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Original Research Paper

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"ROLE OF MRI IN ASSESSMENT OF CARDIAC FUNCTION AND MYOCARDIAL VIABILITY AND COMPARISON WITH ECHOCARDIOGRAPHY AND THALLIUM – 201 SPECT"

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ABSTRACT

Background: Ischemic heart disease (I.H.D) is among the most common serious chronic life threatening illnesses in the developed and developing world. **Materials and Methods:** Thirty two patients with documented old myocardial infarction (1> month) and in a stable condition were included in the study. Patients underwent:- Detailed clinical examination with emphasis on cardiovascular system & Relevant routine Hematological investigations and ECG. **Results:** DE-MRI showed 194 (36.81%) segments as normal, 220 (41.75%) as reversible and 113(21.44%) segments were irreversible. SPECT showed 202 (38.33%) segments as normal, 201 (38.14%) as reversible and 124 (25.53%) segments were irreversible. Good correlation (r=0.952, p <0.01) seen between SPECT and MRI in differentiating reversible from irreversible ischemic segments with linear bivariate correlation. **Conclusion:** The results of our study indicate that MRI and 2D echocardiography correlate very well in evaluation of myocardial function including measurement of ejection fraction, and in detection and grading of regional wall motion abnormality. In detection myocardial viability and in differentiating reversible from irreversible segments, MR showed significant correlation with Thallium – 201 SPECT and was 96.62% sensitive and 96.04% specific as compared to SPECT.

KEYWORDS : Ischemic heart disease, Cardiac event, Echocardiography & Thallium-201 SOECT

INTRODUCTION:

Ischemic heart disease (I.H.D) is among the most common serious chronic life threatening illnesses in the developed and developing world[1]. Ischemic may be transient as in angina pectoris or prolonged when it can lead to myocardial necrosis and or scarring, with or without a clinical picture of myocardial infarction. Coronary atherosclerosis is the most common cause of I.H.D. Other causes that can limit coronary blood flow are spasm, arterial thrombi, coronary embolism or a congential abnormality. Men have higher risk of developing I.H.D than women. This gender related difference decreases after women attain menopause, which could be due to loss of hormonal protective effects. Incidence of I.H.D. increases exponentially with age. Thus atherosclerosis and consequent coronary artery disease are associated with risk factors such as old age, hyperlipidemia, hypertension,obesity, diabetes smoking etc[2]. In patients with I.H.D the extent and degree of myocardial injury after an acute ischemic event are strong predictors of patient outcome[3]. Early interventions to restore myocardial perfusion are the treatment of choice in such patients[4].

Cardiac size and function provide important prognostic information in I.H.D and a variety of acute and chronic cardiac diseases[5]. In clinical practice, variety volumes, ejection fraction and wall motion are subjectively assessed using 2D transthoracic echocardiography and recently by using magnetic resonance Imaging (MRI)[6]. Wall motion of global and regional myocardium can be assessed and abnormal segments are characterized as hypokinetic, akinetic or dyskinetic. Motion of each segment is assessed using 17 segments model of American Heart Association[7].

Limitation of echocardiography include large inter and intra-observer variation compared to MR, as echocardiography requires geometric assumptions for volumetric measurement. Cardiac pathology distorts cardiac symmetry making geometric assumption less accurate. MR imaging data is 3 dimensional which allows direct measurement without geometric assumption and thus MR has less inter and intra-observer variation than transthoracic echocardiography in evaluating ventricular function[8].

Following ischemia, the myocardium may be infarcted or reversibly injured[9].Reversibly injured myocardium maybe either "stunned" or "hibernating". "Stunned" myocardium occurs following an acute ischemic episode with early reperfusion, where myocardium is dysfunctional but viable "Hibernating" myocardium is viable but dysfunctional because of chronic ischemia[10].

The detection of residual myocardium viability in a patient with regional or global severe left ventricular dysfunction in a setting of ischemic heart disease is of clinical importance in the planning of a therapeutic strategy. Identification of viable myocardium is not only important for surgical planning before revascularization but also important in predicting which patient will have improved survival after revascularization[11]. Hibernating and stunned segments improve in function after revascularization[12]. Hibernating stunned and infracted myocardium all appear as regional wall motion abnormality of various degrees. Wall motion abnormality temporarily persists in myocardium stunning during the period of ischemic and becomes normal after blood few is restored. The problem is to distinguish dysfunctional myocardium caused by stunning or hibernation, which may be recoverable[13]. Current methods for evaluating viability include 'Dobutmine Stress echocardiography', 'Single Photon Emission Computed Tomography' (SPECT), 'Positron Emission Tomography' (PET) and 'Magnetic Resonance Imaging' (MRI).Each of the above has different accuracy in different clinical setting[14].

