ORIGINAL ARTICLE

# Accuracy of Thallium Scintigraphy Versus Coronary Angiography for Coronary Artery Disease in Diabetics

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## ABSTRACT

**Objective**: To determine the sensitivity and specificity of thallium scintigraphy in detection of coronary artery disease in diabetic patients.

**Study Design**: Cross-sectional validation study.

**Place and Duration of Study**: The study was carried out from July to December 2007 in the Cardiology Department of the Pakistan Institute of Medical Sciences, Islamabad.

**Methodology**: A total of 60 diabetic patients suspected of having coronary artery disease were studied. Systematic probability sampling technique was used during their selection. All the patients underwent thallium scintigraphy followed by coronary angiography, which was used as gold standard test.

**Results**: Out of 60 patients, 44 had positive thallium scintigraphy and 16 were negative. Likewise, 46 had positive angiography and 14 were negative. Out of 46 patients with positive angiography, thallium scintigraphy was positive in 41 subjects (sensitivity 89%) and false negative in only 5 of the 46 patients. Out of 14 patients with negative angiography, 11 patients had a negative thallium scintigraphy (specificity 79%) and the remaining 3 had a positive thallium scintigraphy. This gives thallium scintigraphy a positive predictive value of 93% and a negative predictive value of 69% when compared with angiography.

**Conclusion**: Thallium scintigraphy is a useful modality in the detection of coronary artery disease in diabetic patients.

**Key words:** *Sensitivity. Specificity. Thallium scintigraphy. Coronary angiography. Diabetes mellitus. Coronary artery disease.*

## INTRODUCTION

Diabetes causes microvascular diseases such as nephropathy, neuropathy and retinopathy and macro-vascular disease, like atherosclerosis.[1-3] Atherosclerosis of coronary, cerebral and peripheral arteries accounts for approximately 80% of mortality and 75% of hospitalization in persons with diabetes.

Prevalence of diabetes is approximately 18% in the U.S population.[4,5] Globally, 200 million individuals have diabetes and projections by the World Health Organization and others suggest that its prevalence will exceed 300 million by 2025 and 360 million by 2030.[6] Patients with diabetes have a two to four fold increased risk of coronary artery disease.[7] For every age stratum, ethnic background and risk factor level, men with diabetes had an absolute risk of coronary artery disease death more than three times higher than that in the non-diabetic cohort, even after adjustment for established risk factors.[8]

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In the general population, women usually develop coronary artery disease approximately 10 years later than men. However, diabetes blunts the cardiovascular benefit of the female gender increasing the risk of death after myocardial infarction (MI) more than in men.[9] In a state wide analysis of MI, the risk of death in diabetic subjects was 87% greater than in non-diabetics aged 30 to 49 years but only 17% greater in the 70 to 89 years age group.[10] Younger diabetic patients are at greater risk of death due to MI.

Thallium scintigraphy (Thallium) is a good test to detect coronary artery disease in suspected cases. It is a monovalent cation with biological properties similar to potassium. It is transported across the myocyte cell membrane by a $Na^+$,$K^+$ adenosine triphosphatase (ATPase) transport system and by facilitated diffusion. It emits 80 KCV of photon energy and has a physical half life of 73 hours. Because potassium is the major intracellular cation in muscle and is virtually absent in scar tissues, Thallium 201 is a well suited radionuclide for differentiating normal and ischemic from scarred myocardium.[11]

Accurate cardiovascular risk stratification of patients with Diabetes mellitus is necessary because diabetic patients have a higher prevalence of coronary artery disease,[12] experience more diffuse, calcified and extensive coronary artery disease, often have more advanced coronary artery disease at the time of diagnosis and more often experience silent ischemia.

Accordingly, early accurate diagnosis of coronary artery disease in diabetic patients is needed and reliable prognostication is mandatory. The American Diabetic Association has recommended an algorithm whereby diabetic patients are referred for either evaluation by a cardiologist or stress echo or stress perfusion imaging. For patients who are at high risk for coronary artery disease, imaging studies would be preferred.[13]

Based on the high prevalence of atherosclerosis and silent ischemia and the high risk for cardiovascular events, the issue of screening for coronary artery disease in asymptomatic diabetes has been raised and debated intensively.[14-16] Published data regarding detection and screening of coronary artery disease in diabetic patients using thallium scanning in Pakistan is scanty. The present study was carried out to determine the sensitivity and specificity of thallium scintigraphy in detection of coronary artery disease in diabetic patients.

## METHODOLOGY

The present study comprised of 60 patients selected using systematic (probability) sampling technique at the Cardiology Department of the Pakistan Institute of Medical Sciences, Islamabad from July to December 2007. Patients above the age of 30 years of either gender who had diabetes mellitus and suspected coronary artery disease by history and risk factors were included in study.

Consent was taken from all the patients regarding invasive and non-invasive tests and for further treatment (percutaneous coronary intervention/coronary artery bypass grafting) depending on the nature of the disease. Patients who gave consent were included in the study. Approval was taken from the hospital ethical committee. Patients who were non-diabetic, had atypical chest pain, cervical spondylosis, renal failure, peripheral arterial disease, neoplasm and those already diagnosed with coronary artery disease were excluded from the study.

