The effect of lifestyle modification on depression amongst myocardial infarction patients after revascularization

by

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As the candidate's supervisor I have approved this thesis for submission.

Signed:  Name: DP Naidoo__ Date: 30 October 2020

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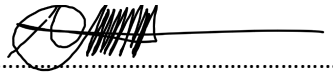
Signed:  Date: 2020/10/20

Dedication

This work is dedicated to my loving parents and my late Aunty Hajiya Aisha Yusuf for their unconditional love and support.

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SUMMARY

Studies have shown that depression is very common amongst coronary artery disease (CAD) patients. It is believed to be a major independent risk factor for CAD as well a poor prognostic factor and is associated with reduced quality of life (QOL). Post-infarction inflammatory and neurohormonal changes are postulated to link CAD to the development of depression. Patients undergoing CABG and PCI patients differ greatly in terms of injury severity score, metabolic and inflammatory response, as such theoretically the prevalence of depression and response to lifestyle modification (LSM) is expected to differ between the two groups. It is not known to what extent the mode of revascularization [coronary artery bypass graft (CABG) vs percutaneous intervention (PCI)] influences the prevalence and severity of depression. However, most of the studies on this topic have been performed in developed countries, where patents have easy access to care and rehabilitation after myocardial infarction (MI). Since little data exists in developing countries on the relationship between depression and CAD, we studied the prevalence of depression in subjects with MI undergoing revascularisation at Inkosi Albert Luthuli Central Hospital (IALCH) and analysed how LSM affects that.

In this study we evaluated the risk factor profile, depression characteristics and changes in lifestyle in 100 consecutive participants undergoing coronary revascularization over a 15-month period (Jan 2017- March 2018). The Beck Depression Inventory II (GDI-II) was used to assess depression and the Goldin leisure-time exercise (GLTE) questionnaire to assess the physical activity (PA) component of lifestyle modification.

The prevalence of depression and depression traits among subjects immediately after coronary revascularization was 51%. After LSM the incidence of depression fell from 51.0% to 34.7% (P=0.022), with fewer PCI subjects having depression and depression traits compared to CABG {PCI 8 (23.0%) vs CABG 25 patients (72.0%), p= 0.000}. The mean depression scores also fell from 21.91±7.75 prior to LSM to 14.98±9.61 (p=0.002), with a greater point score reduction in the PCI compared to CABG group (7.90 vs 4.30), (p=0.000) respectively. In addition, we found the prevalence of depression and depression traits to be significantly lower amongst LSM-compliant subjects post LSM (1 person), compared to 32 subjects in partly-compliant subjects (p=0.001). Further analysis revealed that the participants who were fully compliant in both CABG vs PCI groups derived similar benefits in terms of reduction in prevalence of depression and depression severity, (P=0.191). The main predictors of depression were female gender (OR 3.29, 95% CI 1.51-11.03, p = 0.008),

CABG (OR 1.86, 95% CI 1.68-5.77, p = 0.003), heart failure (OR 2.65, 95% CI 5.87-13.62, p = 0.000), Kidney failure (OR 1.41, 95% CI 1.30-5.23, P = 0.041), atrial fibrillation (OR 1.60, 95% CI 1.40-4.77, P = 0.023), low PA (OR 1.97, 95%, CI 11.23-3.20, P = 0.000), previous history of depression (OR 8.99,95% CI 1.90-7.89, p = 0.002) and low income (OR 2.21, 95% CI 1.40-2.85, p = 0.000).

In this study we found that depression and depression traits are common in subjects who had sustained MI and undergone revascularisation, but commoner among CABG patients. The participants in the PCI group derived greater benefit from lifestyle intervention than the CABG group probably related to early ambulation after PCI. After LSM, depression and depression traits were significantly less common amongst LSM-compliant subjects, regardless of the mode of revascularisation. Furthermore, failure to implement changes in PA after revascularisation was a major barrier to managing depression after coronary revascularisation. Other aspects of LSM like cigarette smoking cessation and dietary modification did not influence the outcome of depression.

Table of Contents

CHAPTER 1: Literature Review

I. Introduction

The prevalence of non-communicable diseases of lifestyle is increasing in developing countries, including South Africa. [1-5] This has resulted in worsening mortality, morbidity and adverse psychosocial outcomes amongst coronary artery disease (CAD) patients in contrast to developed countries where modern therapies and lifestyle modification (LSM) has been shown to reduce morbidity, mortality and effectively manage psychosocial adverse outcomes. [6-14]

Epidemiological and observational studies have reported a high prevalence of depression amongst CAD. [15-20] It is established that patients with depression are more prone to developing CAD and that CAD patients have an increased risk of depression. [15-20] This identifies depression as an independent risk factor for CAD as well a poor prognostic factor.[21-23] Coronary artery disease patients with depression have been observed to have worse adverse cardiac outcomes and reduced quality of life (QOL). [21-23] The Baltimore cohort of the Epidemiologic Catchments Area study follow-up revealed that major depression significantly increased the risk of acute myocardial infarction (OR 4.54, 95% CI 1.65-12.44). [24] A systemic review by the American Heart Association also found that depressed myocardial infarction patients had a significant increase in all-cause mortality, cardiac mortality and chances for recurrence, compared to non-depressed patients. [25]

Although the incidence of CAD is increasing globally, morbidity and mortality are steadily decreasing in the developed countries [3-9]. This has been attributed principally to better therapy and LSM which has shown promising results in the secondary prevention of CAD, reducing adverse cardiac outcomes and depression, as well as improvement in the QOL. [9-14] In contrast to the developed world there is little data from the developing countries regarding the prevalence of depression and the effect of lifestyle changes on depression amongst patients with CAD. [12-16] However, even in the developed countries, to the best of our knowledge no study has examined the effect of LSM on depression amongst patients who undergo coronary artery bypass graft surgery (CABG) *vs* percutaneous coronary intervention (PCI). These two modalities of therapy differ greatly in terms of injury severity score, convalescence, metabolic and inflammatory responses. [26-27] Furthermore, there appears to be a causal relationship between depression and

post-infarction inflammatory and neurohormonal changes [28-34], thus we hypothesized that the prevalence of depression and response to LSM would differ between CABG and PCI groups. In this study we analysed the prevalence of depression amongst MI patients after revascularisation and examined the effect of LSM on incidence of depression between CABG vs PCI groups.

We evaluated the risk factor profile, depression characteristics and lifestyle changes of 100 consecutive participants undergoing coronary revascularization over a 15-month period (Jan 2017 to March 2018). The Beck Depression Inventory II (BDI-II) was used to assess depression and the Goldin leisure-time exercise questionnaire (GLTEQ) to assess physical activity (PA).

II). Prevalence of depression

Numerous studies have reported that depression is very common amongst CAD patients with prevalence varying from 10% to 65% [15-19]. In contrast to the developed countries there is little data from the developing nations regarding the prevalence of depression amongst CAD patients. [3-5] In a recent study, Ranjith et al analysed depression in patients with myocardial infarction (MI) in South Africa and reported a prevalence of 49% [20]. To the best of our knowledge no study has investigated the effects of LSM and revascularisation procedures on depression amongst CAD patients in Africa.

In a prospective study Gu G, et al investigated the incidence of depression amongst patients with CAD before and after PCI in China. They randomly selected one hundred and seventy (170) CAD patients who underwent PCI between September 2013 and February 2014. The patients completed the Hospital Anxiety and Depression Scale (HADS) and a preoperative questionnaire one day before PCI and the same questionnaire was re-administered a day after the procedure, and at one, three, six, and twelve months later. They showed that PCI was significantly associated with the symptoms of anxiety and depression ($p < 0.01$) at each follow-up time point. They concluded that the incidence of anxiety and depression significantly increases the day before and the day after PCI procedure, and thereafter decreased with time. The predictors of anxiety and depression in their study were a low level of education, apprehension regarding quality of nursing care, heart failure, and surgical complications. [35]

Amongst the studies that analyzed incidence of depression after acute coronary syndrome (ACS), the "Depression after First Hospital Admission for Acute Coronary Syndrome: A Study of Time of Onset and Impact on Survival" was prominent. It was conducted at Research Center for Prevention and Health, Copenhagen University, by Osler M et al. They examined incidence of depression after ACS and assessed whether the timing of onset of depression influenced long term survival. The ACS patients (cases) were identified through the National Patient Register, and a comparable reference population sample (control) was matched on 1:1 basis. Both samples were followed for depression and mortality outcomes from the beginning of the study until the end of follow-up (2 years for depression and 12 years for mortality). The results showed that 19,520 (20.0%) out 97,793 ACS patients recruited developed depression within 2 years of follow up, while in the reference population 14,386 persons (14.7%) developed depression. Higher rates of depression were seen in single persons, people with a basic education, and people with previous depression or other disease comorbidity. Although the depression rate was higher in women than men this finding was not significant. At the end of 12 years follow-up, 39,523 (40.4%) ACS patients and 27,931 (28.6%) members of the reference population died. Mortality rate was higher amongst depressed patients compared to those without depression in both the ACS patients and the reference population. This study concluded that depression is common in ACS patients and it is associated with increased mortality independent of its time of onset. [36]

III). Pathogenetic mechanisms linking CAD to depression

Several underlying pathophysiological changes are postulated to link CAD to the development of depression. One aspect that has been studied is heart rate variability (HRV) as a method of assessing cardiac autonomic function and a measure of allostatic load (dysfunction of autonomic system homeostasis over time as a result of chronic exposure to stress) after myocardial injury. [32-34] Reduced heart rate variability (HRV) is manifestation of sympathetic hyperactivity and reduced parasympathetic activity (vagal tone) and has consistently been shown to be associated with depression. It is believed to be caused by autonomic system and hypothalamic–pituitary–adrenal (HPA) axis dysregulation that occurred after myocardial infarction. [32-34] Although the exact mechanism is not known it is possible that the magnitude of myocardial injury may be contributory factor through activation of neurohormonal mechanisms.

