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SCINTIGRAPHIC ASSESSMENT OF CARDIOVASCULAR DISEASES IN ASYMPTOMATIC DIABETIC BLACK PATIENTS

Mboyo Di Tamba Willy Vangu

A thesis submitted to the Faculty of Health Sciences, University of the

Witwatersrand,

in fulfillment of the requirements for the degree of

Doctor of Philosophy

Johannesburg, 2011

DECLARATION

I, Mboyo Di Tamba Willy Vangu declare that this thesis is my own work. It is being submitted for the degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

_____ _____

MDTHW VANGU Date

I certify that the studies contained in this thesis have the approval of the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg.

Human Research Ethics Committee protocol number: M990236

Candidate: Mboyo Di Tamba Willy Vangu Date

Supervisor Karen Sliwa-Hahnle Date

DEDICATION

For my family,

For my friends and colleagues,

For all who believe in medicine and are giving the best they can to improve the health of the people.

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS STUDY AND OTHERS

PUBLICATIONS

I. Forming part of the PhD

Left ventricular systolic function: evaluation by M-Mode Echocardiography vs ECG-Gated myocardial perfusion imaging in patients with and without heart disease
Libhaber CD, Libhaber E, Zambakides CA, Esser JD, Perumal NS, Essop MR, Vangu MDTHW. S Afr Med J 2005; 95: 810

The effect Dipyridamole induced myocardial ischaemia on NT pro-B type natriuretic peptide excretion
De Greef J, Govender R, Libhaber CD, Libhaber E, Perumal S, Mkhize N, Malan N, Vermaak WJH, Vangu MDTHW. S Afr Med J 2006; 96: 1106

Clinical evaluation of women with suspected and known coronary artery disease with myocardial perfusion imaging
Libhaber CD, Libhaber E, Perumal NS, Mkhize N, Malan N, Zambakides CA, Esser JD, Essop MR, Vangu MDTHW. S Afr Med J 2006; 96:1113

Myocardial perfusion imaging in the diagnosis and risk stratification Of CAD in diabetic patients
Libhaber CD, Libhaber E, Perumal NS, Mkhize N, Malan N, Zambakides CA, Esser JD, Essop MR, Vangu MDTHW. S Afr Med J 2006; 96:1116

Evaluation of Patients Post Percutaneous Coronary Intervention with Myocardial Perfusion imaging.
Libhaber CD, Libhaber E, Perumal S, Jogi H, Purbhoo K, Zambakides CA, Esser JD, Essop MR, Vangu MDTHW. S A Heart 2007; 4: 73

Value of Myocardial Perfusion Imaging in Patients Post Coronary Artery Bypass Graft Surgery.
Libhaber CD, Libhaber E, Perumal S, Jogi , Purbhoo K, Zambakides CA, Esser JD, Essop MR, Vangu MDTHW. S A Heart 2007; 4: 75

Does Dipyridamole induce ischemia affect NT pro-BNP secretion?
Jacques De Greef, Radha Govender, William Vermaak, Nalini Perumal, Elena Libhaber, Mboyo-Di-Tamba Vangu. Cardiovasc J Afr 2007; 18: 371-374

Obesity as a predictor of Myocardial Ischemia in Patients referred for Myocardial Perfusion Imaging
Libhaber CD, Libhaber EN, Norton G, Woodiwiss A, Purbhoo K, Essop MR, Dhoodhat S, Zambakides CA, Esser JD, Vangu MDTHW. S A Heart 2008; 5:219

NT pro-BNP and the diagnosis of exercise induced ischaemia.
J. De Greef, M. Funk, W. Vermaak, N. Perumal, C.Libhaber, M.D.T.H Vangu. Cardiovasc J Afr 2008; 19: 254-258

II. Not related to PhD

Effects of ECT on regional cerebral blood flow measurement by 99m Tc-HMPAO SPECT.
MDT Vangu, JD Esser, IH Boyd, M Berk. J Neuropsychopharm 1999;2:S215

