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RESEARCH ARTICLE

ASSESSMENT OF SELECTIVE FACTORS AFFECTING MYOCARDIAL REVERSIBILITY IN ISCHEMIC HEART DISEASE USING ^{99M}TC-MIBI

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ABSTRACT

The aim of this retrospective study was to assess selective factors affecting the reversibility of the ischemic heart. The methodology carried out based on cardiac study at stress and rest for the distribution of ^{99m}Tc-MIBI with consideration to age, weight and gender. The results revealed that: the uptake in cunt/second/pixel (c/s/p) in stressed cardiac study for the affected heart segment (ischemic segment) has been decreased as the age increases, indicating the aging is a negative factor for ischemic reversibility, while there was a significant ($R^2 = 0.8$) increasing uptake during the stress phase for whole heart uptake, Rt/Lt lungs and the gastrointestinal tract (GIT). And there were significant ($R^2 = 0.7$) decreasing uptakes by whole heart, GIT and Rt/Lt lungs as the age increases with superior significant uptake by GIT during stress and rest at $R^2 = 0.6$ and 0.5 respectively. And in the correlation between weights in Kg versus count/sec at stressed cardiac study, the analysis revealed significant increased uptakes by GIT, Rt lung, Lt lung, and whole heart ($R^2 \approx 0.6$) as the weight increases whereas the same organs (GIT, Lt lung, Rt lung and the whole heart) showing significant ($R^2 \approx 0.7$) decreasing uptake as the weight increases as well as the affected heart segment The study also showed there were high frequencies percent of obese and overweight patients 52% and 32% respectively with ischemic heart segment reversibility of 37% among female relative to 30% among male, while the irreversible cases were greater among male 15% relative to only 4% among female and the incidence % of IHD is predominant among male 55% compared with 45% among female. The stress cardiac study enhance the uptake by the reversible ischemic segment hence gives further knowledge about ischemic reversibility% that could be managed by simple medications.

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INTRODUCTION

Ischemic (or ischemic) heart disease (IHD) is a disease characterized by reduced blood supply to the heart; Ischemia means a "reduced blood supply". The coronary arteries supply blood to the heart muscle and no alternative blood supply exists, so a blockage in the coronary arteries reduces the supply of blood to heart muscle. Most ischemic heart disease is caused by atherosclerosis, usually present even when the artery lumens appear normal by angiography, initially there is sudden severe narrowing or closure of either the large coronary arteries and/or of coronary artery end branches by debris showering downstream in the flowing blood, coronary artery (CAD) is presenting the start of many cardiomyopathy including reversible and irreversible ischemic diseases or myocardial infarction (MI), This disease is also affecting the myocardium wall motion causing wall motion abnormalities (WMA) due to lack of blood supply to different myocardium territories, ^{201}Thallium (*half-life ~72 hr emitting 70~80 Kev*) is considered as highly specific agent in detection of perfusion deficits of the myocardium in patients with severe coronary artery disease (CAD) compared to Methoxy Isobutyl Isonitrile (MIBI) which can be labeled with ^{99m}Tc (*Technetium half-life ~ 6 hrs emitting 141 Kev*) known as Sestamibi or Cardiotle, also proven high specificity and sensitivity in detection Ischemic heart disease (IHD), Nevertheless, the prognostic values of both radiopharmaceuticals (^{201}Thallium, ^{99m}Tc-Sestamibi) depending of their bio-distribution over particular myocardium territories is a matter of debate (Babak *et al*, 2014), investigations with the isonitrile complexes have shown them to undergo pattern of biologic distribution different from that of ^{201}TI (Raymond *et al*, 1997), Another study revealed that patients could be shown

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to have significantly higher heart-to-lung ratios as compared to those in both other groups, both heart-to lung- and heart-to-whole body ratios tended to decrease with a higher degree of CAD (Agnieszka *et al*, 2007). Ischemic Heart diseases are appearing as hypo intense areas throughout the heart segments acquired in nuclear medicine procedure of myocardial perfusion imaging (MPI) according to their specific territories within the myocardium.

MATERILS AND METHODS

A sample of fifty four patients underwent treadmill stress, Bruce's model of stress, using Philips/ADAC Forte SPECT (Philips Medical) Gamma Camera used for acquisitions, SPECT is using LFOV with LEHR Collimators, two basic executing systems", Synovia (Siemens Healthcare) and (Cedars) & (Corridor4DM) QPS for processing purposes.