Studies have shown a causal relationship between depression and post-infarction inflammatory and neurohormonal changes. Numerous inflammatory markers have been found in patients with CAD e.g. C-Reactive Protein (CRP), Interleukin 6 and soluble intercellular adhesion molecules. The surge in the inflammatory markers significantly influences the neurohormonal milieu and HPA axis, manifesting physically as mental and psychological changes of depression and anxiety. [28-32] In view of this, we hypothesize that patient who undergo CABG are likely to be more depressed compared to PCI subjects, because the patients selected for CABG surgery generally have more severe and extensive coronary artery disease (triple vessel disease or left main coronary artery involvement) and are expected to generate a greater inflammatory response compared to milder disease (single or double vessel disease) in the majority of patients undergoing PCI.

V). Lifestyle modification program and its effect on depression

Lifestyle modification (LSM) is the main component of cardiac rehabilitation (CR) program. The American heart association (AHA), Australian Cardiovascular Health and Rehabilitation Association (ACRA), European Society of Cardiology (ESC), and many other international health bodies consistently recommend LSM as an important integral part of comprehensive care to patients with cardiovascular disease. [37-39] It comprises a customized program of exercise, health education and behavioral changes that aimed to help CAD patients recover from heart disease and live a normal or near normal life, largely through their own effort. It involves a structured training program of aerobic exercises and health education, ranging from healthy eating patterns, stress management, and cigarette smoking cessation [37-39,40] The European Guidelines on Cardiovascular Disease Prevention in Clinical practice (2016 version) [39], included the following as components of CR programs:

1) Cognitive behavioural strategies to lifestyle changes including cigarette smoking cessation

2) Professional nutritional counseling (<5 g of salt per day, 200 g of fruit per day (2–3 servings), 200 g of vegetables per day (2–3 servings), fish at least twice a week)

3) Long term individual exercise and physical activity (PA)

4) Professional management of stress and psychosocial risk factors.

Several studies have highlighted the beneficial effect of LSM in improving depressive symptoms amongst CAD patients [41-45]. A study conducted in the United states of America (USA) by Carl JL, et al, examined the effect of LSM program on exercise capacity, CAD risk factors, behavioural characteristics, and QOL in young and elderly patients. It was found that LSM improved depression, anxiety and other psychological risk factors with fewer adverse clinical events occurring amongst both groups. The study also showed significant benefits in terms of exercise capacity, QOL and reduction in CAD risk factors. They concluded that LSM is beneficial in both the elderly and in young adults, and leads to modest improvement in lipids, obesity indexes, behavioural characteristics, as well as marked improvement in exercise capacity. They emphasized that elderly patients had greater improvements than younger patients in both exercise capacity and mental health. [46]

In addition to improvement in psychosocial functioning, LSM is believed to enhance quick recovery, and to decrease morbidity and mortality as well as increase QOL. [47-54] The Lifestyle Heart Trial was amongst the pioneer studies that investigated the effect of lifestyle changes on CAD. It was a randomized controlled trial (RCT) that compared the effect of LSM amongst the experiment group (the LSM group) and control groups (those on regular CAD treatment only). The study demonstrated that LSM leads to significant reduction in CAD risk factors, reduction in risk of subsequent fatal MI, and generalized improvement in QOL. Baseline comparison of experimental and control group showed no significant differences in terms of demographic and clinical characteristics. At the end of the first year of the study, LDL cholesterol decreased by 40% and remained 20% below baseline at 5 years amongst experimental group even though they were not on anti-lipid medications. In the control group, LDL cholesterol levels decreased by 1.2% at 1 year and by 19.3% at 5 years (P= 0.007). High density lipoprotein, triglycerides and blood pressure did not differ significantly between the 2 groups at the end of the trial. Weight loss was higher among the experimental group (10.9 kg)) at 1 year and 5.8 kg at 5 years, while there was negligible change in weight in the control group at the end of the trial (P= <0.000). Experimental group patients had a 91% reduction in reported frequency of angina after 1 year and a 72% reduction after 5 years, while the control group patients had an 186% increase in reported frequency of angina after 1 year and a 36% decrease in frequency of angina after 5 years (P= 0.058). At 5 years, secondary MI was much higher in the control group (2.25 events per patient) compared to the experimental group (0.89

events per patient), and the control group patients were more likely to have fatal MI than experimental group patients. [55]

The tremendous improvement gained from LSM has been attributed to reduction in modifiable cardiac risk factors, and rebuilding the patient's life physiologically, physically and psychologically. [41-45, 46, 47-54, 55] Despite its documented benefits, most CAD patients are not referred to LSM program centres in the developed countries, whilst in the developing countries the LSM programs services are rarely available. [56-59] Even among the recruited patients, LSM compliance is poor with only about 33% compliance after 6 months of initiating LSM. [60-61] Of concern is the report that benefits gained from LSM are proportional to the duration of attendance, with possibly reversal of the benefits after discontinuation of the program. [62]

Motivation for the study

The aforementioned studies have shown that depression is common in subjects with CAD and that both depression and its adverse outcomes are amenable to LSM program. Coronary artery disease is an emerging disease in the third world countries such as South Africa where the epidemiological transition to a westernised lifestyle is currently progressing on course.[5-6] However, unlike developed nations, there is a scarcity of information regarding the prevalence of depression amongst CAD and effect of LSM on the depression. There is probably also a widespread underestimation of depression in this population. One local study has reported a high prevalence of depression amongst patients with myocardial infarction (MI) in South Africa, [16] but no study has examined the influence of the mode of revascularisation and LSM on the incidence of depression following MI. The combination of depression and CAD is of great socioeconomic importance given that these two conditions are amongst leading causes of global health burden.

This study will provide information on prevalence of depression after revascularization and will investigate the role of LSM in managing depressed CAD patients. Information generated from the study might also shed light on the effectiveness of LSM in managing depressed CAD patients. This is of importance to clinicians and policy makers in formulating more effective strategies in the aftercare of patients with MI.

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CHAPTER 2: Manuscript

The effect of lifestyle modification on depression amongst myocardial infarction patients after revascularization

ABSTRACT

Background: Patients with Coronary Artery Disease (CAD) are prone to depression, and its presence is associated with poor adverse cardiac outcomes. Although lifestyle modification (LSM) has been shown to be beneficial in managing depression in patients with CAD, it is not known whether the mode of cardiac intervention (coronary artery bypass graft surgery {CABG} vs percutaneous coronary intervention {PCI}) influences the outcome

Objectives*:* We examined the prevalence of depression and depression traits amongst myocardial infarction (MI) patients after revascularisation and compared the effect of LSM on incidence of depression and depression traits in patients who underwent CABG versus PCI

Method: We evaluated the risk factor profile, depression characteristics and lifestyle changes of 100 consecutive participants undergoing coronary revascularization over a 15-month period (Jan 2017 to March 2018). The Beck Depression Inventory II (BDI-II) was used to assess depression and the Goldin leisure-time exercise (GLTE) questionnaire to assess physical activity (PA).

Results: 100 patients were recruited (mean age males 60.73±4.52 yr and females 60.29±3.64 yr), with 5 dropouts leaving 95 patients for complete analysis. Most of the patients were low-income earners 53 (53.0%) and 21.0% had tertiary level education. The majority had multiple CAD risk factors and comorbidities (79.0%). Prior to the LSM program 51 patients (51.0%) had depression and depression traits {CABG 34 (66.7%) *vs* PCI 17 (33.3%), p = 0.047)}. After LSM the overall prevalence of depression and depression traits fell to 33 patients (34.7%), {PCI 8 (23.0%) vs CABG 25 patients (72.0%), p = 0.001}. The mean depression scores also fell from 21.11±7.75 to 14.98±9.61 (p = 0.002). At baseline PCI patients were more physically active compared to CABG {3 (60.0%) vs 2 patients (40.0%), P = 0.715} respectively. After the LSM, more PCI patients undertook PA compared to CABG {24 (60.0%) vs 14 patients (35.0%) respectively, p = 0.012}. The PA

score was also higher amongst the PCI group compared to CABG {14.16±9.73 vs 9.40±10.94 respectively, p = 0.024}. In fully compliant subjects the benefit derived was similar regardless of the mode of intervention {OR 1.10, CI 0.98-4.23,P = 0.191}. Using multivariate analysis the main predictors of depression and depression traits were female gender (OR 3.29, 95% CI 1.51-11.03, p = 0.008), CABG (OR 1.86, 95% CI 1.68-5.77, p = 0.003), heart failure (OR 2.65, 95% CI 5.87-13.62, p = 0.000), Kidney failure (OR 1.41, 95% CI 1.30-5.23, P = 0.041), atrial fibrillation (OR 1.60, 95% CI 1.40-4.77, P = 0.023), low PA (OR 1.97, 95%, CI 11.23- 33.20, P = 0.000), previous history of depression (OR 8.99,95% CI 1.90-7.89, p = 0.002) and low income (OR 2.21, 95% CI 1.40-2.85, p = 0.000).

Conclusions: Depression and depression traits are common among subjects undergoing coronary revascularization, more so amongst CABG compared to PCI participants. Lifestyle modification reduces the prevalence of depression and depression traits, with fully compliant CABG vs PCI groups deriving nearly the same benefits from the LSM regime. No significant reduction in depression and depression was recorded amongst LSM partly-compliant patients. This study suggests that failure to implement lifestyle changes and engage in PA are major barriers to managing depression after coronary revascularisation.