Dysfunctional but viable myocardium retains residual contractile reserve which shows improvement of systolic function upon inotropic stimulation by low dose Dobutamine infusion[15].This is the basis of assessment of viability by stress echocardiography.

In recent years, MRI has been proposed as an alternative test to assess myocardium viability. The two methods used to assess myocardium viability Include contrast enhanced MRI to look for myocardial delayed enhancement (MDE) and by stress MRI techniques. On stress MR, hibernating or stunned myocardium shows increase in contractile function due to presence of viable myocytes on injection of ionotropic or vasodilator agents. However due to potential side effects associated with stress, complexity of the technique cardio-respiratory resuscitation machine which is not feasible at every centre, stress MR technique is not used commonly in the assessment of myocardial viability. MDE gives better definition of transmural extent of non Q._wave (subendocardial) myocardial infarction which is a sensitive marker of future ischemic events[16].Non Q-wave subendocardial infarction have higher incidence and mortality rate than Q-wave subendocardial infarction[17].

In summary, MRI has the potential to provide safe, accurate and comprehensive assessment of cardiac function and differentiation of viable myocardium from nonviable infracted or scarred myocardium. This study has been undertaken to assess feasibility of MRI to assess myocardial function and viability without using stress agents in stable patients with ischemic heart disease in our setup.

MATERIALS AND METHODS:

This prospective study was under taken at department of Radiodiagnosis in association with department of Cardiology, Cardiovascular & Thoracic Surgery and Nuclear Medicine, Major SD Singh Medical College and Hospital, Farrukhabad, Uttar Pradesh during the period from February, 2018 to January, 2019. Thirty two patients with documented old myocardial infarction (1> month) and in a stable condition were included in the study. Patients underwent:-

- Detailed clinical examination with emphasis on cardiovascular system.
- Relevant routine Hematological investigations and ECG.

All patients underwent Echocardiography, Coronary angiography including ventric ulography, Thallium Single photon emission computed tomography (SPECT), and Magnetic resonance imaging (MRI) with in 2 to 4 weeks of each other after informed consent.

Exclusion criteria for MR study

1. Unstable angina.
2. Acute cardiac event (<4 weeks)
3. Cardiac arrhythmia.
4. Congestive heart failure.
5. Inability to lie down for 30 to 45 minutes in MR gantry due to any reason.
6. Patients with pacemaker and those having claustrophobia.

RESULTS AND DISCUSSION:

Age distrubuttion

Age of patients ranged from 43 to 81 years.

Table -1. Age distribution

Age (years)	Number of patients	Percent
<40	0	0%
41-50	6	18.75%
51-60	10	31.25%
61-70	12	37.50%
71-80	3	9.38%
>80	1	3.13%

- All the patients in this study were above 40 years.
- Maximum number of patients were in fifth (31.25%) and sixth (37.50%) decades.

Sex distrubuttion

Gender distribution shown in table -2

Table -2. Gender distribution

Gender	Number of patients	Percent
Male	31	96.88%
Female	1	3.13%
Total	32	100%

- Out of 32 patients, 31(96.88%) are male and only one (3.13%) female aged 65 years.

Table – 3 Correlation of reversible/irreversible ischemia (segments).

Correlation	SPECT	DE-MRI	
Normal	202	194	r = 0.952, p<0.01
Reversible	201	220	
Irreversible	124	113	
	N=527	N=527	

- DE-MRI showed 194 (36.81%) segments as normal, 220 (41.75%) as reversible and 113(21.44%) segments were irreversible.
- SPECT showed 202 (38.33%) segments as normal, 201 (38.14%) as reversible and 124 (25.53%) segments were irreversible.
- Good correlation (r=0.952, p <0.01) seen between SPECT and MRI in differentiating reversible from irreversible ischemic segments with linear bivariate correlation.

In the management of ischemic heart disease (I.H.D) after a cardiac event, important prognostic factors include cardiac function and myocardial viability. Ventricle volumes, ejection fraction and wall motion can be assessed by both 2D – transthoracic echocardiography and magnetic resonance imaging (MRI). Echocardiography, thought a simple, noninvasive and faster imaging technique without any side effect, is limited by large inter and intra-observer variations, as it requires geometric assumptions for volumetric measurement. Cardiac pathology distorts cardiac symmetry making geometric assumption less accurate. MR imaging data is three dimensional allowing direct measurement without geometric assumption and thus MR has less inter and intra observer variation than transthoracic echocardiography in evaluating ventricular function.

