PATTERN OF PERFUSION DEFECTS SEEN IN ISCHEMIC HEART DISEASE PATIENTS ON TECHNETIUM (Tc$^{99m}$) TETROFOSMIN SCANNING

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Background: Cardiovascular disease is common cause of death in developed as well as developing countries. The most common cause of Ischemic Heart disease is narrowing of coronary arteries, a process called as atherosclerosis. The objective of the present study is to determine the pattern of ischemic changes detected by technetium tetrofosmin (Tc$^{99m}$). Methods: Sixty five patients presenting as known or suspected ischemic heart disease over a period of two years (December 1995 to December 1998) at Ziauddin Hospital were included in the study. Each patient underwent Tc$^{99m}$ tetrofosmin stress and rest studies. Tetrofosmin study was performed according to one day protocol. Results: By segmental analysis (five segment per patient), 35 patients had perfusion defects by SPECT Tc$^{99m}$ tetrofosmin imaging. Out of 95 perfusion defects, reversible ischemia and mixed defects were more common in inferior wall and fixed defect in left ventricular apex. Conclusion: Reversible ischemia and mixed defects were more common in inferior wall and fixed defect in left ventricular apex.

Key words: Reversible, Ischemia, Imaging, Fixed Defects, Myocardial perfusion,

INTRODUCTION
Cardiovascular disease is the leading cause of morbidity and mortality in developed as well as developing countries. The most common cause of Ischemic Heart Disease is narrowing of coronary arteries, a process called as atherosclerosis. 1 Chronic injury to vascular endothelium is caused mainly by a disturbance in the pattern of blood flow in certain parts of arterial tree, such as bending points and areas near branching vessels. Local shear forces, which are probably enhanced in hypertension, several factors including hypercholesterolemia, advanced glycation end products in diabetes (particularly insulin dependant), chemical irritants in tobacco smoke circulating vasoactive amines, immune complexes and infections may potentiate chronic endothelial injury leading to accumulation of lipids and monocytes (macrophages). 2

Ischemic heart disease may present as silent or acute myocardial infarction, unstable angina, stable angina, non Q wave myocardial infarction, Q wave myocardial infarction or sudden death from ventricular fibrillation or cardiac failure. Acute myocardial infarction is most dreaded and cardiac arrhythmia is most dangerous complication of atherosclerotic narrowing of coronary arteries. 3 Recently Tc$^{99m}$ agents including hexakis-isonitriles, boronic acid adducts and diphosphine (Tetrofosmin), sestamibi and teboroxime have been approved for clinical use in humans. Tc$^{99m}$ tetrofosmin is a lyophilic, cationic diphosphine developed for myocardial perfusion imaging in humans. 4 Studies have shown that it has excellent early myocardial uptake and a relatively slow clearance (approximately 1% at 2 hours). This study focuses on determination of pattern of of ischemic changes by technetium tetrofosmin.

MATERIAL AND METHODS
Sixty five patients presenting as known or suspected ischemic heart disease over a period of two years (December 1995 to December 1998) at Ziauddin Hospital were included in the study. Thirty five patients (30 males and 5 females) had previously documented evidence of myocardial infarction or clinical symptoms suggestive of coronary artery disease, abnormalities in exercise electrocardiography, and reversible ischemia as documented by previous myocardial scan, or angiographic evidence of one or more than one of the major coronary arteries were included. Those with normal finding (i.e confirmed free IHD by myocardial perfusion scan) were taken as controls. Patients with left bundle branch, vulvular heart disease, history of coronary artery bypass surgery, cardiomyopathies, arrhythmias and major chronic illness were excluded. Each subject had signed the written informed consent.

Each patient underwent Tc$^{99m}$ tetrofosmin stress and rest studies. Tetrofosmin study was performed according to one day protocol which is as follows. In stress test, after a graded treadmill exercise, Tc$^{99m}$ tetrofosmin (10mCi) was injected intravenously at peak of exercise and the patient was asked to continue exercise for another one minute if possible. The images were then acquired after 30 minutes on Siemens Scintillation Orbiter 75 Gamma Camera with Micro delta computer processing System. In rest studies, 30mCi of Tc$^{99m}$ tetrofosmin
was injected intravenously four hours after stress imaging and rest imaging performed. Imaging was done half an hour after fatty meal (glass of milk to facilitate hepatic excretion in both phases of study. Spect images were assessed in five segments: anterior, septal, inferior, lateral and apical. The nature of abnormality was characterized as either fixed or reversible, based on the changes observed in the resting images. The images were read in pairs of stress rest. Each segment was scored as normal, fixed defect, reversible ischemia and mixed defect.