Keywords: Depression, Coronary Artery Disease, Coronary artery bypass graft surgery, percutaneous coronary intervention, Lifestyle modification, Beck depression inventory-II, Goldin leisure time-exercise questionnaire

Introduction

Several studies have shown that depression is very common amongst CAD patients with a prevalence varying from 10.0% to 65.0% [1-7]. Depression is thought to be a risk factor for CAD as well a poor prognostic factor. [8-12]. Patients with CAD who have depression have been shown to have worse adverse outcomes and reduced quality of life (QOL). [4, 6-7] It is well established that CAD with depression has higher chances for MI recurrence and increased risk of death. [13-18] In the Baltimore cohort of the Epidemiologic Catchments Area study follow-up, major depression significantly increased the risk of acute myocardial infarction (OR 4.54, 95% CI 1.651-12.440). [19] A systemic review by the American Heart Association also found that depressed myocardial infarction patients had a significant increase in all-cause mortality, cardiac mortality and chances for recurrence compared to non-depressed patients. [12] Although the incidence of CAD is

increasing globally, morbidity and mortality are steadily decreasing in the developed countries [20-23] and this has been attributed principally to better therapy as well as LSM which has shown promising results in the secondary prevention of CAD, reducing adverse cardiac outcomes and depression, as well as improving QOL. [24-28] In contrast to the developed world there is little data from the developing countries regarding the prevalence of depression and the effect of lifestyle changes on depression among patients with CAD. [21-23] In a recent study Ranjith et al analysed depression amongst myocardial infarction (MI) patients in South Africa and reported a prevalence of 49.0% [29].

To the best of our knowledge, no study has compared the effects of LSM on depression amongst patients who undergo Coronary artery bypass graft surgery (CABG) versus percutaneous coronary intervention (PCI). These two modalities of therapy differ greatly in terms of injury severity score, metabolic responses, convalescence and prognosis. [30-31] Furthermore studies have shown a causal relationship between depression and post-infarction inflammatory and neurohormonal changes [32-38]. Thus, we hypothesized that the prevalence of depression and response to LSM would differ between the two groups.

In this study we analysed the prevalence of depression amongst MI patients after revascularisation and examined the effect of LSM on incidence of depression between CABG vs PCI groups.

Methods

Study design

The risk factor profile, depression characteristics and physical activity (PA) profile were prospectively examined in 100 consecutive participants undergoing coronary revascularization over a 15-month period (Jan 2017 to March 2018). The study was conducted in the Department of Cardiology and Cardiothoracic surgery at Inkosi Albert Luthuli Central Hospital (IALCH), Durban, South Africa. After informed written consent was obtained, patients who met the inclusion criteria were enrolled within two (2) to four (4) weeks after revascularisation.

The demographic, anthropometric measurements, vital signs and other clinical data, as well as blood samples, were obtained from the patients at the beginning of the study and thereafter the interview was performed.

Questionnaire administration

During the interview, the Beck depression inventory-II (BDI- II) and Goldin Leisure-Time Exercise (GLTE) questionnaires were administered by the researcher (AA) to determine depression status and level of PA. The GLTE questionnaire is a validated and reliable questionnaire that is used to assess the level of PA. [39] Briefly, the patients indicate the number of times they engage in mild, moderate or strenuous exercise for more than 15 minutes within a week. The level of PA is categorised as: 'sufficiently active' (≥24 units/week), 'moderately active' (14-23 units/week), and 'insufficiently active' (<14 units/week). [39] For strenuous PA, the GLTE questionnaire demonstrated moderate to strong associations with measured indices of PA particularly maximal oxygen consumption determinations (VO2max), and percent body fat by hydrostatic weighing (% BF), but a lesser degree of association with the Caltrac accelerometer (CALTRAC) readings. For moderate PA, it was modestly correlated with the above measures, but for mild PA it showed less association with these measures. By and large it gives a reliable and fairly accurate assessment of PA. [40]

The Beck Depression Inventory-II (BDI-II) is a 21-item, simple, reliable, and validated questionnaire, rated on a four-point scale (0-3). [41] It is one of the most widely used psychometric instrument in both research and clinical practice for assessing depression. [42] Based on the total score obtained, a patient is classified as normal (1-10), mild mood disturbance (11-16), borderline depression (17-20) moderate depression (21-30), severe depression over (31-40) and extreme depression (>40). [41] The BDI-II adequately corresponds to diagnostic and statistical manual of mental disorders (DSM-IV) criteria and has high reliability and validity. Based on available psychometric evidence, the BDI-II is considered as a cost-effective questionnaire for measuring the severity of depression, with broad applicability for research and clinical practice worldwide. Although the questionnaire was originally designed to measure the severity of depression, existing evidence shows that the BDI-II can be effectively used to screen for major depression with a sensitivity of more than 70%. Its major shortcoming is variability of the cut-off score to screen for depression according to the type of sample.—Non-clinical samples displayed the lowest range of cut-off points (from 10 to 16) to detect major depression, medical samples had an intermediate cut-off (from 7 to 20), and psychiatric samples had the highest cut-off (from 19 to 31). As a self-report measure there may be reporting bias since the educational level attained, status or gender may affect the respondent's response. [41-42]

Cardiac rehabilitation, recruitment and follow up

Eligible patients were enrolled in a supervised exercise based LSM program and after a few sessions, an individualised aerobic exercise regimen was prescribed based on the standard guidelines. [43-45] Psychological counselling, smoking cessation and dietary advice were given as well. At the time of discharge, a referral letter and written instructions about the individualised LSM were given to the patients and they were advised to continue the program at home. The written instructions included how to monitor the level of exertion manually using their heart rate and the Borg's rating of physical exertion at home. Studies have shown that homebased LSM is safe and not inferior to centre-based LSM. [46-48] Patients continued the LSM at home with a monthly follow-up at their community clinics. After a 12 weeks period, the patients underwent a final assessment by the researcher (AA). At the final visit, anthropometric measurement, vital signs, blood samples and clinical evaluation were repeated and documented. The BDI-II and GLTE Questionnaires were re-administered, and the results documented.

Inclusion criteria

Male or female eligible adult patients over the age of 18 years with a documented AMI who underwent CABG or PCI in IALCH within the period of the study and consented to participate in the study

Exclusion Criteria

Any patient with a terminal illness or a debilitating comorbidity *such as* incapacitating CVA, severe arthritis and other severe diseases, which would preclude moderate physical activity.

Study outcome

The primary outcome was depression status before and after LSM as assessed using the BDI-II questionnaire. The secondary outcome was an improvement in physical function and endurance, which is reflected by changes in the level of PA.

Data analysis

Data analysis was conducted using SPSS version 25. The demographic, social and clinical characteristics of the patients were analysed. Descriptive statistics were used to analyse the demographic data, disease characteristics, LSM compliance and depression. The prevalence of depression was established, and predictors of depression were determined

using multivariate analysis. The results for all the variables were compared before and after initiating LSM. Chi-square-test was used to determine the association between the disease characteristics and outcome variables (depression and physical activity) at baseline and after LSM, amongst CABG and PCI patients. A general linear model was used to evaluate the mean and SD values, and the differences between the group outcomes (depression severity and number of subjects with depression) at the baseline, and after three months of LSM as a function of the main effect (group differences). The changes in the study outcome values (depression and LSM compliance) from baseline to the final visit were expressed in both the CABG and PCI groups.

Results

During recruitment, four (4) patients were excluded due to severe congestive cardiac failure (n=3) and debilitating CVA (n=1). 100 patients were recruited (58 males and 42 females), and of these there were 5 dropouts who did not appear for follow up after the 3 months of LSM, leaving 95 patients for complete analysis at the end of the study.

The mean age of the participants was 60.56±4.09 years, with males and females having mean ages of 60.73±4.52 vs 60.29±3.64, respectively. The ages of males and females were normally distributed ($p = 0.667$) and ($p = 0.794$) respectively (Shapiro-Wilk score = 0.829). The sample comprised mainly Indians (73.0%), the remaining 27.0% about evenly split amongst the other race groups. Most of the patients were low-(53.0%) or moderate-income earners (40.0%). Nine patients (9.0%) had a background history of depression prior to the cardiac event and 55 patients (55.0%) reported significant alcohol use. All the patients had previously sustained MI and had angiographically confirmed CAD. Most patients had multiple CAD risk factors and nearly half of the patients 48 (48.0%) had at least one comorbidity, the commonest being chronic kidney disease (43.0%). (Table 1)

Predictors of depression

The overall prevalence of depression and depression traits in this sample was 51.0%. The main predictors of depression and depression traits were female gender (OR 3.29, 95% CI 1.51-11.03, $p = 0.008$), CABG (OR 1.86, 95% CI 1.68-5.77, $p = 0.003$), heart failure (OR 2.65, 95% CI 5.87-13.62, $p = 0.000$), Kidney failure (OR 1.41, 95% CI 1.30-5.23, $P = 0.041$), atrial fibrillation (OR 1.60, 95% CI 1.40-4.77, $P = 0.023$), low PA (OR 1.97, 95%, CI 11.23- 33.20, $P = 0.000$), previous history of depression (OR 8.99,95% CI 1.90-7.89, $p = 0.002$) and low

income (OR 2.21, 95% CI 1.40-2.85, p = 0.000).The level of education (OR 0.60, 95% CI 0.17-2.14, p = 0.430), age (OR 0.56, 95% CI 0.71-2.00, p = 0.099), COPD (OR 1.30, 95% CI 0.30-2.98, P = 0.327) as well as the other coronary artery disease risk factors, complications and comorbidities did not show any significant influence on the outcome of depression. (Table 2)

Effect of the LSM Intervention on the entire sample

***Protocol* compliance**

Prior to initiation of LSM program, 5 participants (5.0%) were already physically active, 6 (6.0%) had changed their diet on their own to a Mediterranean diet, and 11 (11.0%) had stopped smoking cigarettes; however only 3 participants (3.0%) were fully compliant with LSM ab initio. After 3 months of the LSM program 32 (33.7%) complied fully with the protocol. Fifty-eight participants (61.1%) complied with the dietary changes, 72 (75.8%) with cigarette smoking cessation, and 38 (40.0%) complied with the minimum accepted PA. (Table 3)