In the present study, MRI and 2D echocardiography of 32 patients were compared for the assessment of myocardial function. The regional wall motion abnormality as well as ejection fraction were assessed. In MR, 12 (31.25%) out of 32 patients showed severe LV dysfunction, 10 (31.25%) showed moderate LV dysfunctional and 7 (21.88%) showed mild LV dysfunction. In echocardiography 7(21.88%) out of 32 patients had mild LV dysfunction, 13 patients (40.63%) had moderate LV dysfunction and 9 had severe LV dysfunction. MR was 100.00% sensitive, with positive predictive value 89.66% and negative predictive value 100.00% in measuring ejection fraction as compared to echocardiography. There was strong significant correlation (r=0.897, p<0.01) between two modalities in measuring ventricular volumes and ejection fraction. Similar results have been reported by others. Bellenger et al compared the agreement of left ventricular volumes and ejection fraction by M-mode echocardiography, 2D – echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance performed in 52 patients with chronic stable heart failure. The mean left ventricular ejection fraction by 2D echo Simpson's biplane was 31±10, by radionuclude ventriculography, it was 24±9 and by magnetic resonance it was 30±11. All the mean left ventricular ejection fractions by each technique were significantly different from all other technique (p<0.001), except for ejection fraction by MR and 2D echocardiography using Simpson's rule (p=0.03)[18]. Chaung et al (2000) determined the concordance between biplane and volumetric echocardiography and magnetic resonance imaging (MRI) strategies. Biplane echocardiography underestimated LV volume with respect to the other strategies (p<0.01). They concluded that volumetric MRI and volumetric echocardiography measures of LV volume and LVEF agree well and give similar results[19].

In our study there were disagreement in ejection fraction in three (9.38%) patients were MR overestimates the severity of LV dysfunction as compared to echocardiography. Possible reasons could be due to use of geometric assumptions in measurement of ejection fraction by echocardiography.

We analyzed 544 segments for regional wall motion abnormality. In MR, out of 544 segments 201(36.95%) segments were hypokinetic, 35 (6.43%) were akinetic and 6 (1.1%) were dyskinetic. By echocardiography out of 544 segments 209(38.42%) were hypokinetic, 30 (5.51%) were akinetic and 7 (1.29%) were dyskinetic. Sensitivity, specificity, positive predictive value and negative predictive value of MR for assessment of regional wall motion wall abnormality were 97.55%, 98.68%, 98.34% and 98.03% respectively as compared to echocardiography. There was strong significant correlation (r=0.862, p<0.01) between two modalities in detecting regional wall motion abnormality. White et al (1988) studied relative capabilities of magnetic resonance (MR) imaging and two-dimensional echocardiography evaluation of regional contractile dysfunction in the left ventricle after a myocardial fraction. Results from 22 concurrent MR (orthogonal - transaxial, ECG-gated, multiphasic, single-spine echo) and 2DE examinations were compared and a significant correlation (r = 0.795, p<0.01) between scorings was found[20]. Harald et al (2004) compared cardiac magnetic resonance (MR) imaging examinations with harmonic two-dimensional echocardiography were included. Data from corresponding two-,three-, and four-chamber long axial views and a midventricular short axial view were acquired with each modality. Image quality and depiction of segments wall motion were scored semiquantitatively by using the 16-segment model of the American Society of Echocardiography. There was significant correlation (p<0.001) between these two modalities[21].

There is disagreement between echocardiography and MR in measuring wall motion abnormality in 10 (1.84%) segments including 4 (0.74%) overestimations and 6 underestimations (1.14%). Positive reasons could be low temporal resolution of MRI in patients who have heart rates of greater than 100 beats per minute and in some cases to poor breath hold leading to decreased spatial resolution.

Following ischemia, the myocardium may be infracted or reversible injured. Reversible injured myocardium may be either "stunned" or "hibernaing". "Stunned" myocardium occurs following an acute ischemic episode with early reperfusion, whereas "Hibernating" myocardium is viable but dysfunctional because of chronic ischemia. Hibernating, stunned and infracted myocardium all appear as regional wall motion abnormalities of various degree. The aim is to distinguish dysfunctional myocardium caused by stunning or hibernation, which may be recoverable after revascularization from post infarct scar, which is not recoverable. Current methods for evaluating viability include 'Dobutamine Stress echocardiography', 'Single Photon Emission Computed Tomography' (SPECT), 'Positron Emission Tomography' (PET) and 'Magnetic Resonance Imaging' (MRI). Each of the above has different accuracy in different clinical settings.In 'Dobutamine Stress echocardiography' upon inotropic stimulation by low dose Dobutamine infusion, dysfunctional but viable myocardium shows improvement of systolic function. Poor acoustic window in patients of chest wall deformity and side effect due to dobutamine stress are few limitations of Stress Echocardiography.

