Assessment of the integrated role of myocardium perfusion gated SPECT study in patient with parathyroid adenoma by ^{99m}Tc-sestamibi

Original Article

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ABSTRACT

Introduction: The purpose of this study is to assess the integrated role of scintigraphy by Tc99m MIBI in diagnosis of parathyroid adenoma and its impacts on the myocardium, and to evaluate whether myocardium perfusion gated SPECT study could be a complementary routine workup for patient with positive parathyroid adenoma on Tc99m MIBI parathyroid scan.

Methods: Rest myocardium perfusion gated SPECT study was performed on the same day of parathyroid scintigraphy, the stress study were completed on the next day for complete assessment of the myocardium perfusion and LV functions.

Results: Population included 30 patients; 56% were positive for parathyroid adenoma and compared to 44% negative for parathyroid adenoma, the latter was considered as control group, the gated SPECT EF was normal in 62.5% and abnormal 37.5%. Myocardial perfusion was abnormal in 43.75%, the overall hemodynamic disorder including EF abnormalities as well as the perfusion defects in the study group were 62.5% compared to 27.5% in the controlled group with statically significant relationship (P value=0.03).

Conclusion: The risk of premature cardiovascular death in p HPT is a serious problem and the present study indicates that scintigraphically detected parathyroid adenoma has an impact on the overall hemodynamic of the myocardium and the complementary role of rest/ stress two days protocol Tc99m MIBI myocardium perfusion gated SPECT study may be promising , but its usage as routine workup specially in patient with positive parathyroid adenoma and have high risk warranted further evaluation and reassessment.

Key words: Tc99m MIBI parathyroid scintigraphy; Myocardium perfusion gated SPECT; Parathyroid adenoma

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INTRODUCTION

Parathyroid hormone (PTH) has central role in calcium homeostasis, yet primary hyperparathyroidism (pHPT), mobilizes calcium to the blood stream and induce symptoms of hypercalcaemia [1], pHPT caused by solitary parathyroid adenomas in 85% of cases and a diffuse hyperplasia in most of the remaining cases [2].

It has been reported that patients suffering from pHPT have increased premature death which seems to be mainly due to an overrepresentation cardiovascular death [3]. pHPT is reported to be associated with hypertension, disturbances in the renin–angioten- sin–aldosterone system, cardiac arrhythmia as well as structural and functional alterations in the vascular wall [4]. It has found that the vascular actions of PTH may result in an altered regulation of vasomotor tone and thus in impaired perfusion. This abnormality might be particularly relevant in those tissues such as the myocardium [5]. The functional properties of the heart might be affected by the hyperparathyroid [6]. Cardiovascular diseases such as myocardial Infarction, stroke and heart failure seem to be excessively prevalent causes of death among pHPT patients [7].

Parathyroid imaging has involved a number of different radiotracers that were used in many different ways. Technetium -99m sestamibi (99mTc-MIBI) scanning has become the imaging modality of choice [8]. The sensitivity of MIBI for detection of solitary adenomas ranges from 68 to 95% [9].

On other hand SPECT myocardial imaging provides useful information about the myocardial perfusion, extent and severity of fixed or reversible perfusion defects and the use of electrocardiographic gating has deeply modified the scenario of myocardial perfusion single-photon emission computed tomography (SPECT). The available gated SPECT processing software can measure the left ventricular volumes and ejection fraction improved the diagnostic capability of myocardial perfusion imaging. Other studies have shown that assessment of the use of gated SPECT as a reliable modality for examining the left ventricular contractile reserve on both a regional and a global basis has become a reality, with different possible applications [10].

The aim of this study is to assess the integrated role of scintigraphiy by Tc99m sestamibi in diagnosis of parathyroid adenoma and its impacts on the myocardium, clarify the connection between pHPT and cardiac morbidity as well as to evaluate if the myocardium perfusion gated SPECT study could introduced as a routine workup for patient with positive parathyroid adenoma on Tc99m sestamibi parathyroid scan.

METHODS

Among all questionable cases of hyperparthyroidsm came to our nuclear medicine unite (48) perform Tc-99 m MIBI parthyroid scintigraphy studies between January 2011 and Febrauray 2013; planar view of parathyroid scintigraphy were performed 5 min and 2 h after intravenous administration of 20 mCi of 99mTc-MIBI with a low-energy, high-resolution collimator. The field of view in planar image encompasses the neck and thorax additional whole body scan was performed to evaluate ectopic parathyroid glands or brown tumors. Double phase99mTc-MIBI parathyroid scintigraphy was based on the time related differential washout of radioactivity between the thyroid gland and a parathyroid tumor. Subtraction technique using Tc99m pertechnetate to outline the thyroid was performed to highly suspicious patients for parathyroid adenoma.