After the LSM intervention the total number of subjects who were physically active increased from 5 at baseline to 38 (40.0%) three months later and the number who were insufficiently active fell from 95% at baseline to 57 patients (60.0%), (both p = 0.000). The PA score improved from 2.81±4.410 at baseline to 11.65±10.600 (p = 0.000) after LSM. (Table 3)

At baseline, 51 participants (51.0%) had depression and depression traits and 49 (49.0%) were not clinically depressed (36.0% had mild mood disturbance and 13.0% were psychologically normal). Amongst those with depression and depression traits, 18 (18.0%) had borderline depression, 23 (23.0%) moderate depression, and 10 (10.0%) severe depression at baseline. After the LSM intervention, the number of participants with depression and depression traits fell from 51 (51.0%) to 33 (34.7%), p = 0.022 and the number without depression and depression traits increased from 49 (49.0%) to 62 (65.3%), p = 0.022. (Table 3). Of the latter group, 11 patients (17.7%) had mild mood disturbance and 51(82.3%) had no psychological disturbance at all. Amongst the 33 who had depression post LSM, 13 (39.4%) had borderline depression, 13 (39.4%) moderate, and 7 (21.2%) had severe depression. The mean depression scores fell from (21.91±7.747) at baseline to 14.98±9.610 (p = 0.002), indicating a significant reduction in the severity of depressive symptoms post LSM. (Table 3)

The prevalence and severity of depression and depression traits after the LSM intervention were compared in compliant and noncompliant subjects. Both the depression severity and the number of subjects with depression were significantly lower in compliant subjects (both p= 0.000). Only 1 (3.0%) fully compliant patient had depression out of the total 33 persons with depression post LSM (p = 0.000). (Table 4)

Effects of LSM in CABG vs PCI

Fifty-two patients underwent CABG {m-27, (51.9%); f-25(48.1%)}, and 48 patients had PCI, {(m-31, (64.6%); f-17, (35.4%)}. The mean ages in these groups were similar and normally distributed (p = 0.140)

Physical activity

Most of the 95 (95.0%) participants were insufficiently active at baseline, with only 5 (5.0%) being physically active. After LSM the number who reached the desired PA level increased from 5 (5.0%) at baseline to 38 (40.0%), (p = 0.000) 3 months later. The PA score improved from 2.81±4.410 at baseline to 11.65±10.600 (p = 0.000) after LSM. (Table 3)

The PA scores were low for both CABG and PCI groups at baseline, though slightly higher for PCI (2.15±4.160 and 3.53±4.603 respectively), (p = 0.119). After 12 weeks of the LSM regime, more patients undertook PA in the PCI group compared to the CABG group: 27 (61.1%) vs 15 (33.9%) patients participated often, 7 (73.9%) vs 2 (21.1%) sometimes and 11 (23.7%) vs 33 (71.3%) rarely, (p = 0.012). The mean PA scores were also higher in the PCI compared to the CABG group {(14.16±9.73 vs 9.40±10.94 respectively), (p = 0.024)}. At the end of the study 24 (60.0%) subjects in the PCI group and 14 (35.0%) in the CABG group reached a satisfactory level of PA based on the GLTE questionnaire cut-off points (p = 0.012).

Depression status

At baseline, there were fewer PCI subjects with depression compared to the CABG group {17 (33.3%) vs 34 (66.3%) respectively, (p = 0.047). The mean depression scores were lower in the PCI group compared to CABG {(19.20±7.50) vs (22.10±7.60), (p = 0.049)} respectively, indicating more severe depressive symptoms amongst CABG subjects at baseline. (Table 5)

After 3 months of LSM, the number of participants with depression and depression traits fell from 51 (51.0%) to 33 (34.7%), (p = 0.022). Fewer cases of depression and depression

traits were seen in the ~~P~~PCI compared with the CABG group {8 (23.0%) vs 25 (72.0%) (p = 0.001)} respectively. There was a corresponding increase in the number of non-depressed patients in both groups, with a greater increment amongst the PCI subjects {37 (56.7%) vs 25 (38.3%) (p = 0.001)}. The mean depression scores followed the same pattern, with a greater point score reduction in the PCI compared to CABG (7.90 vs 4.30), (p = 0.000) respectively, suggesting that the PCI group derived greater benefit than the CABG group from the LSM regime. (Table 5)

In addition, we found the prevalence of depression and depression traits to be significantly lower amongst LSM-compliant subjects post LSM (1 person), compared to 32 subjects in partly-compliant subjects (p=0.001). Further analysis revealed that the participants who were fully compliant in both CABG vs PCI groups derived similar benefits in terms of reduction in prevalence of depression and depression severity, P=0.191), where 8 CABG *vs* 5 PCI patients had depression and depression traits amongst the fully complaint patients at baseline respectively (P = 0.125), which reduced to 1 CABG *vs* no PCI patient with depression traits post LSM (P = 0.063). (Table 6)

Discussion

In this prospective study we evaluated the prevalence of depression and depression traits amongst MI patients after revascularisation and analysed the effect LSM on depressive symptoms. We found a high prevalence of depression and depression traits (51.0%) amongst CAD patients who had sustained MI and undergone revascularisation, with Similarly, several previous studies have shown that depression is common amongst MI patients, ranging from 10-65%. [1-7] Most of these studies were conducted in the developed countries, but a recent study by Ranjith et al analysed depression amongst MI patients in South Africa and reported a prevalence of 49.0%. [29] In addition to evaluating the prevalence of depression amongst these patients, we also analysed the effects of LSM on incidence of depression and compared the findings between CABG and PCI patients. We found that LSM significantly reduced both the incidence and severity of depression and traits amongst MI patients undergoing revascularisation, with compliant PCI vs CABG patients deriving similar benefits. To the best of our knowledge, no previous study had compared the effect of LSM in these two categories of patients.

Many factors could have contributed to the high prevalence of depression and depression traits in our study, among them being gender, low income, previous history of depression, low PA, as well as the presence of complications and other comorbidities. Similar to other studies [16,19,29], we have shown those participants with low income, previous history of depression and female gender were more frequently associated with depression. In addition, it appears those participants with more severe CAD requiring CABG and the sicker patients (those with heart and kidney failure) were more likely to experience depressive symptoms. This is in contrast to the study of Pelletier et al which showed that disease severity does not influence the outcome of depression in MI patients. [14]

The high prevalence of depression in our study could also be related to the fact that all our subjects had sustained previous MI resulting in compensatory haemodynamic and neurohormonal consequences of myocardial damage. Factors such as reduced heart rate variability (HRV) caused by autonomic dysregulation and post-infarction inflammatory and neurohormonal changes are common amongst MI patients and have been shown to manifest physically as mental and psychological changes of depression and anxiety. [33-38] Patients undergoing CABG probably generate an even greater inflammatory response than PCI subjects since they generally have more severe coronary disease affecting all three coronary arteries or the left main coronary artery compared to patients selected for PCI who are more likely to have single or two vessel disease. The higher prevalence of depression amongst CABG compared to PCI subjects in our study could therefore be related to the severity of myocardial injury and the greater burden of atherosclerotic disease in CABG participants (frequent triple vessel disease and heart failure compared to single and double vessel involvement in the PCI group).

An important finding in our study was that LSM led to a significant reduction in the prevalence of depression from 51.0% pre-LSM to 34.7% after LSM intervention. In addition, we recorded a six-point reduction in the mean depression scores post LSM, (table 3), indicating reduction in the severity of the depressive symptoms with LSM intervention. After LSM, depression was three times more frequent amongst CABG than PCI patients, (table 5), suggesting that the PCI group benefited more from the antidepressive effect of LSM. We attributed the marked difference in depression scores in the PCI compared to the CABG group {7.90 vs 4.30 points reduction respectively, (P= 0.000)}, to early ambulation with better improvement in PA in the PCI group. It is noteworthy that PA scores were similarly low for both CABG and PCI groups at baseline (P = 0.119). There was a large increase in the PA scores from a mean of 2.81 at baseline to

11.65 after LSM intervention (table 3). The PCI group attained higher PA scores compared to the CABG subjects (P = 0.024) by the end of the study period because of their more immediate mobility post revascularisation. (Table 5)

While the adherence to LSM measures showed improvement in dietary changes and cigarette smoking cessation amongst the majority of the participants, only 40.0% complied with aerobic exercise recommendations; overall, only one third of subjects adhered fully to LSM. Poor compliance with LSM recommendations has been reported in previous studies. [54-55] Similar to these studies, the reasons for non-adherence to LSM measures in our study were mainly lack of motivation, bodily discomfort and fear of an adverse outcome, though no exercise-related adverse effects were reported amongst the participants. Thoracic cage and lower limb discomfort as well as fear of potentially adverse outcomes after early ambulation post bypass surgery was another possible factor accounting for the lower exercise scores amongst the CABG subjects. It is therefore not surprising that twice as many PCI subjects participated in frequent physical activity compared to the CABG group. This may explain the higher prevalence and severity of depression after LSM amongst the CABG group. This is an important limitation of our study which to some extent may have been averted if the interview after the LSM intervention had been performed six months after surgery instead of three months.

Although the prevalence of depression in partly-compliant participants fell after LSM, (51.0% at baseline to 33.7% post LSM) there was a marked reduction recorded in LSM compliant subjects (51.0% patients at baseline to 1.1% post LSM), (p = 0.001). Also, a greater point reduction in depression score was seen for subjects who adhered fully to LSM measures, indicating a better reduction in severity of depressive symptoms with LSM intervention. (Table 4) An important finding in our study was that fully compliant CABG and PCI patients derived similar benefit from the LSM program, emphasizing the role of adherence to LSM in reaping maximum benefit after revascularisation, independent of the type of procedure.