Radiopharmaceuticals

In stress myocardial perfusion studies (MPS), the injected radiopharmaceuticals are delivered to the myocardium in proportion to flow. There is reduced tracer uptake in the regions with reduced flow and incensed tracer uptake in the region with increase blood flow. The currently used radiotracers in MPS are ^{201}Tl-chloride, ^{99m}Tc- sestamibi and ^{99m}Tc- tetrofosmin.

^{99m}Tc sestamibi

^{99m}Tc-cardiospect-MIBI (Cardio-SPECTTM, Medi-Radiopharma Ltd., Budapest; Hungary) most commonly used radiopharmaceuticals in MPS. The extraction efficiency is approximately 65% in the physiological flow range, the uptake is proportional to flow, and the deposition of the tracer does not increase linearly with flow, but rather tends to level off at higher flow rate. The distribution of ^{99m}Tc-related radionuclides remains relatively fixed over several hours. This allows imaging to be delayed up to several hours after injection, thereby facilitating the evaluation of patients presenting with acute chest pain. Hepatobiliary excretion of ^{99m}Tc may result in liver and/or gut activity obscuring the inferior wall of the left ventricle (LV). To immunize adjacent sub-diaphragmatic activity; imaging is delayed for at least 30 minutes after a stress injection and 60 minutes after a rest injection.

Image Analysis

Visual analysis of all images was performed by three experienced physicians, the images were post-processed in separate serverSyngo.via (Siemens Healthcare), using Corridor 4DM and Cedars QPS an individual ROIs were drawn around each study at LAD (Left Anterior descending artery) segments affected ischemic territories i.e.(17, 13, 14, 7, 8, 1, 2), calculated counts were registered and classified according to the respective pathological condition (Reversibility), Next, all calculated data were analyzed using Excel (Microsoft).

RESULTS

The following results shows the selected factors affecting the tissue reversibility in left anterior descending artery (LADR) of the heart as well as the radiopharmaceutical uptake ratio in whole heart, right/left (Rt/Lt) lungs, gastrointestinal tract (GIT-(*Liver, Gallbladder, spleen*)), the affected heart segment (territory) for the stress and rest in addition to patients weight distribution and the reversibility percent.

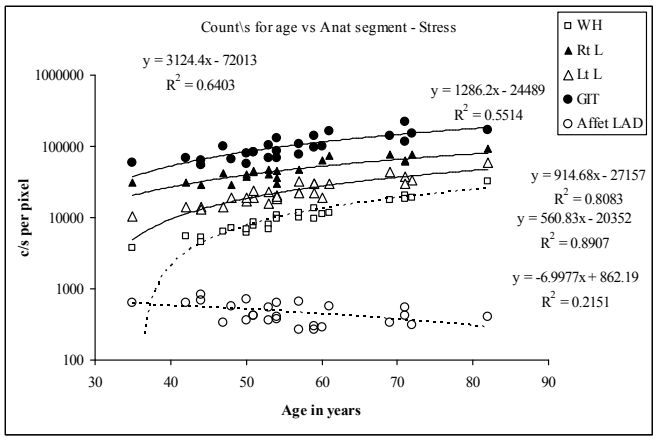

Figure 1. Shows the correlation between Age versus count/sec at stressed cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment at stress

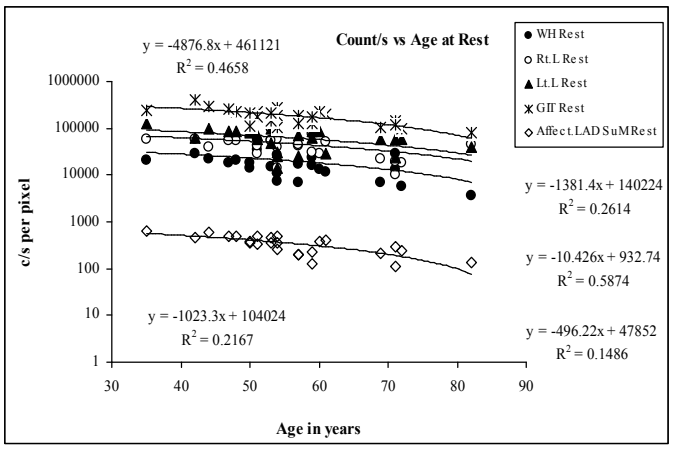

Figure 2. shows the correlation between Age versus count/sec at rest cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment at rest