All the positive cases of parathyroid adenoma by scintigraphy (16) without a history of coronary artery disease (CAD), chest pain or dyspnea or other exclusion criteria: previous evidence of arrhythmias, valvular heart disease, left ventricular dysfunction, history of CAD, history of more than mild hypertension (diastolic blood pressure >95 mmHg), renal failure (chronic kidney disease with estimated glomerular filtration rate <60 ml/min) and long standing diabetes mellitus; The myocardium perfusion gated SPECT study was two days protocol; The rest phase was on the same day and by the same dose of parathyroid scintigraphy at 45–60 min after intravenous administration of the tracer ; The stress test was on the next day, stress test used was exercise in 19 patients and dipyridamole in 11 patients, exercise stress test (Treadmill) Exercise endpoints were 85% or more of the maximum predicted heart rate, symptoms of severe angina, or 2-mm ST-segment depression on ECG and written inform consent was obtained.

The negative cases of parathyroid adenoma by scintigraphy control group (14) followed the same and matched with case group as regard the for mentioned exclusion criteria; The rest phase was on the same day and by the same dose of parathyroid scintigraphy and The stress test was on the next day.

Data acquisition, reconstruction and image analysis for the gated SPECT myocardial imaging stress study; 20mCi of 99mTc-MIBI was intravenously injected at peak exercise with stress continuing for another minute. Gated SPECT myocardial imaging acquisition started 30 min later. Gated SPECT myocardial imaging data were acquired in the supine position with a single-head SPECT gamma camera (Siemens, symbia e; Siemens Medical Solutions USA Inc) equipped with a general purpose low-energy collimator. Sixty four projection images over a 180_ non-circular orbit were acquired. Time per projection was 15s, matrix size 64 X 64, zoom 1.45, and gating eight frames per cardiac cycle.

The reconstructed data were projected as myocardial tomographic slices in the short axis, vertical-long axis, and horizontal long axis views. Gated SPECT myocardial imaging data were then processed and analyzed using software Quantitative Gated SPECT (QGS, QPS Cedars-Sinai Medical Center, Los Angeles, CA).The left ventricular EDV, ESV, and EF were also determined by QGS software.

The presence of perfusion defects was classified the defects as reversible (including partially reversible) or fixed (irreversible). To determine the presence, location and severity of any perfusion abnormalities, SPECT images were assessed in the following manner: the left ventricle was divided into 20 segments, and each segment was assigned a score using a five-point scoring system (0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced; and 4, absent uptake). The sums of segment scores at stress (SSS), scores at rest summed rest score (SRS) and differences between the stress and rest scores summed difference score (SDS) were calculated. All images were interpreted by experienced consultant in nuclear medicine.

For the statistical analysis, chi-square tests were performed using the Epi 6 and a p-value less than 0.05 was considered to be significant.

RESULTS

During the indicated time interval, 33 patients fulfilled the selection criteria and any patient with high risk or known history of CAD was excluded from the study. Of them, three didn't come at the next day for the stress phase of the cardiac study. Therefore, the final patient population included 30 patients; 12 (40%) were men, and 18 (60%) were women (mean age; 42; age range, 19–67 years) ; of the 30 patients , 16 (56%) had a positive 99mTc-MIBI scintigraphy and localize parathyroid adenoma and were categorized as study group includes 10 male (62.5%) and 6 female (37.5%), compared to 14 (44%) who were negative for parathyroid adenoma and considered as control group. The control group included 7 male (50%) and 7 female (50%) with mean age 44 (Table 1).

These parathyroid adenomas were represented by a sestamibi-avid focus located at the left inferior parathyroid gland (6 patients) right inferior parathyroid gland (5 patients) and more than one parathyroid gland (5 patients).

By analyzing the demographic data and its impact on the overall cardiovascular disease (CVD), In the study group, there was no statistically significant difference between the positive cases for CVD and the negative cases for CVD as regard the demographic characters(age and sex) (Table 2).

Table 1. Demographic distribution of the parathyroid adenoma among the study and control groups.

Variables	Positive for parathyroid adenoma	Negative for parathyroid adenoma
Total	16 (56%)	14 (44%)
Men	10 (62.5%)	7 (50%)
Women	6 (37.5%)	7 (50%)
Mean age	37.5	44.9

In the control group, there was no statistically significant difference(P value > 0.05) between positive cases for CVD and negative cases for CVD as regard the demographic characters (age and sex) (Table 3). From previous both table, it was found that demographic characters had no neither risk in developing CVD either in study nor control group.