The reduction in depression achieved in partly compliant participants is probably due to modest increments in PA from baseline without which depressive symptoms may have persisted over time. This has been highlighted by May et al in their ground-breaking study, which showed that depression status may not improve completely after MI and is associated with two-fold increased risk of death. [16] Our findings are consistent with previous studies showing that LSM improves mental functioning and reduces depression.

[50-53] In a meta-analysis on mental health treatment and LSM for improving clinical outcomes and depression among patients with CAD, Rutledge et al [19] demonstrated that not only did LSM reduce depression to the same extent as mental health treatment, but it was also superior in reducing all-cause mortality risk. In another study Richard VM and Carl JL [13], established that LSM reduces depressive symptoms by 63% and all-cause mortality by 73.0%.

Limitations

Our study has methodological limitations and challenges. Although subjects were prospectively evaluated, the convenience non-random sampling method used in this study limits the ability to generalise our findings to all CAD subjects. Only participants undergoing revascularisation who were able to participate in the LSM recommendations were recruited into the study. Participants recruited were referred by state institutions, so that most participants were from the lower income group. Furthermore, the PA levels were self-reported and were not objectively verified at follow-up through stress testing. However, studies have shown that self-reported activity has significant concordance with objectively measured physical activity using actigraphy-assessed PA. [39-40]

A further important consideration is that the 12-week period after revascularisation might have been too short for assessing the response to LSM in CABG patients since the operation involved mediastinal surgery and lower limb vein grafts which may have required a longer period of physical recovery before full physical activity could be resumed compared to PCI subjects who were almost immediately ambulant after their procedure. A re-evaluation after six months of LSM would have provided a fairer comparison between the two groups. The limited time frame of three months for the LSM intervention in our study also does not permit long term inferences to be made from our findings since persistence of depression over time has been reported by May et al [16]. Also, a more informed assessment of the exercise parameters and incidence of depression would have been obtained in subjects matched for ejection fraction and disease severity. A longer term randomised controlled study is needed to verify our findings and to relate these findings to haemodynamic severity of the underlying disease and adjust for other confounding factors such level of income and domestic issues which we have shown to be predictors of depression.

The main strength of our study lies in its prospective evaluation of the effects of LSM on the incidence of depression after coronary revascularisation and provides some insight

into the varying responses of the intervention amongst CABG and PCI participants. The findings suggest that LSM changes may be safely implemented without fear of potential adverse cardiovascular events. Despite its limitations the study is consistent with previous studies showing that LSM improves mental functioning and reduces depression and depression traits. [50-53]

Clinical Implications

Our findings have important clinical applicability, since they emphasize the relationship between mental and physical well-being and suggest a successful outcome particularly in participants who are able to adhere fully to LSM guidelines regardless of the mode of revascularisation. Lower levels of PA short of the required target also appeared to have had some anti-depressive benefits since a modest benefit accrued in those who were partly compliant with LSM guidelines. These findings suggest that ongoing emphasis on counselling patients to overcome the barriers to engaging in adequate PA such as lack of motivation and the fear of adverse outcomes are critical to a successful outcome, particularly in CABG subjects. This may well translate into morbidity and mortality benefits in participants who fully adhere to LSM recommendations.

Conclusion

This study confirms a high prevalence of depressive symptoms in MI subjects undergoing coronary revascularisation and showed that participants in the PCI group derived greater benefit from lifestyle intervention than the CABG group, probably because of early ambulation. Although depression is amenable to intervention by LSM measures, the beneficial effect of LSM is mainly seen among LSM compliant subjects. Fully compliant subjects derived equal benefit, regardless of the mode of revascularisation, emphasizing the importance of counselling to overcome the barriers to full participation in LSM and undertaking PA. A long-term randomised study is needed to verify these findings.

Summary

Depression is common amongst coronary artery disease (CAD) patients and is associated with a reduced quality of life (QOL) in these subjects. This study examined the prevalence of depression in 100 subjects undergoing coronary revascularisation and sought to determine the effect of LSM on depressive symptoms and whether the mode of revascularization [coronary artery bypass graft (CABG) vs percutaneous intervention (PCI)] had any influence on the outcomes. The authors evaluated the risk factor profile, and

depression characteristics in 100 consecutive participants undergoing coronary revascularization and re-evaluated the participants after three months of lifestyle intervention using the Beck Depression Inventory to assess depression and the Goldin leisure-time questionnaire to assess the physical activity (PA) component of lifestyle modification.

The prevalence of depression among subjects immediately after coronary revascularization was 51.0%. After LSM the incidence of depression fell from 51.0% to 34.7% (P = 0.022), with fewer PCI subjects having depression compared to CABG {PCI 8 (24.2%) vs CABG 25 patients (75.8%), p = 0.000}. The mean depression scores also fell from 21.11±7.75 prior to LSM to 14.98±9.61 (p = 0.002), with a greater point score reduction in the PCI compared to CABG group (7.90 vs 4.30), (p = 0.000) respectively. After LSM, both the incidence of depression and depression scores was significantly lower amongst LSM-compliant subjects. An important finding in our study was that fully compliant CABG and PCI patients derived similar benefit from the LSM program, emphasizing the role of adherence to LSM in reaping maximum benefit after revascularisation, independent of the type of procedure. The main predictors of depression were female gender (OR 3.29, 95% CI 1.51-11.03, p=0.008), CABG (OR 1.86, 95% CI 1.68-5.77, p=0.003), heart failure (OR 2.65, 95% CI 5.87-13.62, p=0.000), Kidney disease (OR 1.41, 95% CI 1.30-5.23, P= 0.041), atrial fibrillation (OR 1.60, 95% CI 1.40-4.77, P=0.023), low PA (OR 1.97, 95%, CI 11.23- 33.20, P=.000), previous history of depression (OR 8.99,95% CI 1.90-7.89, p=0.002) and low income (OR 2.21, 95% CI 1.40-2.85, p=0.000).

This study confirms a high prevalence of depressive symptoms in MI subjects undergoing coronary revascularisation and showed that participants in the PCI group derived greater benefit from lifestyle intervention than the CABG group probably related to early ambulation after PCI. After LSM, depression and depression traits were significantly less common amongst LSM-compliant subjects, regardless of the mode of revascularisation.

Ethical issues

Approval was obtained from the Biomedical Research Ethics Committee (BREC/443/16) of the University of KwaZulu-Natal before starting the study.

Abbreviations

Coronary Artery Disease (CAD), Coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), Lifestyle modification (LSM), Cardiac rehabilitation (CR), Home-based cardiac rehabilitation (HCR), Beck depression inventory-II (BEC-II), Goldi leisure time-exercise questionnaire (GLTEQ), physical activity (PA), Confidence interval (CI), Odds ratio (OR).

Competing interest: We have no competing *interests* to declare.

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Table 1: Demographic data and baseline characteristics

Characteristics	Variables	n=100 (%)
Gender/ Age (mean+SD)	Male 60.73±4.52	58.0
	Female 60.29±3.64	42.0
Race	Black	5.0
	Coloured	8.0
	Indian	78.0
	White	9.0
Yearly income	Low	53.0
	High/moderate	47.0
Educational level	Primary school	11.0
	High school/Tertiary	89.0
Depression history	Yes	9.0
	No	91.0
CAD diagnosis	STEMI*	89.0
	NSTEMI#	11.0
CAD risk factors	Hypercholesterolaemia	84.0
	Diabetes	78.0
	Hypertension	78.0
	Sedentary lifestyle	76.0
	Family history of CAD	53.0
	Cigarette smoking	70.0
	Obesity	45.0
Comorbidities	Kidney disease	43.0
	Arthritis	19.0
	Other vascular diseases**	17.0
	Hypothyroidism	7.0
	COPD	*4.0*
	Other comorbidities ##	10.0
Complications	Heart failure	28.0
	Atrial fibrillation	8.0

* STEMI: ST elevation myocardial infarction

NSTEMI: Non-ST elevation myocardial infarction

**other vascular disease: 11 peripheral vascular disease, 6 CVA

##other comorbidities: 2 valvular heart diseases, 2 RVD, 4 psoriasis, 2 SLE

The sample comprised largely Indian subjects with multiple risk factors and comorbidities

Table 2: **Predictors of depression**

Characteristics	Variables	Depressed n=51 (%)	No depression n =49(%)	Total	OR (95% CI)	p- value
Age (years)	(mean±SD)	71±1.122	71±2.34		0.56 (0.71-2.00)	0.099
Gender	Male	23 (45.1)	35 (71.4)	58		
	Female	28 (54.9)	14 (28.6)	42	3.29 (1.51-11.03)	0.008
Income	Low	42 (82.4)	11 (22.4)	53		
	High	9 (17.6)	38 (77.6)	47	2.21 (1.40-2.85)	0.000
ACS intervention	PCI	17 (33.3)	31(63.3)	48		
	CABG	34 (66.7)	18 (36.7)	52	1.86 (1.68- 5.77)	0.003
Depression history	No	42 (82.35)	49 (100)	91		
	Yes	9 (17.65)	0 (0)	9	8.99 (1.90-7.89)	0.002
Educational level	Low	5 (9.8)	6 (12.2)	11		
	High	46 (90.2)	43 (87.8)	89	0.60 (0.17-2.14)	0.430
Physical activity	Low	50 (53.0)	45 (47.0)	95		
	High	1 (20.0)	4 (80.0)	5	1.97(1.23- 33.20)	0.000
CAD risk factors	↑cholesterol	43 (84.3)	41 (83.7)	84	1.05 (0.36-3.06)	0.930
	Diabetes	43 (84.3)	35 (71.4)	78	1.75 (0.79-5.70)	0.120
	Hypertension	43 (84.3)	35 (71.4)	78	1.77 (0.80-4.50)	0.120
	Sedentary life	39 (76.5)	37 (75.5)	76	1.05 (0.42-2.64)	0.910
	Cigarette smoking	40 (78.4)	30 (61.2)	70	0.30 (0.80-1.60)	0.061
	Obesity	27 (52.9)	24 (47.1)	51	0.95 (0.90-7.21)	0.567
Comorbidities and complications	Kidney disease	27 (52.9)	16 (32.7)	43	1.41 (1.30-5.23)	0.041
	Heart failure	24 (47.1)	4 (8.2)	28	2.65 (5.87-13.62)	0.000
	Arthritis	11 (21.6)	8 (16.3)	19	1.41 (0.51-3.87)	0.504
	Other vascular **	10 (19.6)	7 (14.3)	17	1.16 (0.71-4.21)	0.479
	Thyroid disease	4 (7.8)	5 (10.2)	9	0.75 (0.19-2.97)	0.679
	Atrial fibrillation	1 (2.0)	7 (14.3)	8	1.60 (1.40-4.77)	0.023
	COPD	3 (5.9)	1 (2.0)	4	1.30 (0.30-2.98)	0.327

OR: odds ratio, ACS: Acute coronary syndrome; COPD: chronic obstructive pulmonary disease.
PCI: percutaneous coronary intervention; CABG: Coronary artery bypass graft surgery

Depression was commoner in women, those with low income, kidney disease and heart failure, and in those undergoing CABG compared to PCI.