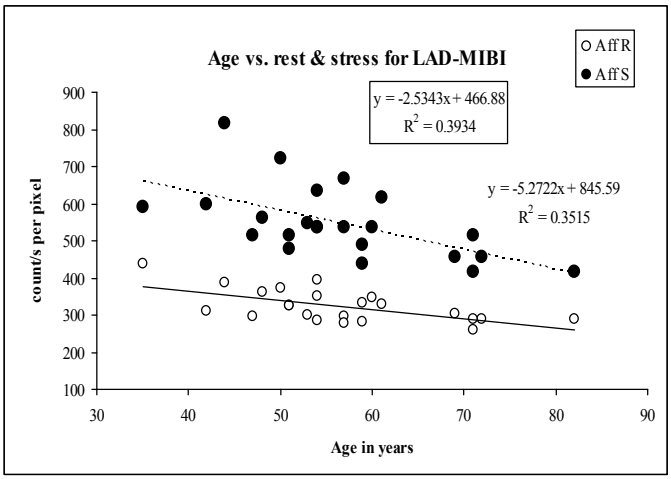

Figure 3. shows the correlation between Age in years versus count/sec at rest & stress for cardiac study of ischemic heart segment (left anterior descending artery)

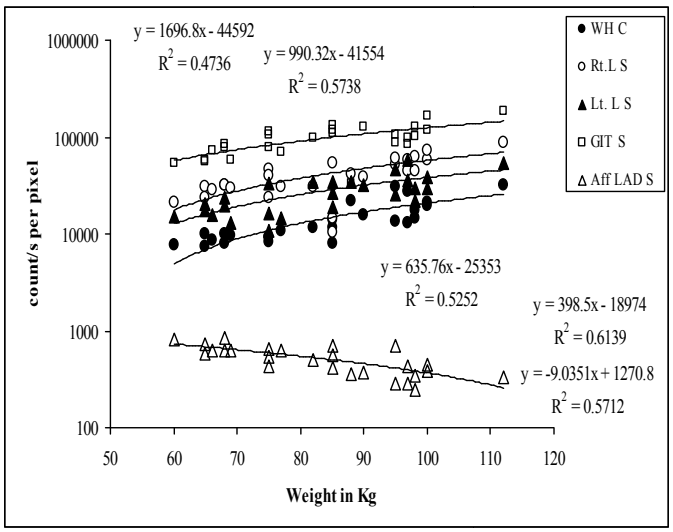

Figure 4. shows the correlation between weight in Kg versus count/sec at stressed cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment

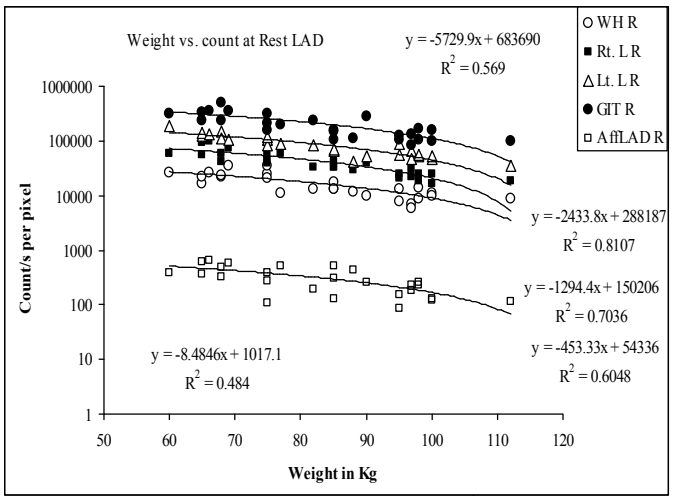

Figure 5. Shows the correlation between weight versus count/sec at rest cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment

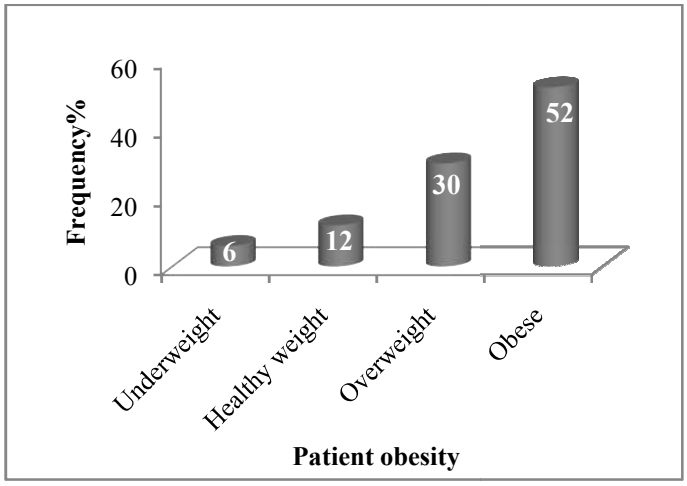

Figure 6. Shows the general patient weight distribution based on the body mass index (BMI)