Table 2. The effect of demographic distribution of study group in developing cardiovascular disease (CVD).

Variables		Positive CVD	Negative CVD	X^2	P value
Sex	Men	5 (50.0%)	5 (50.0%)	0.02	0.89
	Women	2 (33.3%)	4 (66.7%)		
Age	≤ 37.5	2(33.3%)	4(66.7%)	0.30	0.83
	>37.5	7(70.0%)	3(30.0%)		

Table 3. The effect of demographic distribution of control group in developing cardiovascular disease (CVD).

Variables		Positive CVD	Negative CVD	X^2	P value
Sex	Men	2 (28.6%)	5 (71.4%)	0.35	0.55
	Women	2 (28.6%)	5 (71.4%)		
Age	≤ 44.9	2(33.3%)	4(66.7%)	0.07	0.80
	>44.9	2(25.0 %)	6(75.0%)		

Table 4. Effects of parathyroid adenoma on LV EF at both stress and rest sets of the gated perfusion SPECT study.

	Case Group (Positive for adenoma)	Control Group (Negative for adenoma)	T test	P value
Mean LV EF-Stress	49.8	56.7	1.25	0.22
Mean LV EF-Rest	52.9	56.6	0.61	0.50

Table 5. The mean LV EF at both the study and control groups.

	Case Group (Positive for adenoma)	Control Group (Negative for adenoma)	T test	P value
Mean LV EF-Stress	49.8	56.7	1.25	0.22
Mean LV EF-Rest	52.9	56.6	0.61	0.50

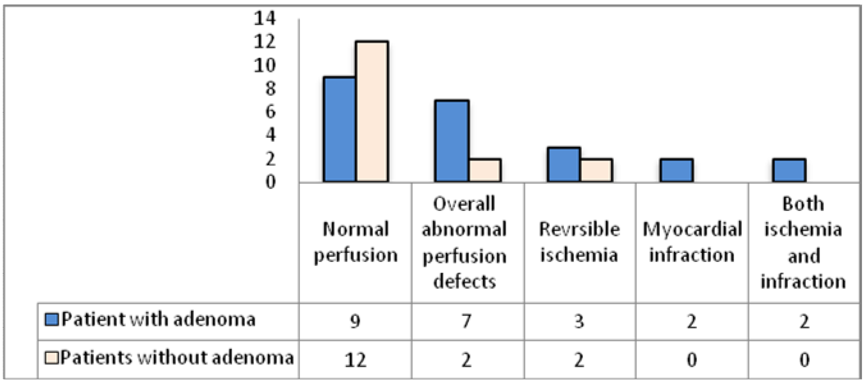

Fig 1. Cardiac events (perfusion defects) in patients with and without parathyroid adenoma.

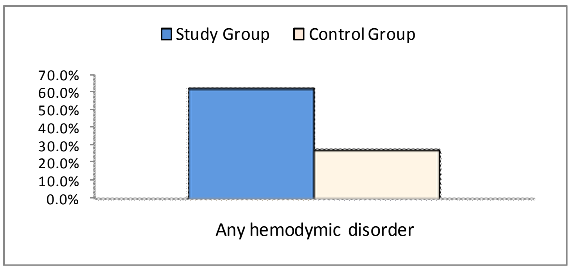

Fig 2. Overall perfusion and functional abnormalities in both groups ($X^2 = 4.57$, $p = 0.03$).