Thallium 201 or Technitium 99 Sestamibi SPECT acts as a marker of viability because of dependence on intact cell membrane and active transport for the radionucleide uptake. Viability can be assessed from resting and redistribution images. There is a direct correlation between uptake of radioisotope and tissue viability. The combination of scarred and hibernating myocardium in the same poorly contracting segment of myocardium is a particular problem. There may be sufficient viable myocardium for tracer uptake but not enough for functional recovery following revascularization. Relatively poor spatial resolution of SPECT in the detection of subendocardial scar is a problem and an alternate technique with better spatial resolution is needed. Recently MRI has been proposed as an alternative modality to assess myocardial viability. The methods used to assess myocardial viability include contrast enhanced MRI to look for first pass perfusion, myocardial delayed enhancement (MDE) and stress MRI. Myocardial perfusion is used for evaluating the adequacy of blood flow to the myocardium. Ischemic area may show hypoenhancement during first pass perfusion. Hypoperfused myocardium appears as persistent dark area as compared to enhancement normal myocardium[22]. However first pass perfusion is not very useful for assessment of myocardial viability because hypoperfusion in first pass MRI can also be expected in patients with severe coronary artery stenosis, even without structural myocardial abnormality. In the study of Van hoe et al no significant correlation was found between the result of first pass perfusion MRI and functional recovery. Standstede et al suggested that hypoenhancement during first pass is not a reliable criteria of non predictor of non viability. Standstede et al showed that out of 73 segments 25 segments shows both hypoperfusion is first pass enhancement as well as delayed enhancement with disagreement in 10 segments (13.7%)[23]. Out of 10 segments 1 segments shows normal perfusion in first pass and hyperenhancement in delayed phase and 9 segments shows hypoperfusion in first pass with absence of delayed enhancement. In our study, out of 527 segments,338 segments show delayed enhancement. Out of 338 segments, 314 segments shows hypoperfusion in first pass enhancement with disagreement in 24 segments (4.55%) which is comparable with the study of Standstede et al[23]. Out of 24 segments 21 segments shows delayed enhancement with no hypoperfusion and 3 segments shows hypoperfusion in first pass with no delayed enhancement . Reason for false positive segments could be reduced blood flow due to coronary artery stenosis without structural damage. Increased capilliary permeability and increased interstitial volume might be the reason for hyperenhancement without hypoperfusion[24]. Since stress agents were not used during first pass perfusion, which might be another cause for hyperenhancement without hypoperfusion.

Hence to assess myocardial viability, standard accepted protocols are myocardial delayed henhancement (MDE) and stress MR studies. On stress MR, hibernating or stunned myocardium shows increase in contractile function due to presence of viable myocytes[25]. However due to potential side effects associated with stress, complexity of technique, difficult patient monitoring and need for appropriate MR compatible cardio-respiratory resuscitation machine, stress protocol is generally not used in the assessment of myocardial viability. Van hoe et al showed that likelihood of functional recovery after revascularization was 91% for segments without delayed hyperenhancement, 43% for segments with delayed hyperenhancement with transmural extent of 75% or less, and 8% for segments with delayed hyperenhancement with transmural extent of more than 75% (p<0.05). Improved function at dobutamine stress MRI indicated functional recovery in 87%, whereas functional recovery was observed in only 30% of segments not responding at dobutamine stress MRI (p < 0.05) . They suggested that simple protocol consisting of baseline contractility and delayed enhancement MRI studies is adequate to differentiate dysfunctional but viable from nonviable myocardium. Dobutamine stress and perfusion MRI studies offer little or no additional information.

MDE gives better definition of transmural extent of non Q-wave (subendocardial) myocardial infarction which is a sensitive marker of future ischemic. In the region of increased extracellular space (infarction), gadolinium compound accumulates in higher concentration with slower clearance showing high signal intensity on T1 – weighted sequence. After myocardial infarction there is fourfold increase in extracellular space compared to pre infarction due to inflammation and fibrosis giving more than 400% increase in signal intensity between infracted and normal myocardium in T1 weighted inversion recovery sequence[26,27]. On delayed imaging following gadolinium administration (10 to 30 minutes) region with infarction appears white in relation to normal black myocardium.