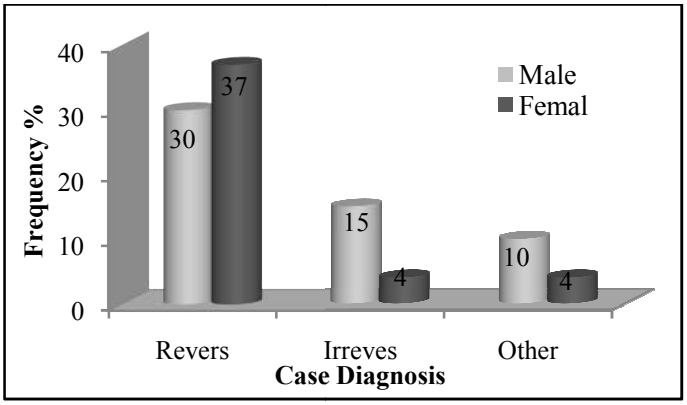

Figure 7. shows the frequency of reversibility% for ischemic heart segment among the gender

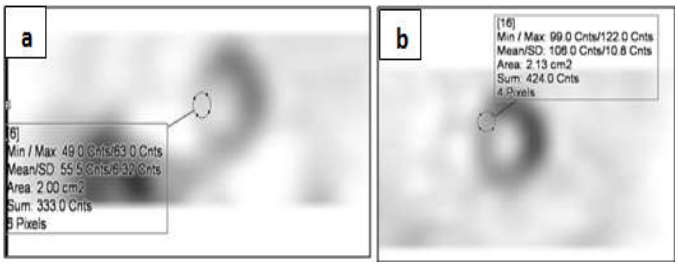

Figure 8. shows the uptake of apical heart & at ROI during rest (a) and stress (b) where the ischemic segment (17) manage to take a little amount of radiopharmaceutical, indicating the reversibility of the case

DISCUSSION

Regarding the study of myocardial ischemic heart disease; which is ascribed to defect of the Left Anterior Descending Artery (LADA) that supplying the heart segments (17, 13, 14, 7, 8, 1, 2) as classified by American Heart association (Cerqueira *et al*, 2002) and as well it is commonly involved y stenosis due to atherosclerosis, such segments radiopharmaceutical perfusion or uptake in count/second per pixel indicating the extend of LADA defect, which in turn reveals the vitality of the myocardial territory, the Bio distribution of the injected radiopharmaceutical as well as the ischemic reversibility. In Figure (1), which shows the correlation between Age versus count/sec at stressed cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment, it revealed that: the c/s per pixel (c/s/p) for the affected segment has been decreased as the age increases, such decrement could explain that: the aging is a negative factor for ischemic reversibility if occur or it could be ascribed to the fact that: elderly people likely to develop complete or partial occlusion of one or more coronary arteries (Earl *et al*, 2002). While the aging effect in c/s for the whole heart uptake, Rt/Lt lungs and the GIT was a significant increasing uptake during the stress phase where R^2 = 0.6, 0.6, 0.8 and 1 respectively, such results could be ascribed to significant promoted blood flow during blood pool phase of imaging of heart, muscles and GIT (Mitchell &Blomqvist, 971; João and Dominique, 2004) by exercise, also the higher uptake of MIBI by GIT is considered as a part of MIBI normal bio distribution property, as well it could be ascribed to un optimum heating of MIBI

(100°C); that causing the radiopharmaceutical miss its target and goes to salivary gland or thyroid in a form of free pertechnetate ($^{99m}TcPCO_4$). And in case of expiration date of the radiopharmaceutical, the body treats the radiopharmaceutical as foreign body and further being captured in liver (Baskot *et al*, 2011). Figure (2) shows the correlation between Age and count/sec at rest cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment, it revealed that: there were decreasing uptakes by whole heart, GIT and Rt/Lt lungs as the age increases, however the GIT shows significant uptake ($R^2 = 0.5$) relative to other anatomical structures; but less significant when compared with the values of stress where $R^2 = 0.6$, and the Rt/Lt lungs came secondly with less significance at $R^2 = 0.3$, and 0.2 respectively. Figure (3): shows the correlation between Age in years versus count/sec at rest & stress for cardiac study of ischemic heart segment (*left anterior descending artery*).