Regional cerebral perfusion of Tc 99m-HMPAO SPECT in Trichotillomania.
C Gordon, MDT Vangu, M Berk, JD Esser, IH Boyd. J Neuropscychopharm 1999;2:S215

A study using 99m Tc-MDP showing that the quality of bone scan is not improved by hydration.
MDT Vangu, I Boyd, D Mabelane. Nucl Med Func Metab Imaging 2001;25:601

Peritoneal pleural fistula: A case study.
MDT Vangu, M adams. Nucl Med Func Metab Imaging 2001;25:600

Non-toxic multinodular goiters.
wJ Kalk, MDT Vangu. S A J Endocrinol Metab Diabetes 2002;7:10-13

New onset seizures in HIV-infected patients without intracranial mass lesions or meningitis. A clinical, radiological and SPECT scan study.
Modi G, Modi M, Marthinus I, Vangu MDT. J Neurol Sciences 2002;202:29-34

Effects of electro-convulsive therapy on regional cerebral blood flow measured by 99m Technetium hexamethylpropylene amine oxime single photon emission computed tomography.
MDT Vangu, JD Esser, IH Boyd, M Berk. Progress Neuropscychopharm Biol Psychiatry 2003;27:15-19

A case for the provision of positron emission tomography (PET) in South African public Hospitals.
MM Sathekge, J Warwick, MDT Vangu, A Ellmann, M Mann. S Afr Med J 2006;96:598-601

Gastric emptying scintigraphy
NS Perumal, MDTH Vangu. The specialist forum 2007;7:34-40

Nuclear cardiology in clinical practice.
CD Libhaber, NS Perumal MDTH Vangu. SA J Cardiol Stroke 2007;1:26-32

Dacryoscintigraphy in patients with epiphora.
NS Perumal, MDTH Vangu. SA J Ophtamol 2007;2:11-13

Value of nuclear cardiology for the diagnosis and risk stratification of coronary artery disease.
CD Libhaber, MDTHW Vangu. SA Heart 2008;5:106-114

An unusual complication of thyroid carcinoma: pericardial effusion.
NS Perumal, CD Libhaber, N Malan, MDTHW Vangu. Eur J Nucl Med Mol Imaging 2008;35:S216-S402

Spontaneous perforation of the common bile duct.
NS Perumal, B Banieghbal, MDTHW Vangu. Eur J Nucl Med Mol Imaging 2008;35:S216-S402

The use of radionuclide in the evaluation of renal transplant.
NS Perumal, MDTHW Vangu. The specialist forum 2009;9:57-63

Chilaiditi's syndrome demonstrated by SPECT-CT.
Perumal NS, Purbhoo K, Dhoodhat S, Vangu MDTHW. S J Radiol 2009.

PUBLISHED CONFERENCE PROCEEDINGS

I. Related to PhD

I.I. International

- 54th SNM Annual Meeting held in Washington DC from June 2 –June 6, 2007. USA

Work presented:

Does dipyridamole or exercise induced myocardial ischemia affect NT pro-B type Natriuretic Peptide (NT pro-BNP) excretion?

I.II. Regional and National

- Work presented at the eleventh biennial Congress of the South African Society of Nuclear Medicine, October 2004, Pretoria

1. Myocardial Perfusion Imaging in the Evaluation of Coronary Artery Disease in Patients with LBBB.

2. The Use of Myocardial Perfusion Imaging in the Clinical Evaluation and Risk Stratification of Coronary Artery Disease.

3. Comparison Between Left Ventricular Ejection Fraction Measured by M-Mode Echocardiography and By ECG-Gated Myocardial perfusion Imaging Using QGS.

4. Left Ventricular Ejection Fraction using Gated Tc-99m Sestamibi SPECT: Is Immediate Post-Stress Imaging Feasible?

- Work presented at the twelfth biennial Congress of the South African Society of Nuclear Medicine held in Port Elizabeth in September 2006

1. Role of Myocardial Perfusion Imaging in the Clinical Evaluation of Diabetic Patients with Suspected and Known Coronary Artery Disease.

