response had a combination of all the reversible perfusion defects in 18 segments, micro infarcts in 2 and subendocardial infarcts in 9 on CMR and showed fixed defects 7 and reversible defects in 22 on SPECT. The data suggested that only presence of transmural infarcts on CMR showed no improvement in the wall motion on DMR seen as either no response or monophasic response while for all other types of reversible or fixed defects seen on both the modalities DMR was required to predict the contractile reserve of the myocardium.

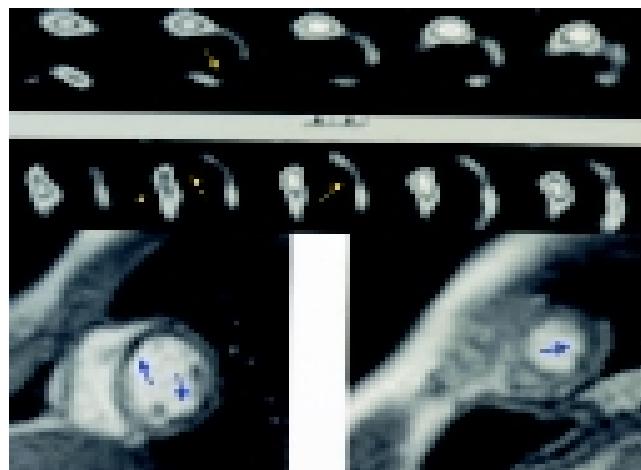


Figure 1: Stress 99mTc -sestamibi and CMR showing perfusion defects in the inferior, lateral and anterior walls(arrows) with the septum showing normal perfusion (small arrow).

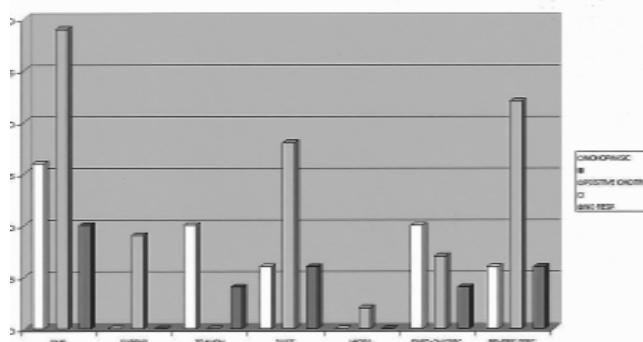


Figure 2: Bar diagram showing correlation of the CMR, SPECT and the response on DMR.

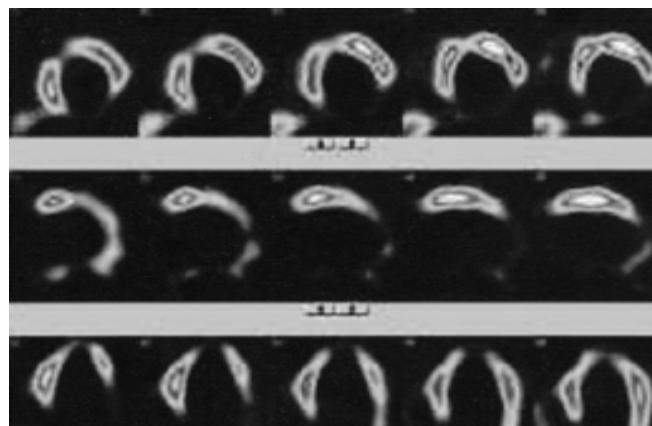


Figure 3a: Stress ^{99m}Tc -sestamibi scan showing perfusion defects in the Inferior wall in the short axis and vertical long axis(arrowhead) with remaining myocardium being normal.



Figure 3 b): On CMR delayed enhancement with TMI alongwith reduced wall thickness in the whole of inferior wall(arrow) with a subendocardial infarct in the septum (arrow head), lateral wall and septo anterior segment . 3 c): Cine resting and dobutamine MR systolic frame showing dilated LV cavity with no change of wall thickness following low dose dobutamine (arrowhead).