Table 3: Effects of LSM on lifestyle parameters and depression

Variables	Pre LSM n=100 (%)	Post LSM n=95* (%)	P value
Aerobic exercise compliance	5(5.0)	38(40.0)	0.0001
Cessation of smoking	11(11.0)	72(75.8)	0.0001
Diet modification	6(6.0)	58(61.1)	0.0038
Total LSM compliance	3(3.0)	32(33.7)	0.0001
Aerobic exercise score (mean±SD)	2.81±4.41	11.65±10.60	0.0001
Depression score (mean±SD)	21.11±7.75	14.98±9.61	0.0019
Depression	51(51.0)	33(34.7)	0.0216
No depression	49(49.0)	62(65.3)	0.0216

* At the beginning 100 patients were recruited, but there were five dropouts during the study, leaving 95 participants for analysis after the LSM intervention.

Lifestyle modification yielded improved aerobic scores and a four-point reduction in the depression scores with a reduction in the incidence of depression after LSM.

Table 4: Effects of LSM in compliant and non-compliant groups

Variables	LSM Compliant	LSM partly compliant	P-value
Aerobic exercise score post LSM (mean±std)	15.94±12.00	10.80±9.80	0.018
Depression score post LSM (mean±std)	10.20±7.00	16.70±10.30	0.0001
Depression (n)	1 (2.9%)	32 (92.1%)	0.0001
No depression (n)	31 (47.5%)	31 (47.5%)	0.0001

LSM: Lifestyle modification yielded improved exercise scores and a fall in depression scores with a reduction in the incidence of depression in compliant subjects.

Table 5: Effect of LSM : CABG vs PCI group

Lifestyle parameters		CABG n=52* n (%)	PCI n=48* n (%)	p-value
Aerobic exercise score	Pre LSM	2.15±4.16	3.53±4.60	0.119
	Post LSM	9.40±10.94	14.16±9.73	0.024
Aerobic exercise compliance	Pre LSM	2 (40)	3 (60)	0.715
	Post LSM	14 (35.0)	24 (60.0)	0.012
Dietary measures compliance	Pre LSM	3 (50.0)	3 (50.0)	0.200
	Post LSM	30 (49.1)	28 (45.9)	0.200
Smoking cessation compliance	Pre LSM	6 (54.5)	5 (45.5)	0.590
	Post LSM	40 (52.8)	32 (42.2)	0.593
Total LSM compliance	Pre LSM	1 (33.3)	2 (66.7)	0.217
	Post LSM	12 (35.6)	20 (59.4)	0.022
Depression score	Pre LSM	22.10±7.60	19.20±7.50	0.049
	Post LSM*	17.80±10.60	11.30±6.60	0.000
Depression status Pre LSM	Depressed	34 (66.7)	17 (33.3)	0.047
	Not depressed	18 (36.7)	31 (63.3)	0.047
Depression status Post LSM*	Depressed	25 (72.0)	8 (23.0)	0.001
	Not depressed	25 (38.3)	37 (56.7)	0.001

LSM: Lifestyle modification; PCI: percutaneous coronary intervention

CABG: Coronary artery bypass graft surgery

LSM was more effective after PCI, with lower depression scores and reduced incidence of depression, as well as improved aerobic and dietary compliance in PCI subjects

*The lower participant numbers reflect the changes recorded in 95 participants after LSM because there were five dropouts .

Table 6: Effects of LSM: compliant CABG vs compliant PCI groups

Variables	Compliant CABG n=12	Compliant PCI n=20	OR(95% CI)	P-value
Total LSM compliance	12(35.6)	20(59.4)	1.70 (2.30-5.67)	0.022
Aerobic exercise score (mean±std)	14.96	18.91	1.10 (1.31-4.82)	0.049
Depression score (mean±std)	10.81	7.62	1.21 (1.12-3.92)	0.046
Depression pre LSM	*5(41.7)	®8(40.0)	0.91(0.89-3.97)	0.125
Depression post LSM	1 (7.9)	0(0.0)	0.96(0.80-3.30)	0.063
No depression pre LSM	7 (58.3)	12(60.0)	1.0(0.91-2.94)	0.097
No depression post LSM	©11(87.1)	×20 (95.0)	1.19(0.75-4.10)	0.113

*The prevalence of depression fell from 5 persons pre LSM to 1 post LSM (80.0% reduction) amongst fully compliant CABG group.

®There was no person with depression post LSM from the initial 8 depressed fully compliant PCI subject (100.0% reduction) amongst fully compliant PCI group.

The difference in reduction between fully compliant CABG and PCI was 80.0% vs 100.% (OR 1.10, CI 0.98-4.23,P= 0.191), which was not statistically significant.

© The number of patients with no depression increased from 7 persons pre-LSM to 11 post LSM in fully compliant CABG group (57.1%).

× There was 66.7% increment in the number of subjects with no depression post LSM, from the initial 12 to 20 patients amongst fully compliant PCI group.

The difference in increment between the fully compliant CABG and PCI was 57.1% vs 66.7% (OR 0.91, CI 0.97-3.23,P= 0.210), which was not statistically significant.

CHAPTER 3: Appendices

Appendix I: Study protocol

Effect of lifestyle modification on depression in coronary artery disease patients after revascularization

Problem Statement:

The prevalence of noncommunicable diseases of lifestyle is increasing in developing countries, including South Africa. This has resulted in worsening morbidity, mortality and psychosocial adverse outcome of coronary artery disease (CAD) in contrast to developed countries, where modern therapies and lifestyle modification (LSM) has been shown to reduce morbidity, mortality and improve quality of life (QOL), particularly reduction in the prevalence of depression. The purpose of this study is to evaluate prevalence of depression amongst CAD patients after revascularization and analyze the effect of LSM on depression and QOL.

Research Questions:

- How common is depression amongst CAD after revascularization?
- What is the effect of LSM on depression and QOL after revascularization?
- Do confounders like comorbidity, type of revascularization, income status, previous history of depression and gender affect depression after revascularization?

Hypothesis:

Lifestyle modification reduces prevalence of depression and improves QOL and after myocardial infarction (MI)

Aim:

To evaluate the prevalence of depression and analyse the effect of LSM on depression and QOL amongst MI patients after revascularization

Objectives:

1. To determine the baseline clinical profile (signs and symptoms) of the patients' pre-LSM and post LSM period.
2. To determine the status of prevalence of depression at baseline (three weeks/more)
3. To re-evaluate the prevalence of depression three months later after LSM

4. To determine the effects LSM on depression and QOL amongst the patients pre and post LSM
5. To determine the effects of confounding factors such as comorbidity, type of revascularization, income status, previous history of depression, physical activity profile and gender on depression and QOL.

Literature review:

Background:

Studies have shown that depression is common amongst CAD patient with a prevalence varying from 10% to 65%. [1-6] Depression is thought to be a risk factor for CAD as well a poor prognostic factor [3-6] and is associated with a worse adverse outcome and reduced health-related quality of life. [7-10] It is well established that CAD with depression have increased chances for MI recurrence and are more risk of death. [7-10] In the Baltimore cohort of the Epidemiologic Catchments Area study follow-up, major depression significantly increased the risk of acute myocardial infarction (OR 4.54, 95% CI 1.65-12.44). [11] A systemic review by the American Heart Association also found that depressed myocardial infarction patients had a significant increase in all-cause mortality, cardiac mortality and chances for recurrence, compared to non-depressed patients. [12]

Although prevalence of CAD is increasing globally, morbidity and mortality are noticed to be reducing in advanced countries. [13-19] In contrast, morbidity and mortality is increasing in developing countries, with more CAD patients having difficulties resuming normal lifestyle patterns, including return to work and participation in social and recreational activities. These difficulties result in a poorer QOL and depression in these patients. The decrease in morbidity and mortality and improvement in QOL reported in developing nations has been attributed principally to the introduction of better therapies as well as LSM which shows promising results in primary and secondary prevention of CAD, reduction in major adverse cardiac event (MACE) as well as improvement in QOL and depressive symptoms. [13-19]

Lifestyle modification regime is a standardized program of exercises, health education, and behavioral changes that aim to help CAD patients live a normal or near-normal life. [20-22] It involves training in aerobic exercises and health education, ranging from healthy eating, stress management and cessation of smoking. [20-22] For LSM to be successful, compliance with the regimen needs to be ensured. Compliance can be gauged using an established international guideline that recommend a minimum of 45 minutes of aerobic exercise, at least

5 times a week. Cessation of cigarette smoking and Mediterranean type of diet, which include a large portion of vegetables and fruits, fish, and less red meat/saturated fatty acid. [20-22]

Many studies have highlighted the beneficial effects of LSM after MI. It enhances early recovery, reduces subsequent fatal MI, increases QOL, as well as decreases mortality from CAD. [23-32] The tremendous improvement noticed is believed to be due to generalized reduction in modifiable cardiac risk factors, and improvement in the patient's life physiologically, physically, and psychologically. [23-32] This improvement is believed to account for the increase in QOL and decline in the mortality rate observed in many developed countries. [23-32]. Due to its benefits, several international guidelines {American heart association (AHA), Australian Cardiovascular Health and Rehabilitation Association (ACRA), and European Society of Cardiology (ESC)} have recommended LSM as an important component of comprehensive care to cardiovascular patients [33-35].