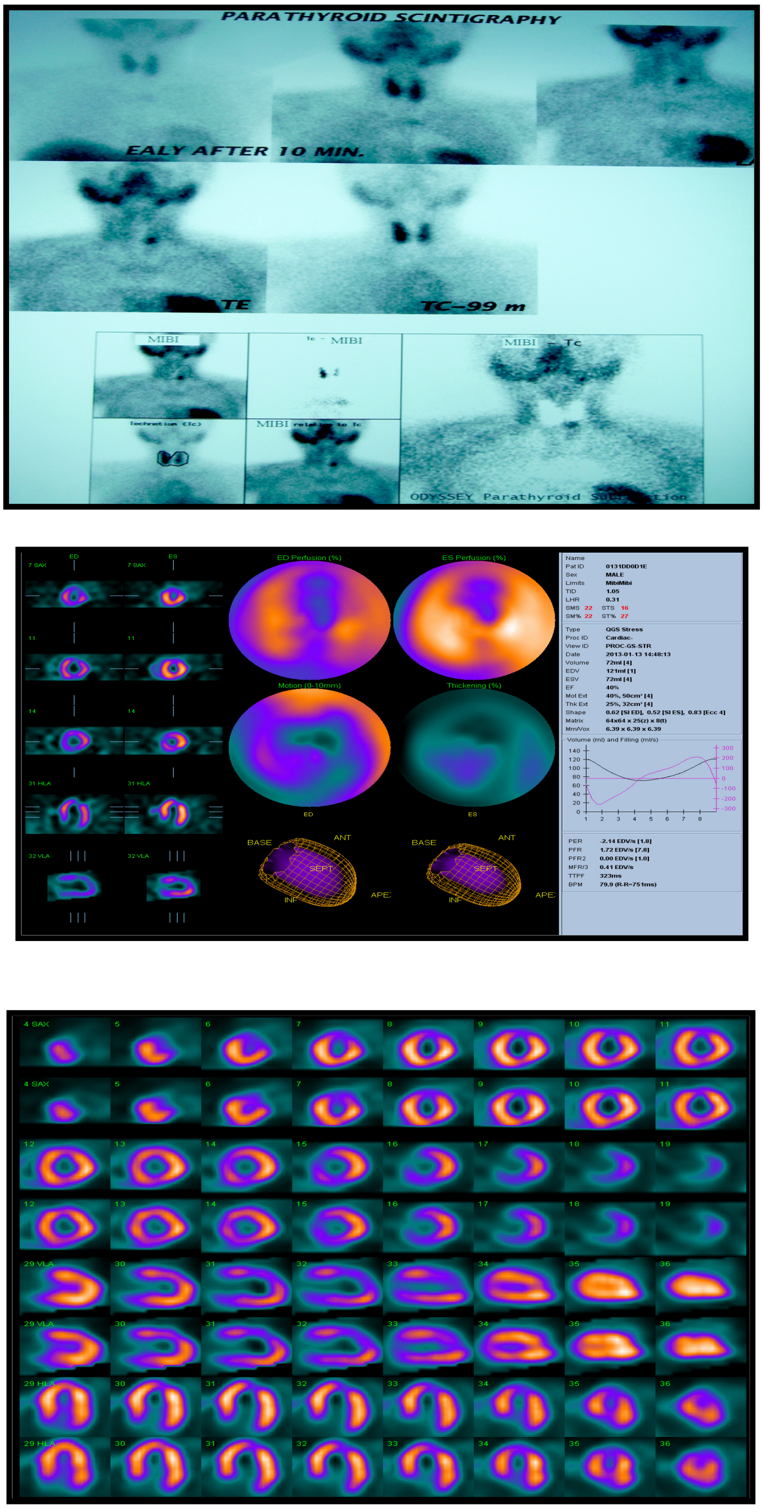

Fig 3. A 42-year old female patient complains of generalized bone ache; her PTH was remarkably elevated, dual phased Tc99m seat MIBI parathyroid scintigraphy with complementary thyroid scan revealed sizeable left inferior parathyroid adenoma, The myocardium perfusion gated SPECT study showed hemodynmically significant myocardium perfusion defect deduced from marked ischemic change at the antero-apical wall with reduced LV EF post stress (40%) .

In the study group (patient with adenoma), the resting gated SPECT was normal in 10 patients (62.5%) and abnormal in 6 patients (37.5%). The resting EF was (mean 52.9 ± 20.6, range 25-88) , we considered the value of LV EF normal if it is = 50% or higher in female and more than 42% in male [11], among 6 patient, 5 patient has reduced EF associated with perfusion abnormalities and 1 patient his EF is reduced without perfusions defects (Table 4).

In stress gated SPECT, gated SPECT was normal in 10 patients (62.5%) and abnormal in 6 (37.5%), The post stress EF was (mean 49.8 ± 19.9, range 22-76), among 6 patient 5 patient has reduced EF associated with perfusion abnormalities and 1 patient has reduced EF without perfusions defects.

In the control group (patient without adenoma), the resting gated SPECT was normal in 10 Patients (83.4%) and abnormal in 2 (16.6%), The resting EF was (mean 56.6 ± 9.4, range 40-74), In stress gated SPECT, was normal in 10 Patients (83.4%) and abnormal in 2 (16.6%), The post stress EF was (mean 56.7 ± 10.4, range 35-75).

There was no statistically significant difference between case and control groups as regard the mean LV EF at both rest and stress (Table 5).

Myocardial perfusion was abnormal in 7 patients (43.75%) among all 16 patients had adenoma, by reviewing the rest and stress phases; 3 patients had reversible ischemic changes, 2 patients with myocardial infarction while 2 patients had both reversible ischemic changes and myocardial infarction. The remaining 9 patients with adenoma (56.25%) exhibited normal perfusion pattern and unremarkable for any hemodynamically Significant perfusion defects, in the stress and the rest phases (P value= 0.3). Only 2 (14.2%) patients in the controlled group had significant CAD and both perfusion defects were reversible ischemic changes (Figure 1).