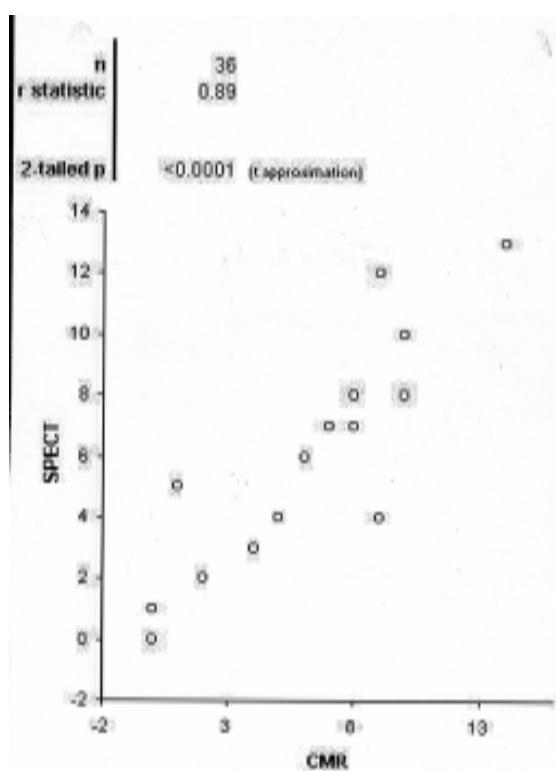


Figure 4: Scatter plot showing correlation of perfusion defects seen by SPECT and CMR with r value of 0.89 with 95 % CI of 0.77 to 0.95.

CMR examination claustrophobia was experienced by 4 patients while poor breath holding was seen in 6 patients which resulted in breathing artifacts.

Statistical analysis.

Correlation of the results of CMR and SPECT was performed for detection of myocardial ischemia using Pearson correlation and showed a good correlation with $r = 0.89$ with 95%CI 0.77 to 0.95 and 2 tailed p value of <0.0001 which is statistically significant (Figure 4).

ROC analysis of the above results comparing the sensitivity and specificity of the SPECT and CMR in assessing perfusion deficits also revealed a good area under the curve for both CMR and SPECT of 0.97-- with the a p value of <0.001 thereby suggesting a good diagnostic value of both the modalities (Figure 5). CMR however showed a higher sensitivity for detection of myocardial scars/ fixed defects on the SPECT.

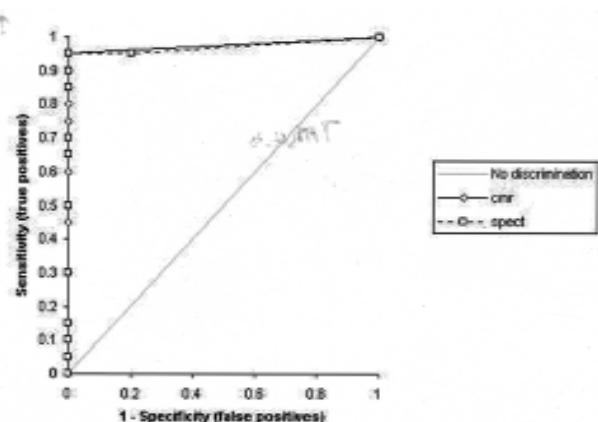


Figure 5: ROC curve between SPECT and CMR showing 0.97 area under curve with a good diagnostic value for both CMR and SPECT.

DISCUSSION:

The present study revealed a higher sensitivity of CMR of 92.8% than SPECT 82.6% in detecting both myocardial ischemia and non viable myocardial tissue (Tables 1,2). CMR had a sensitivity of 100% while for SPECT it was 79.3% in diagnosing non viable myocardium(Figure 6). Similar results were also reported by Saadi et al(6), Regenfus et al(7) who showed good correlation between SPECT and CMR with the latter showing 100% sensitivity in the detection of myocardial infarcts versus SPECT which had a sensitivity of 89%. The reasons cited for improved results are due to inherent superior resolution of the CMR compared to SPECT. The advantage of CMR was observed in the detection of subendocardial and micro infarcts which were missed by SPECT in 12 patients in this study all of which were missed by SPECT resulting in lower sensitivity as compared to CMR.