2. Evaluation of Patients Post Percutaneous Coronary Intervention with Myocardial Perfusion imaging.

3. Clinical Evaluation of Patients Post Coronary Artery Bypass Graft Surgery with Myocardial Perfusion Imaging.

4. The Effects of Dipyridamole Induced Myocardial Ischaemia on N-Terminal Pro B Type Natruretic Peptide Levels.

- Eighth Annual Congress of the South African Heart Association (SAHA). Sun City, 22-25 Nov, 2007

1. Evaluation of patients post percutaneous coronary intervention with myocardial perfusion imaging.

2. Value of myocardial perfusion imaging in patients post coronary artery bypass graft surgery.

- Work presented at the thirteenth biennial Congress of the South African Society of Nuclear Medicine held in Port Windhoek, Namibia, 21-25 August 2008

Can obesity predict myocardial ischaemia in patients referred for myocardial perfusion scan?

- Ninth Annual Congress of the South African Heart Association (SAHA). Wild Coast Sun, 2-5 Nov 2008

Obesity as a predictor of myocardial ischaemia in patients referred for myocardial perfusion imaging

II. others

II.I. International

- XXIst CINP Congress Collegium Internationale Neuro-Psychopharmacologicum, 12-16 July,1998, Glasgow, Scotland:

Work presented:

1. “Effects of ETC on regional cerebral blood flow measured by 99m Tc- HMPAO SPECT”

2. “Regional Cerebral perfusion pattern of Tc-99m -HMPAO SPECT in Trichotillomania”

- 2nd Congress of the African Association of Nuclear Medicine and the 39th French Language Nuclear Medicine colloquium, 10-12 November 2001, Saint Denis and 13-15 November 2001, Saint Gilles, Reunion.

Work presented:

1. “A Study using 99mm-Tc- MDP Showing that the Quality of Bone Scintigraphy is not improved by Hydration”

2. “ Peritoneal- Pleural Fistula- A Case Study”

- International Symposium on Nuclear Oncology, 19-23 January 2004, Porto Allegre, Brazil.

Work presented:

Clinical Presentation and Outcome in Patients Treated for Papillary and Follicular Carcinoma of the Thyroid: patterns in Johannesburg.

- The American Association of Chemical Pathology held in San Diego, USA in July 2007.

Work presented:

Estimating Glomerular Filtration Rate in South Africa.

- Annual Congress of the European Association of Nuclear Medicine (EANM) 2009. Munich, Germany

1. An unusual complication of thyroid carcinoma: Pericardial Effusion

2. Spontaneous Perforation of the common bile duct

- 56th SNM Annual Meeting held in Toronto, Canada June 13-17, 2009

Work presented:

Organizer, moderator and speaker on the following continuing education (CE):

Thyroid carcinoma: Role of F18-FDG in patients with “TENIS” syndrome-Myth or Reality

II.II Regional and National

- Work presented at the tenth Biennial Congress of the South African Society of Nuclear Medicine, December 2002 , Stellenbosch:

1. The use of Indium-111 Octriotide in Oncogenic Osteomalacia: Case Presentation.

2. Myocardial Perfusion Imaging- The Johannesburg Experience.

3. Does the area selected for Background Correction Influence the Relative "Renal Function" on 99m Tc- DMSA done on Patients with poor Renal Function?

4. Radionuclide Studies in Differentiation between Herniated Liver and Pulmonary Sequestration: Case Report.

5. Usefulness of V/Q Lung Scans in the Diagnostic Approach to PTED: Clinical and Scan Evaluation.

6. Comparison of Emory Cardiac Tool Box (ECTb) with Quantitative Gated Spect (QGS) in Clinical Use.

- Work presented at the eleventh biennial Congress of the South African Society of Nuclear Medicine, October 2004, Pretoria

1. Nuclear Medicine in South Africa: current status.

2. Retrospective audit of patients presenting to our department for venoscintigraphy.

3. Brain Metastases from Thyroid Carcinoma: study of cases.

- Work presented at the first national workshop in Nuclear medicine in Nigeria. Ibadan, April 2006

Nuclear Medicine: The Johannesburg experience with focus on Pediatric nephro-urology

- Twentieth biennial congress on surgical emergencies and new technologies. Sandton, 28-31 May 2006

PET scanning for surgeons

- Surgical Oncology, Hepato-biliary congress. Johannesburg, 9-11 october 2007

Radioisotopes in diagnosis and therapy of neuroendocrine tumours.