However the overall hemodynamic disorder including functional EF abnormalities and the perfusion defects in the study group were assessed in 10 patient (62.5%) compared to 4 patients (27,5%) in the controlled group , There was statically significant relationship (P value=0.03) (Figure 2).

Figure 3 shows parathyroid and myocardial perfusion studies of a 42-year old female patient.

DISCUSSION

Hyperparathyroidism is one of the most common endocrine disease worldwide, the pathologic findings of primary hyperparathyroidism are adenomas (80%-85%), hyperplasia (15%-20%) and carcinoma (<1%) [12]. The fact that specific tracer for parathyroid tissue does not exist. In fact, the tracers utilized in routine parathyroid nuclear medicine imaging, like 99mTc-sestamibi, are myocardial perfusion tracers and are taken up by the hyper-functioning parathyroid glands; ^{99m}Tc-MIBI parathyroid imaging is most likely to yield identification and localization of a parathyroid adenoma [8].

Primary hyperparathyroidism (PHPT) is associated with increased cardiovascular mortality. However, data on the association between PHPT and cardiovascular risk are lacking [13], with conflicting data concerning their extent and clinical significance, In this study the myocardium perfusion and ejection fraction was assessed as a marker for coronary artery disease and the myocardium function respectively.

In view of the fact that PTH has many effects on the heart; to alter heart rate, coronary blood flow, peak pressure, and rate of rise of left ventricular pressure, it is reasonable to hypothesize that PHPT could be associated with abnormalities in vascular function. Studies assessing the nature of vascular function in PHPT have focused on vascular reactivity, which measures small vessel or endothelial function, and vascular compliance, a measure of large vessel function [14]. It is well documented that PTH have several effects on the cardiovascular system, the results of several more recent studies have been interpreted as indicating that both PTH and PTHrP have direct positive inotropic effects.

In conclusion, of Marini et al [15] study indicates that pHPT is associated with a profound dysfunction of the coronary crocirculation. These findings represent a novel window to understand the cardiovascular actions of PTH in pHPT.

Ogaered et al [16], were previously study the relation between the scintigraphcially depicted parathyroid adenoma and its impact on the myocardium perfusion on Gated SPECT study; they surprisingly found 23% of patient without known ischemic heart disease, had significant myocardial perfusion defects, Patients with perfusion defects has also reduced LVEF, compared with patients without perfusion defects, The main limitation of this study that the assessment were only in the rest phase and it is actually incomplete study, so the reported coronary artery disease were limited only for patients with silent myocardial infarction, so addition of stress phase in our study is more reliable and more conclusive for better assessment of myocardium perfusion and functions. The other limitation Ogaered et al study that the study population was small and there was no control group. In the current study the rest myocardium perfusion gated SPECT study was performed on the same day of parathyroid scintigraphy prior to late parathyroid gland scan for easier acquisition and less radiation exposure, the stress study was completed on the next day to complete the assessment of the myocardium perfusion and LV functions. The abnormal perfusions were depicted in 7 (43.75%) patients among the 16 patients who were positive for adenoma, and 4 patients (25%) had silent myocardium infraction this result is nearly similar to Ogaered et al study, yet the addition of the stress study had an adding value as it showed that 2 patients had associated reversible ischemic changes with the infraction and 2 patients (12.5%) had reversible ischemic changes without infraction. Despite this apparent high percentage of myocardium perfusion defects previously reported; however when these findings compared to the control group; There was no statistically significant relationship and p=0.19; so the limitations of physical artifact should be considered during interpretations.

Most of the patients with perfusion defects had also associated reduced EF (71% of the patients) and one patient only had reduced EF without abnormal perfusion, again when the reduced LV EF in the study group compared to the control group the relationship was statically insignificant.

Finally, when the overall hemodynamic disorder included both perfusion defects and LV EF abnormalities in the case group compared to the control group we found that there was statically significant relationship, and the idea of performing two day protocol rest/ stress myocardium is apparently worthwhile and has an adding clinical value.

CONCLUSION

The risk of premature cardiovascular death in pHPT is a serious problem and the present study indicates that scintigraphically detected parathyroid adenoma has an impact on the overall hemodynamic of the myocardium and the complementary role of rest/ stress two days protocol Tc99m MIBI myocardium perfusion gated SPECT study may be promising , but its usage as routine diagnostic workup specially in patients have positive parathyroid adenoma on the scintigraphic base with high risk factors warranted further evaluation and reassessment.

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