Although the combined use of Stress and resting 99mTc sestamibi gated SPECT is an established modality for the diagnosis of myocardial ischemia but it has a higher false-positive rate varying from 14% to 38% (8,9,10). In this study we found the incidence of false positive to be 26.9% and with the application of the corrected algorithm it was reduced to 7%; the corrected algorithm uses the presumption that the fixed defects caused by infarcts should demonstrate decreased wall motion and thickening, while those caused by attenuation artifacts should demonstrate normal motion and thickening. Also the location of such fixed defects also helps in identifying them as artifactual because most of such defects exist in predictable locations i.e. the inferior wall because of the diaphragmatic attenuation and in the anterior wall, the apex in especially obese patients (9,11). The above correction may not be 100% accurate for all patients with fixed defects and there are false negatives which vary from 4% seen by Depuey(11) to as high as 24% in the study by Holly (8). This study showed a incidence of false negative to be 14%. The reason for these false negative cases is that some of the ischemic segments do not cause wall motion abnormalities and thus are presumed to be normal.

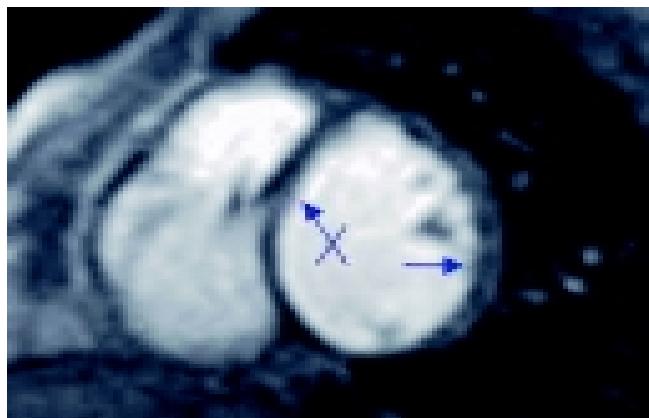


Figure 6: First pass perfusion CMR showing subendocardial perfusion defect due to magnetic susceptibility artifact due to passage of contrast in the lateral wall(arrows) and true perfusion defect in the whole of the septum(crossed arrow).

Data analysis of CMR showed only 7% false positive which were due to transient magnetic susceptibility artifacts resulting from the passage of contrast in the initial images of the first pass perfusion study. These were observed characteristically in the subendocardial region at the left ventricle cavity interface and immediately disappeared spontaneously in the subsequent images of the first pass study (Figure 6). The second type of false positive perfusion defect seen was in the septoanterior part in the basal part of the short axis the exact cause for which is not known but is probably due to crossing of the myocardial fibres at the root of aorta (Figure 7). The recognition of these artifacts is important and in the absence of wall motion abnormalities one should be careful not to interpret these as true positive perfusion defects.

Thus if the awareness of the origin of these artifacts is kept in mind one can further reduce the incidence of such false positive defects. The false negatives seen on CMR were also lower i.e. 5% in the present study compared to 15.3% of SPECT and were seen in patients with severe triple vessel coronary artery disease with low flow or balanced hypoperfusion where it was difficult to appreciate the delayed perfusion. However with rapid improvements in analysis of perfusion soft ware on CMR this may even be reduced. CMR has an accuracy of 100% to detect and quantify myocardial infarcts seen as late enhancements and can become a gold standard modality in the detection of such infarcts. The false negative studies on SPECT were those myocardial segments which had subendocardial or micro infarcts with sparing of a large thickness of overlying rim of myocardium thus resulting in no appreciable wall motion abnormality. Detection of such infarcts is beyond the resolution of the SPECT while CMR offers high spatial resolution (2 x 2 x 8-mm voxels) with high image contrast and can be used to detect and quantify such infarcts(4). Many studies have shown a good agreement between histopathologic depiction of infarct and MR imaging findings(12,13,14). The location and quantification of infarct is also important as is its detection and Wagner (14) showed in his study that MR imaging correctly identified 92% segments with subendocardial infarcts while with resting 201TI SPECT only 28% of these segments were correctly identified.