Initially, patients underwent standard thallium scintigraphy. For image interpretation, a semi quantitative visual analysis was applied, in which the myocardium was divided into 17 segments and perfusion in each segment was graded from 0-4, with 0 representing normal perfusion and 4 representing a very severe perfusion defect. Scores for all 17 segments were added to create a summed score. The summed stress score represents the extent and severity of perfusion abnormality related to both ischemia and infarction. The summed rest score represents the extent of the infarction. The patient's thallium scintigraphy was taken as a positive test if there was perfusion abnormality related to ischemia and negative if there was no perfusion abnormality related to ischemia.

Next, the same patients underwent coronary angiography. In angiography, the percentage of coronary artery stenosis was recorded.

Coronary angiography showing 70% stenosis was recorded as a positive test and below that were recorded as negative test. All the patients who had significant disease underwent percutaneous coronary intervention/coronary artery bypass grafting depending on the nature of disease as they have given consent for treatment.

The data was analyzed using SPSS version 10. Mean and standard deviation were calculated for age and fasting blood sugar levels. Frequency and percentages were presented for categorical variables like gender, thallium scintigraphy and coronary angiography results. Sensitivity, specificity, positive predictive value and negative predictive value were calculated by using coronary angiography results as gold standard.

## RESULTS

A total of 60 cases were studied. Out of these, 39 (65%) were males and 21 (35%) were females. The minimum age was 30 years and the maximum was 75 years with a mean age of 51 years. Minimum blood sugar fasting recorded was 139 mg/dl and maximum was 265 mg/dl with a mean blood sugar fasting of 206 mg/dl.

Forty four (73%) had positive thallium scintigraphy and 16 (27%) were negative. Out of 60 cases, 46 (77%) had positive angiography and 14 (23%) were negative. A total of 41 cases were positive both for thallium scintigraphy as well as on angiography (true positive). Three cases were positive for thallium scintigraphy but were negative on angiography (false positive). Like wise, 5 cases were negative for thallium scintigraphy, but were positive on angiography (false negative). Eleven cases were negative both on thallium scintigraphy as well as on angiography (true negative). This showed a sensitivity of 89% and specificity of 79%, with a positive predictive value of 93% and a negative predictive value of 69% for thallium scintigraphy.

## DISCUSSION

The diagnostic and prognostic significance of thallium scintigraphy has been discussed and proven in multiple randomized controlled trials and results have been verified in comparison with angiography. The stratification of coronary artery disease into various categories of low, intermediate and high risk depends upon the population in the study group. Subjects having a high pre-test likelihood of disease will increase the sensitivity and specificity of the test, while subjects with a low pre-test likelihood will make the test less sensitive and specific.

For prognostication, patients are generally classified into three categories. The low risk patients are those with an annual cardiac mortality of less than 1%, the high risk are those with an annual cardiac mortality of more than 3% and intermediate risk patients are those with an annual mortality between 1 and 3%.

In this study population, the subjects picked were diabetic with their history suggestive of coronary artery disease. If the study group had been selected from the general population, the results would have been different. The study results showed a sensitivity of 89% and specificity of 79% as compared to coronary angiography. This gives thallium scintigraphy a positive predictive value of 93% and negative predictive value of 69%. ACC/AHA guidelines summary state the sensitivity of 87% and specificity of 73%.[17] The presently reported percentages of sensitivity and specificity are higher. It could be due to two reasons. Firstly, as there were 65% males in this study, so breast attenuation defects were minimized and secondly, the selected subjects were at high risk for coronary artery disease because of the primary morbidity that was diabetes.

A study conducted in the All India Institute of Medical Sciences, New Delhi showed sensitivity of 87.5% and specificity of 84% in diabetic patients.[18] So, the results of this study are comparable to that study.

Rajagopalan, *et al.* studied 1427 asymptomatic diabetic patients and reported that the prevalence of abnormal scan was 58% with an annual hard event rate of 5.9%, for those with abnormal scan versus 1.6 % for those with a normal scan.[19]

A meta analysis of 31 studies indicates that a normal study is associated with an excellent prognosis.[20] The annual hard event rate (cardiac death, myocardial infarction) was 0.85% with the normal study. This number is comparable with the annual event rate in the general population rate without coronary artery disease. In contrast, the annual hard event rate was 5.9% in patients with moderate to severe abnormal study. The likelihood of an event increases in parallel to the extent of abnormalities on the scan study. Various predictive parameters have been identified on scanning. These include small fixed defect size, increasing defect size, defect reversibility, defect in multiple vascular territories, increasing tracer lung uptake and transient ischemic dilatation of left ventricle.

The findings of this as well as related studies suggest that thallium scintigraphy is a useful modality in detection and screening of coronary artery disease in diabetic patients. It not only detects coronary artery disease in diabetic patients but also predicts the prognosis.

## CONCLUSION

Although no single diagnostic test is best suited for detection and screening of coronary artery disease, it seems reasonable to conclude based on available data, easy accessibility, cost consideration and the non-invasive nature of the test, that thallium scintigraphy is a useful modality in the detection and screening of coronary artery disease in diabetic patients.

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