It revealed that: there is decreasing uptake by the affected heart segment following the patients aging; such decreasing correlation following aging indicates bad prognosis of IHD or irreversible tissue vitality, however there is obvious higher uptake in case of stress relative to rest which is ascribed to exercise that increase the heart ejection fraction and further increasing the blood flow in tissue (João and Dominique, 2004), also (Moretti *et al*, 2005) mentioned that loss of influx in cells at an early stage of apoptosis owing to a decrease in their electrical gradient, lack of retention in resistant cells mediated by multidrug resistant proteins and/or over expression of the anti-apoptotic protein Bcl-2, preventing mitochondrial accumulation, means that there will be poor accessibility of ^{99m}Tc-MIBI to the tumour, decreased viability and electrical gradients in 'over-aged' and hypoxic cells. In Figure (4) which shows the correlation between weight in Kg versus count/sec at stressed cardiac study for whole heart, Rt\Lt lungs, GIT and the ischemic heart segment. It is analysis revealed significant increased uptakes by GIT, Rt lung, Lt lung, and whole heart ($R^2 \approx 0.6$) as the weight increases, with same superior radiopharmaceutical uptake by GIT relative to other organs. Such results could be ascribed to the fact that obesity can alter the biodistribution of ^{99m}Tc-MIBI specifically with patients suffering from (IHD). These obtained results are agreed with the results mentioned by Agnieszka *et al*, (2007). While the affected heart segment remains with same decreasing uptake as the weight increases; this ascertains the irreversibility of tissue vitality of the affected heart segment among elderly people. In comparison with Figure (5) where patient at rest, however the same organs (GIT, Lt lung, Rt lung and the whole heart) showing significant ($R^2 \approx 0.7$) decreasing uptake as the weight increases as well as the affected heart segment, which might ascribed to the "uptake/retention" theory.

Such results are agreed with the results mentioned by Richard *et al*, (2011) in which they ascribed the loss of isotope in ischemic myocardial region by time and as well accounts for "wash-in" as the regions of myocardium supplied by "critically" narrowed arteries and arteries whose (vulnerable plaques) were ready to rupture. Also in the studied sample; the combination of severely disturbed flow through critically narrowed and/or unstable coronary lumen passages and relatively large regions of ischemic myocardium with impaired ability to accumulate sestamibi, results in a delay in initial isotope counts. Regarding the sample distribution based on weight or body mass index (BMI) as in Figure (6), the high frequencies were the obese and overweight patients (52% and 32% respectively), which is consider as a factor for CHD as mention by Canoy *et al*, (2013) that stated: "CHD risk increased with increasing BMI and waist circumference" and although BMI could be influenced by many other factors such as age, socioeconomic status, habits and physical activity (Whitlock *et al*, 2009; Wormser *et al*, 2011) as well as altitude living, however even these proved having direct impact in CHD risk (Roger *et al*, 2012). Figure 7: shows the ischemic heart segment reversibility and irreversibility% among both genders, in which the reversibility% was high among females and represents 37% relative to male 30%, while the irreversible cases were greater among male 15% relative to only 4% among female, such irreversibility of IHD among male could be due to the causative factors which are more common among male. And also the graph deduces that: the incidence % of IHD is predominant among male 55% compared with 45% among female, such high incidence among male is agreed with Jackson *et al*, (1997). While Figure (8) shows that: the uptake of apical heart & at ROI during rest (Figure 8a) with obvious lack of ^{99m}Tc-MIBI uptake and faint distribution, while at stress (Figure 8b) there was increased uptake by myocardium with significant ($P = 0.5$) uptake at ischemic zone of tissue which correspond to the apical segment number (17) within myocardium.

Conclusion

The selective factors such as age, weight, gender and obesity have great effect in IHD reversibility or tissue vitality that supplied by the left anterior descending artery. Also the study confirmed that: IHD is common among male relative female and as well the frequency of reversibility% for ischemic heart is high among female relative to male.

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