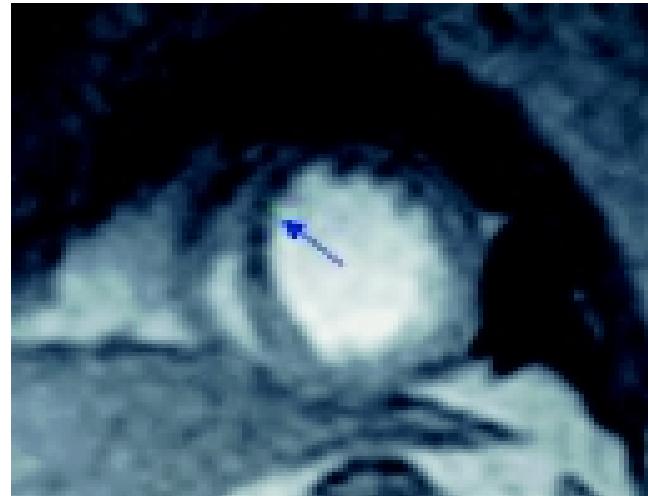


Figure 7: False perfusion defect in the septo anterior segment(arrow) on CMR.

As researchers look for answers to the question of viability on imaging the detection of a TMI can be an important answer to this vexing question. In this study we have compared the information obtained by DMR with that of CMR findings and observed that the quantification of infarct does help to predict the viability/function of the segment and can influence the line of management(15,16). All the patients in the present study who had TMI on CMR showed either monophasic negative or no ionotropic response to

low dose dobutamine thus implying poor contractile function or irreversible myocardial dysfunction; in other words reflecting nonviability. No other finding on SPECT or CMR reliably differentiated between viable and non viable myocardium. 29% segments that showed perfusion defects without late enhancement on CMR indicating viability turned out to have irreversible ischemic dysfunction on DMR. This was true for all other type of defects including late enhancement less than 50%, subendocardial enhancements and microinfarcts. Analysis of the SPECT data in the same set of patients also revealed that 12% of the segments reported as fixed were infact viable on DMR.

Hence the finding of transmural infarct on CMR emerged as the only definite pointer to the non viability of the segment. Whether this means that pharmacological testing can be done away with in such a segment would need further confirmation. Clearly the ability of CMR to detect a transmural infarct independent of wall motion abnormality is an important advantage in determining the therapeutic options in a patient with chronic ischemic heart disease.. Those patients with a non transmural infarct are likely to have some viable myocardium and thus more likely to benefit from reperfusion procedures and improve their ejection fractions and survival(17,18)

CONCLUSION:

The results of the present study show a good sensitivity and correlation of both SPECT and CMR in diagnosing the extent and number of perfusion defects in the myocardium in a patient with chronic ischemic heart disease. CMR is more accurate than SPECT in not only diagnosing myocardial infarcts but also shows its exact location and extent; this is likely to be of use in patients with equivocal SPECT studies and can also provide the most definite evidence of non viability on imaging irrespective of wall motion abnormality by demonstrating a transmural infarct and a dobutamine stress test can be avoided (19). All other findings still remain inconclusive when we begin to address this issue and will require the use of low dose dobutamine study to assess the positive contractile response in the ischemic segment and will thus continue to be a important part of myocardial viability. The main limitation of the present study is the number of patients was only 36 along with disadvantages of CMR like claustrophobia andppor patient breath holding. To conclude the present studies de monstres the edge of CMR over SPECT due to improved resolution and better cardiac morphology and wall motion details in the evaluation of myocardial perfusion and viability it shall be some more time before it is established as a routine diagnostic tool , this is due to lack of free availability also because SPECT has been a established technique for the last two decades to evaluate the myocardial ischemia and viability and has a good acceptability by the cardiologist and the cardiac surgeons where as CMR

being a new technique needs to be more generalized in its usage. Such studies need to performed more frequently by the cardiac radiologists and cardiac physicians before the potential benefits of CMR can be translated into patient care. Lastly, more follow up is needed to evaluate the functional significance of scars detected on CMR and also to determine the final patient outcome based on the decisions based on CMR (20).

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