- Work presented at the thirteenth biennial Congress of the South African Society of Nuclear Medicine held in Port Windhoek, Namibia, 21-25 August 2008

1. Estimating glomerular filtration rate in South Africa.

2. Role of 99mTc-sucralfate scanning in carcinoma of the oesophagus.

3. Ectopic parathyroid adenoma and brown tumours demonstrated on Tc-99m Sestamibi scan.
4. Diagnostic value of nuclear endocrinology in neuroendocrine tumours: a case presentation of MEN2A syndrome

5. Spontaneous perforation of the common bile duct.

6. An unusual complication of thyroid carcinoma: Pericardial Effusion.

7. Gallium scintigraphy in the detection of chest infections in patients with retroviral disease (RVD)

- Surgical oncology congress. Johannesburg 13-15 Feb 2009

Radiological sensitivies

- Critical Care Society of South Africa and the South African Thoracic Society congress. Sun city, 16-20 August 2009

Assessment of therapy response in Non Small Cell Lung Cancer with F-18 FDG PET

ABSTRACT

The association between diabetes and coronary artery disease (CAD) has been recognized as a major public health problem in the developed world. While there is an increased prevalence of silent myocardial ischaemia among asymptomatic individuals with diabetes, diabetic individuals with CAD in their larger number are usually asymptomatic, and when they present with signs of disease, there is extensive and severe CAD. It should be noted that amongst black South African, ischemic heart disease (IHD) remains rare, and there is little data linking diabetes mellitus with IHD. However, contrary to early reports that have suggested a low prevalence of CAD in black population in Africa, many studies have indicated a rapid change on the spectrum of CAD in numerous parts of the African continent. Despite the emerging report of high prevalence of risk factors there are only limited data investigating prevalence of CAD in black African with diabetes.

The purpose of this thesis was to use myocardial perfusion imaging (MPI) at rest and after stress testing to detect CAD in a group of asymptomatic black patients suffering from diabetes and therefore assess the prevalence of CAD; to assess the changes in myocardial perfusion in asymptomatic diabetic black individuals and compare the differences seen in myocardial perfusion changes between the asymptomatic diabetic black and, the asymptomatic diabetic white and Indian individuals; to include data from symptomatic diabetic patients who were referred for MPI as part of their routine clinical management for possible comparison

Consecutive 94 asymptomatic diabetic black patients and 50 asymptomatic diabetic white and Indian patients were recruited from the outpatient diabetic clinic of the Johannesburg hospital. Data from 90 subjects forming a group of symptomatic diabetic patients, 45 blacks and 45 whites and Indians referred for MPI as part of their clinical management were also analyzed. A two-day protocol for SPECT MPI was used in all participants: on the first day the stress testing

MPI while the rest MPI was consistently done on the second day. Both exercise and pharmacologic stress testing were used. Technetium-99m methoxy-isobutyl-isonitrile (MIBI) was used as the myocardial perfusion radiopharmaceutical. Myocardial perfusion was assessed by means of semi-quantitative scoring system to measure the extent and severity of perfusion abnormality. Visual inspection of the reconstructed SPECT MPI images was carried out to assess perfusion deficit where there was a doubt on the extent and severity of perfusion abnormality. The QPS/QGS software allows obtaining resting and post stress left ventricular ejection fraction (LVEF). The means and percentages on study variables were obtained. The Spearmen correlation coefficient was used to calculate correlations between variables. The Kruskal-Wallis test was used to assess differences between black diabetic and white or Indian diabetic patients and Wilcoxon scores (rank sum) two-sided were used to measure differences within these racial groups.