A multicentered study by Carl J et al compared benefit of LSM among elderly (>65 years) and younger patients (<65 years) cardiac patients post-MI. Both groups were statistically similar regarding baseline levels of total cholesterol, LDL cholesterol, behavioral characteristics, and parameters of QOL. The patients underwent a monitored LSM regimen under cardiac rehabilitation exercise programs, which started at 2 to 6 weeks after ACS and 4 to 8 weeks after bypass surgery and lasted approximately 3 to 4 months. The program included exercise sessions and educational programs on diets and other lifestyle changes. The result revealed that elderly patients showed very significant improvement in exercise capacity (+43%, $p< 0.0001$) after cardiac rehabilitation, which was statistically greater than the improvement (+32%; $p <0.0001$) noted in younger patients ($p \sim 0.01$). Improvement in all other parameters were statistically similar in both groups. Behavioral characteristics and QOL measures such as anxiety ($p <0.01$), depression ($p <0.01$), somatization ($p <0.0001$) as well total quality of life (all $p \sim 0.0001$) improved significantly after cardiac rehabilitation and exercise training in both groups. Mental health score improved more in the elderly (+5% vs +2%; $p = 0.05$) than in younger patients, but all other improvements in behavioral characteristics and QOL parameters were statistically similar in both groups. [36].

Amongst the studies that analyzed incidence of depression after MI was the “Depression after First Hospital Admission for Acute Coronary Syndrome : A Study of Time of Onset and Impact on Survival” by Osler M et al. They examined incidence of depression after ACS and assessed

whether the timing of onset of depression influenced long term survival. The ACS patients (cases) were identified through the National Patient Register, and a comparable reference population sample (control) was matched on 1:1 basis. Both samples were followed for depression and mortality outcomes from the beginning of the study until the end of follow-up (2 years for depression and 12 years for mortality). The results showed that 19,520 (20.0%) out 97,793 ACS patients recruited developed depression within 2 years of follow up, while in the reference population 14,386 persons (14.7%) developed depression. Higher rates of depression were seen in single persons, people with a basic education, and people with previous depression or other disease comorbidity. Although the depression rate was higher in women than men this finding was not significant. At the end of 12 years follow-up, 39,523 (40.4%) ACS patients and 27,931 (28.6%) members of the reference population died. Mortality rate was higher amongst depressed patients compared to those without depression in both the ACS patients and the reference population. This study concluded that depression is common in ACS patients and it is associated with increased mortality independent of its time of onset. [37]

In another study conducted by Antonakoudis H. et al, conducted in the department of Cardiology, Asclepeion Hospital, Athens, Greece, in the year 2005/2006, a total of 110 cardiac patients were recruited and followed up for two (2) months. They were divided into three (3) groups, namely A, B and C. Group A consisted of 60 post-AMI patients participating in a LSM under CR program, group B Consisted of 40 post-AMI patients not participating in any LSM program, while the control group C consisted of 10 apparently healthy people. QOL was evaluated by the Velasco-Del Barrio questionnaire, a QOL evaluation questionnaire consisting of 9 items (health, sleep, and rest, emotional behavior, concerns for the future, mobility, social interaction, alertness behavior, communication, work, and leisure time). A five (5) point scale (1= all the time, 5= none of the time) and a special (1 to 8) coefficient for each parameter were used for the evaluation of each parameter. The highest score of 220 indicates the poorest QOL. The result of the study showed that the LSM group A patients had better QOL as compared to non-LSM group B (94±3 vs 114±3, $p<0.001$), and slightly worse QOL compared to the control Group C (94±4 vs 69±3, $p<0.01$). Significant differences were found among LSM Group A and non-LSM group B patients regarding the important QOL parameters evaluated such as angina, dyspnea, depression (17±6.8 vs 22±6.5, $p<0.001$) and social behavior (21±4.2 vs 23±5.5, $p<0.0001$). They concluded that LSM in form of CR program significantly improves QOL including psychosocial function in post-AMI patients. [20]

In conclusion, while a beneficial effect of LSM in improving QOL and depressive symptoms have been reported in several studies, there is minimal information regarding that in developing countries including South Africa.

Rationale

With rapid urbanization and westernization in terms of diet, physical inactivity and smoking in SA, there is documented increase in CAD and its complications, particularly depression. Studies reported that LSM has shown promising results in primary and secondary prevention against CAD, with improvement in QOL and reduction in psychosocial complications. However little data exist in developing countries regarding the effect of LSM on QOL and depression after revascularization. This study aims to analyze that. The information to be generated would help to formulate a code of practice for the implementation of LSM in our clinical care.

Study design

Study type

The study is prospective in nature, in which a cohort of MI patients would be followed longitudinally to determine the prevalence of depression and effect of LSM and prevalence of depression among MI patients who underwent revascularization (CABG or PCI).

Setting

The research will be sited at IALCH Cardiology OPD clinic. Approximately 25 CABGs are done per month. These patients are followed up till six weeks' post-surgery on an out-patient basis by the surgeon. After six weeks, they are referred to Cardiology unit follow-up at 6 months, then yearly till three years' post-surgery.

Methods

The risk factor profile, depression characteristics and lifestyle changes of 100 consecutive participants undergoing coronary revascularization in the department of Cardiology IALCH would be obtained at the beginning of the study. The Demographic and other clinical data would be obtained from patient's file. The Beck Depression Inventory would be used to assess depression and the Goldin leisure-time questionnaire to assess physical activity (PA). The research process would be repeated and documented 3 months later after LSM program

Study population

The study population will be all adult patients who have underwent CABG and or PCI in the Departments of Cardiology of IALCH with in the time of the study and are willing to participate in the research.

Inclusion criteria

Adult Subjects will be recruited who have had documented AMI on coronary angiography and underwent CABG and or PCI during the time of the study.

Exclusion Criteria

Any patient with other major debilitating comorbidity, like advanced cancer, debilitating CVA, Severe arthritis and other severe incapacitating disease, which would preclude physical activity as a parameter of LSM.

Sampling

Convenient non-random sampling will be used. All consenting subjects who have either underwent PCI or CABG after AMI presenting to Cardiology clinic will be consecutively enrolled. The Sample size was calculated to be 150, based on Kwazulu-Natal (KZN) 2016 population estimate of 11, 079, 717 people [Stat SA 2016] and CAD prevalence of 5% [KZN burden of disease]. But almost all unstable angina and many of the MI patient do not undergo revascularization but treated medically, thus our sample size reduced to 100 since we are only to study the patient that undergo revascularization.

Statistical analysis

Recording and analysis

From the data generated, patients are to be stratified by racial group, age, gender, and mode of therapy (CABG vs PCI) for analysis. Demographic and clinical data of patients at the time of admission and after LSM intervention would be obtained from patients' file. Descriptive data will be expressed as mean ±SD. Categorical variables would be reported by frequency and percentage. Continuous variables are to be reported as medians and 25th and 75th percentiles (inter quartile range, IQR) as per their distribution. FS-36 QOL questionnaire would be used to inquire about changes in QOL pre- and post- LSM. From the data generated, patients are to be stratified by mode of revascularization (CABG vs PCI) for analysis. Baseline changes among PCI/CABG groups are to be compared by chi-square analysis and non-paired

test. Baseline and repeat evaluation at three months will be compared in each group by a paired t test, and the changes in data between groups to be analysed with a 2 factor (data pre- and post-intervention, and mode of therapy) repeated measures of analysis of the variance with repeated measures in a 1 factor (data before and after) test. Multivariate analysis/logistic regression will be used to determine predictors of QOL changes post revascularization. A p value < 0.05 will be considered significant. SPSS statistical software would be used for data analysis.

Limitations

The study will be limited to public sector patients at IALCH. This may have an impact on the generalizability of the results. Another major limitation will be the non-random sampling method, which will limit the strength of the study.

Potential Impact of the study

Routine blood tests for HbA1c and lipid profile will be done. This is important for it helps to indicate changes in CAD risk factor and whether treatment targets have been reached in the patients' management or not. This research would be beneficial in that it would assist in delineating prevalence of depression and effect lifestyle modification intervention on depression. It will improve knowledge and high light the importance of LSM in management of MI patients. Feedback will be given to the units involved on the findings of the study. Research findings will be presented at congresses and published in journals.

Ethical issue

Approval will be obtained from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal, as well as the Chief Executive Officer (CEO) of the IALCH before starting data collection.

Informed written consent will be obtained from participants. All questionnaires should be in English and will be administered with self of researcher or research assistant.

The Head of department of Cardiology and Cardiothoracic surgery have given permission to conduct this study. The patients involved in the research will be at minimal risk with regards to their privacy because they will not be identified by name or other particulars, except race,

sex, and age. No recorded material neither video footage nor pictures will be taken. Only routine blood tests for follow up will be taken.

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Appendix II: BREC ethical approval for the study

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

11 January 2017

Dr A Arzet (211560326)
Department of Internal Medicine
School of Clinical Medicine
NRMSM
aminuarzet@gmail.com

Dear Dr Arzet

Title: Effect of life style modification on quality of life conorary artery disease patients after revascularisation.
Degree: MMed

BREC Ref No: BE441/16

EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 12 July 2016.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 13 December 2016 to BREC letter dated 27 September 2016 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given **full ethics approval** and may begin as from 11 January 2017.