In our study, we studied 31 patients and total of 527 segments were analyzed. Entire left ventricle was divided into 17 segments with six at base, six at mid ventricle and five at apex. In myocardial delayed enhancement out of 527 segments, 194 (36.81%) segments showed no enhancement, 143 (27.13%) showed grade 1 enhancement, 77 (14.61%) showed grade 2, 63 (11.95%) showed grade 3 enhancement and 50 (9.49%) segments showed grade 4 enhancement. In Thallium – 201 SPECT out of 527 segments, 136 (25.81%) showed grade – 1 uptake, 65 (12.33%) showed grade – 2 uptake and 124 (23.53%) showed grade – 3 uptake. Grade 3 and 4 enhancement in MR corresponds with grade – 3 of SPECT for comparison. Sensitivity, specificity, positive predictive value and negative predictive value of MR for assessment of viability were 96.62%,96.04%,97.52% and 94.63% respectively as compared to SPECT. There was strong significant correlation ($r = 0.952$, $p<0.01$) between two modalities in detecting myocardial viability. Ansari et al (2004) showed in their study that in patients with LV dysfunction and prior myocardial infarction, MRI delayed hyperenhancement correlayes significantly with thallium - 201 SPECT for demonstration of myocardial nonviability. He analyzed 15 patients. Overall, there was a strong inverse relationship between the area of hyperenhancement on MRI and diminished thallium – 201 uptake on SPECT ($r = -0.51$, $p < 0.001$). There was a significant correlation between the imaging methods for each individual segment, expect for the weaker correlation in the inferior-septal segment ($r = -0.38$, $p < 0.08$)[25]. In a study of 60 patients. Lund et al showed good correlation and agreement ($r = 0.92$, $p<0.01$) between thallium – 201 SPECT and delayed enhancement MRI in assessment of viability and measurement of infarct size[28].

In our study out of 202 segments shown to be normal by SPECT, 194 (36.81%) segments showed no enhancement in MRI with disagreement in 8 (1.52%) segments, which showed hyperenhancement in DE-MRI. Five among these 8 segments were in inferior and inferoseptal wall. Possible reason for this disagreement could be due to higher spatial resolution of MRI as compared to SPECT leading to detection of subendocardial infarct which showed normal tracer uptake in SPECT.

MR underestimated 11 segments where SPECT showed grade 3 tracer uptake and MR showed grade 1 enhancement in 4 segments and grade 2 enhancement in 7 segments. Attenuation artifact in the region of inferior wall could be the possible reason.

Lee et al (2004) showed benefit of contrast enhancement MR in 20 patients equivocal for infarct with SPECT particularly so in the setting of subendocardial infarct. In their study out of 41 equivocal segments by SPECT, infarct was confirmed in 10 segments by MR. These equivocal segments were mainly present in inferior or posterior wall[29].

Transmural extent of hyperenhancement in DE – MRI is considered as a predictor of reversibility. Kitagawa et al[30] suggested that in thallium – 201 SPECT, segments showing tracer uptake >50% (grade – 1 and ll) could be classified as viable or reversible and segments showing tracer uptake 0 to 49% of peak activity (grade - lll) were classified as nonviable or irreversible. Similarly in MRI they suggested that segments showing hyperenhancement >50% of wall thickness were nonviable or irreversible and those with hyperenhancement <50% or without any delayed enhancement could be viable or reversible. In our study MRI showed out of 527 segments 113(21.44%) segments were irreversible and 220 (41.75%) segments were reversible. Thallium showed 124(23.53%) segments were irreversible and 201 (38.41%) were reversible. Sensitivity, specificity, positive predictive value and negative predictive value of MRI were 100.00%,96.04%,97.60% and 100.00% respectively as compared to SPECT in differentiating reversible from irreversible ischemia. There was a strong significant correlation ($r = 0.952$, <0.01) between two modalities. In another study Kim et al showed a striking relationship between transmural extent of hyperenhancement using MDE and likehood of improvement of contractile function after revascularization[11]. Gerber et al reported that absence of delayed hyperenhancement had sensitivity of 82% and accuracy of 74% in predicting recovery of myocardial function after revascularization[31].

The present study has a few limitations. First , a relatively smaller number of patients were included. Studies in more patients are needed to confirm these data. A second limitation is that post revascularization studies were not done in order to confirm the reversibility of ischemic myocardium.

CONCLUSION:

In conclusion, the results of our study indicate that MRI and 2D echocardiography correlate very well in evaluation of myocardial function including measurement of ejection fraction, and in detection and grading of regional wall motion abnormality. In detection myocardial viability and in differentiating reversible from irreversible segments, MR showed significant correlation with Thallium – 201 SPECT and was 96.62% sensitive and 96.04% specific as compared to SPECT. Thus MRI without stress agent has the potential to become a simple, fast, noninvasive and stressless test in patients of ischemic heart disease where it can be used as a single modality to evaluate myocardial function and assess myocardial viability.

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