There were 123 females (52.6%) and 111 males (47.4%) in total. From the recruited participants, 53 (56.4%) asymptomatic females and 41 (43.6%) asymptomatic males were blacks whereas 24 (48%) asymptomatic females and 26 (52%) asymptomatic males were whites or Indians. The symptomatic group was comprised of 26 (57.8%) female and 19 (42.2%) male black patients and 20 (44.5%) female and 25 (55.5%) male white or Indian patients.

Asymptomatic diabetic black participants were younger than the participants from the asymptomatic diabetic white and Indian group with a mean age of 60 (SD±7.2) years Vs 64 (SD±7.7) [p=0.003].

Fourteen percent of asymptomatic black participants had evidence of ischaemia by showing improvement of perfusion on stress testing versus twenty eight percent of white and Indian asymptomatic participants (p=0.62).

Perfusion defects that did not change from rest to post stress testing MPI (fixed defects) were also noted in 20% of asymptomatic black and 26% of asymptomatic white and Indian diabetic participants. These fixed perfusion

defects are indicative of previous myocardial infarctions and therefore suggestive of CAD.

No significant difference was noted on the changes of perfusion that could account either for ischaemia or infract between asymptomatic diabetic black participants and their white and Indian counterparts (p=0.47). The difference on the improvement of perfusion from rest to post-stress MPIs or reversibility of perfusion to suggest only the presence of ischaemia did not also show a significant difference between these two racial groups (p=0.62).

Our data demonstrated a high prevalence of CAD in asymptomatic diabetic black participants similar to other racial groups. Our study has demonstrated evidence to recommend screening of asymptomatic diabetic black individuals in equal manner than other races for the detection of CAD. More importantly, stress MPI should be routinely used as a noninvasive investigation in our environment and be utilized more actively in the management of all asymptomatic diabetic patients.

ACKNOWLEDGEMENT

My gratitude is with the following people:

- My wife and daughters who accept to sacrifice uncountable number of weekends to let me work with almost no social time for them
- Professor J Kalk for igniting the urge in me to start this work
- Professor MD Mann for his continuous support throughout my career
- Professor K Sliwa for accepting to finalize the supervision of this thesis
- Doctor E Libhaber for giving her time to analyse data for this study
- The staff of Nuclear Medicine at the CM Johannesburg Academic Hospital for their willingness to contribute to the success of this study. My special thanks go to Dr N Mkhize for all the effort and dedication in the selection of participants.
- I finally thank God for giving me strength to persevere in collecting data, analyzing them and typing the entire work myself.

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Fig 4. This asymptomatic diabetic participant showed a reversible perfusion consistent with stress induced moderate inferior ischaemia and the SDS was 10.

Fig 5. Severe lateral and inferior stress induced ischaemia with a SDS of 15.

Fig 6. Different degree of perfusion improvement noted in both groups of asymptomatic participants.

Fig 7. No change is noted on the perfusion from rest to stress MPI but there is a large fixed perfusion defect noted in the apical inferior, septal and inferior walls.

NOMENCLATURE

A2A: Adenosine 2A

AHA: American Heart Association

CABG: After coronary artery bypass graft

CAD: Coronary artery disease

cAMP: Cyclic adenosine monophosphate

CD: Cardiac death

CVD: Cardiovascular disease

DIAD: Detection of ischemia in asymptomatic diabetics

ECG: Electrocardiography

EF: Ejection fraction

HbA1C: Glycosylated hemoglobin

HDL: High density lipoprotein

IHD: Ischemic heart disease

LBBB: Left bundle branch block

LDL: Low density lipoprotein

LVEF: Left ventricular EF

MBq: Megabequerel

MI: Myocardial infarction

MPI: Myocardial perfusion imaging

MIBI: Methoxy-isobuthyl-isonitril

PPV: Positive predictive value

PTCA: Post percutaneous transluminal coronary angioplasty

QGS: Quantitative gated score

SPECT: Single emission computed tomography

SD: Standard deviation

SDS: Summed difference score

SRS: Summed rest score

SSS: Summed stress score

3D: Three-dimensional

TG: Triglyceride

THR: Target heart rate

TID: Transient ischemic dilatation

Tl-201: Thallium 201