RESULTS
The study included 35 patients and 30 controls. Mean age in patients was 51.56 years and in controls was 45 years. Using image analysis patients were characterized as normal, reversible ischemia, fixed defect and mixed defect (had both infarction and reversibility). By segmental analysis (five segment per patient), 35 patients had perfusion defects by SPECT Tc\(^{99m}\) tetrofosmin imaging. Out of 95 perfusion defects, reversible ischemia and mixed defects were more common in inferior wall and fixed defect in left ventricular apex (table 1). When compared with angiographic findings for involvement of left anterior descending artery, out of 35 patients 25 were positive and 10 negative on tetrofosmin study, while 27 were positive and 8 were negative on angiography. P value was <0.01, sensitivity 85% and specificity 83%. Positive predictive value was 92% and negative predictive value was 60%.

Similarly out of 35 patients, 22 were positive for involvement of right coronary artery and 13 negative on tetrofosmin study, while 23 were positive and 12 were negative on angiography. P value was <0.01, sensitivity 87% and specificity 83%. Positive predictive value was 91% and negative predictive value was 77%.

Similarly when circumflex artery was studied, out of 35 patients, 15 were positive and 20 negative on tetrofosmin study, while 20 were positive and 15 were negative on angiography. P value was <0.01, sensitivity 70% and specificity 93%. Positive predictive value was 93% and negative predictive value was 70%.

DISCUSSION
The study was undertaken to determine the pattern of perfusion defects in ischemic heart disease patients. Imaging was done using tetrofosmin Tc\(^{99m}\) in patients suffering from coronary artery disease. Myocardial perfusion scans can localize the obstructed coronary vessel(s) via localizing the extent of the heart muscle area with reduced blood flow. It also provides information about the heart’s pumping function, and identify areas of the heart muscle that are scarred from a heart attack. Thus, they are superior to routine exercise stress testing (without imaging) and provide information necessary to help identify patients with an increased risk for a heart attack, who may be candidates for invasive procedures, such as coronary angiography, angioplasty, and heart surgery.

Exercise induced myocardial ischemia can be imaged directly with \(^{18}\)FDG. Combined exercise \(^{18}\)FDG- Tc\(^{99m}\)-imaging provides a better assessment of exercise-induced myocardial ischemia compared with exercise-rest perfusion imaging. Direct ischemia imaging eliminates some of the limitations of presently used myocardial perfusion imaging. Large-scale clinical studies are warranted.

In our study, by segmental analysis (five segment per patient), 35 patients had perfusion defects by SPECT Tc\(^{99m}\) tetrofosmin imaging. Out of 95 perfusion defects, reversible ischemia and mixed defects were more common in inferior wall and fixed defect in left ventricular apex (table 1). P value is <0.01 and marked sensitivity and specificity is seen when compared with coronary artery disease.

In the study by Xiang et al, perfusion abnormalities were seen in myocardial segments corresponding to 25 vascular territories of a total of 51 vessels with ≥ 50% luminal narrowing in 22 patients (sensitivity 49%), whereas increased \(^{18}\)FDG uptake was seen in 34 vascular territories (sensitivity 67%, P=0.008).

Another study by Samady et al demonstrates significant correlation between Tc\(^{99m}\) uptake at rest and unipolar voltage and normalized unipolar voltage for all myocardial segments. Current nuclear techniques appear to be highly sensitive for the detection of myocardial viability in asynergic myocardium.

Table-1: Distribution of perfusion defects in different cardiac segments
The numbers of subjects are shown and percentage is given in parenthesis

<table>
<thead>
<tr>
<th>Perfusion Defects Tc(^{99m}) Tetrofosmin</th>
<th>Inferior Wall No. (%)</th>
<th>Lateral wall No. (%)</th>
<th>Anterior Wall No. (%)</th>
<th>Apex No. (%)</th>
<th>Interventricular septum No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversible Ischemia</td>
<td>14 (24)</td>
<td>12 (20)</td>
<td>10 (17)</td>
<td>10 (17)</td>
<td>13 (22)</td>
<td>59 (62)</td>
</tr>
<tr>
<td>Fixed defect</td>
<td>4 (15)</td>
<td>1 (4)</td>
<td>7 (27)</td>
<td>9 (35)</td>
<td>5 (19)</td>
<td>26 (27)</td>
</tr>
<tr>
<td>Mixed defect</td>
<td>4 (40)</td>
<td>2 (20)</td>
<td>-</td>
<td>1 (10)</td>
<td>3 (30)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Total</td>
<td>22 (23)</td>
<td>15 (16)</td>
<td>17 (18)</td>
<td>20 (21)</td>
<td>21 (22)</td>
<td>95</td>
</tr>
</tbody>
</table>
CONCLUSION
Reversible ischemia and mixed defects were more common in inferior wall and fixed defect in left ventricular apex. Current myocardial perfusion imaging agents appear to be highly sensitive for the detection of myocardial viability in asynergic myocardium.

Acknowledgment
We owe thanks to Mr Salman Arshad for carefully typing the manuscript

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