This approval is valid for one year from **11 January 2017.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its next meeting taking place on **14 February 2017.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor Joyce Tsoka-Gwegweni
Chair: Biomedical Research Ethics Committee

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Appendix III: BREC's approval for change of the study title

UNIVERSITY OF
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI
RESEARCH OFFICE
Biomedical Research Ethics Administration
Westville Campus, Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za
Website http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

19 July 2018

Dr A Arzet (211560326)
Department of Internal Medicine
School of Clinical Medicine
NRMSM
aminuarzet@gmail.com

Dear Dr Arzet

Title: Effect of life style modification on quality of life conorary artery disease patients after revascularisation.
Degree: MMed
BREC Ref No: BE441/16

New Title: The effect of life style modification on Depression amongst coronary artery disease patients after revascularisation.

I wish to advise you that your application for **Amendments to change the title** to the above received on 29 June 2018 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee.

The committee will be notified of the above at its next meeting to be held on 14 August 2018.

Yours sincerely

Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

Appendix IV: Inkosi Albert Luthuli Central Hospital (IALCH)/DOH approval

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE:
Office of The Medical Manager
IALCH

Physical Address: 800 Bellair Road, Mayville, 4058
Postal Address: Private Bag X09, Mayville, 4058
Tel: 0312401059 Fax: 0312401050 E/mail: mrgulanun@ialch.co.za
www.kznhealth.gov.za

30 November 2016

Dr A Arzet
Department of Internal Medicine
School of Clinical Medicine

Dear Dr Arzet

Re: Approved Research: Ref No: BE 441/16: Effect of life style modification on quality of life conorary artery disease patients after revascularisation.

As per the policy of the Provincial Health Research Committee (PHRC), you are hereby granted permission to conduct the above mentioned research once all relevant documentation has been submitted to PHRC inclusive of Full Ethical Approval.

Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

   The Secretariat
   Health Research & Knowledge Management
   330 Langaliballe Street, Pietermaritzburg, 3200
   Private Bag X9501, Pietermaritzburg, 3201
   Tel: 033395-3123, Fax 033394-3782
   Email: hrkm@kznhealth.gov.za

Yours faithfully

.....

Dr L P Mtshali
Medical Manager

Fighting Disease, Fighting Poverty, Giving Hope

Appendix V: Consent form to participate in the study

Information Sheet and Consent to Participate in Research

Date:

Dear prospective research Participant.

My name is Aminu Arzet, a medical Doctor undergoing specialist training under department of Medicine, Nelson Mandela School of Medicine, Durban. I am currently attached to the department of Cardiology Inkosi Albert Luthuli central Hospital, Durban. My mobile cell number is 0797970416, with email address: aminuarzet@gmail.com

You are being invited to consider participating in a study that involves healthy lifestyle changes so as to attain better health. The aim of the study is to assess effect of lifestyle changes on prevalence of depression and quality of life among patients who had heart attack. The study is expected to enroll 100 patients who attend fallow up Cardiology clinic at Inkolis albert luthuli central hospital. It will involve advising patients about lifestyle modification, and taking patients clinic and biographic data, then fallowing the patients for some months to see how lifestyle changes affect depression and quality of life of the patient's life. The duration of your participation if you choose to enroll and remain in the study is expected to be approximately 3 months.

The study involves advising you about healthy living via health talk, like cessation of smoking, if you smoke, and encourage you to exercise, de-stress, then change your diet by reducing saturated and eating more fruits, vegetables, fish and whole grain cereals. Normal routine blood samples will be taken like is done in all your follow up. We hope that the study will improve your quality of life and reducing your chances of having subsequent heart attack.

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number: BE441/16).

In the event of any problems or concerns/questions you may contact the researcher at (provide contact details) or the UKZN Biomedical Research Ethics Committee, contact details as follows: BIOMEDICAL RESEARCH ETHICS ADMINISTRATION Research Office, Westville Campus Govan Mbeki Building Private Bag X 54001 Durban 4000 KwaZulu-Natal, SOUTH AFRICA Tel: 27 31 2604769 - Fax: 27 31 2604609 Email: BREC@ukzn.ac.za

Participation in this research is voluntary and you are at liberty to withdraw participation at any point, and if you do not want to participate you will not incur any penalty or loss of treatment or other benefit to which you are entitled as a patient in this department. However, your disorderly withdrawal can hamper the success of the study, and could affect quality of care the study aim to establish.

Participation is free, and no reimbursements for participation in the study.

Information to be generated from the study will be safe and confidential, for participants will not be identified by names or racial group, rather a code to ensure confidentiality.

CONSENT

I ……..have been informed about the study entitled THE EFFECT OF LIFESTYLE MODIFICATION ON DEPRESSION AMONGS MYOCARDIAL INFARCTION PATIENTS AFTER REVASCULARISATION, by Dr Aminu Arzet.

I have been given an opportunity to answer questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any treatment or care that I would usually be entitled to.

I have been informed about any available compensation or medical treatment if injury occurs to me as a result of study-related procedures.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher at (provide details).

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION Research Office, Westville Campus Govan Mbeki Building Private Bag X 54001 Durban 4000 KwaZulu-Natal, SOUTH AFRICA Tel: 27 31 2604769 - Fax: 27 31 2604609 Email: BREC@ukzn.ac.za

_____ _____ Signature of Participant
Date

_____ _____ Signature of Witness
Date (Where applicable)

_____ _____ Signature of Translator
Date (Where applicable

Appendix VI: Questionnaires

Beck's Depression Inventory

Candidate number: Date:

1.	0	I do not feel sad
	1	I feel sad
	2	I am sad all the time and I can't snap out of it
	3	I am so sad and unhappy that I can't stand it
2.	0	I am not particularly discouraged about the future
	1	I feel discouraged about the future
	2	I feel I have nothing to look forward to
	3	I feel the future is hopeless and that things cannot improve
3.	0	I do not feel like a failure
	1	I feel I have failed more than the average person
	2	As I look back on my life, all I can see is a lot of failures
	3	I feel I am a complete failure as a person
4.	0	I get as much satisfaction out of things as I used to
	1	I don't enjoy things the way I used to
	2	I don't get real satisfaction out of anything anymore
	3	I am dissatisfied or bored with everything
5.	0	I don't feel particularly guilty
	1	I feel guilty a good part of the time
	2	I feel quite guilty most of the time
	3	I feel guilty all of the time
6.	0	I don't feel I am being punished
	1	I feel I may be punished
	2	I expect to be punished
	3	I feel I am being punished
7.	0	I don't feel disappointed in myself
	1	I am disappointed in myself
	2	I am disgusted with myself
	3	I hate myself
8.	0	I don't feel I am any worse than anybody else
	1	I am critical of myself for my weaknesses or mistakes
	2	I blame myself all the time for my faults
	3	I blame myself for everything bad that happens
9.	0	I don't have any thoughts of killing myself
	1	I have thoughts of killing myself, but I would not carry them out
	2	I would like to kill myself
	3	I would kill myself if I had the chance
10.	0	I don't cry any more than usual

	1	I cry more now than I used to
	2	I cry all the time now
	3	I used to be able to cry, but now I can't cry even though I want to
11.	0	I am no more irritated by things than I ever was
	1	I am slightly more irritated now than usual
	2	I am quite annoyed or irritated a good deal of the time
	3	I feel irritated all the time
12.	0	I have not lost interest in other people
	1	I am less interested in other people than I used to be
	2	I have lost most of my interest in other people
	3	I have lost all of my interest in other people
13.	0	I make decisions about as well as I ever could
	1	I put off making decisions more than I used to
	2	I have greater difficulty in making decisions more than I used to
	3	I can't make decisions at all anymore
14.	0	I don't feel that I look any worse than I used to
	1	I am worried that I am looking old or unattractive
	2	I feel there are permanent changes in my appearance that make me look unattractive
	3	I believe that I look ugly
15.	0	I can work about as well as before
	1	It takes an extra effort to get started at doing something
	2	I have to push myself very hard to do anything
	3	I can't do any work at all
16.	0	I can sleep as well as usual
	1	I don't sleep as well as I used to
	2	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep
	3	I wake up several hours earlier than I used to and cannot get back to sleep.
17.	0	I don't get more tired than usual
	1	I get tired more easily than I used to
	2	I get tired from doing almost anything
	3	I am too tired to do anything
18.	0	My appetite is no worse than usual
	1	My appetite is not as good as it used to be
	2	My appetite is much worse now
	3	I have no appetite at all anymore
19.	0	I haven't lost much weight, if any, lately
	1	I have lost more than five pounds
	2	I have lost more than ten pounds
	3	I have lost more than fifteen pounds
20.	0	I am no more worried about my health than usual

	1	I am worried about physical problems like aches, pains, upset stomach, or constipation
	2	I am very worried about physical problems and it's hard to think of much else
	3	I am so worried about my physical problems that I cannot think of anything else
21.	0	I have not noticed any recent change in my interest in sex
	1	I am less interested in sex than I used to be
	2	I have almost no interest in sex
	3	I have lost interest in sex completely

INTERPRETING THE BECK DEPRESSION INVENTORY

Now that you have completed the questionnaire, add up the score for each of the twenty-one questions by counting the number to the right of each question you marked. The highest possible total for the whole test would be sixty-three. This would mean you circled number three on all twenty-one questions. Since the lowest possible score for each question is zero, the lowest possible score for the test would be zero. This would mean you circles zero on each question. You can evaluate your depression according to the Table below.

Total Score_____ Levels of Depression

1-10_____ These ups and downs are considered normal
11-16 _____ Mild mood disturbance
17-20 _____Borderline clinical depression
21-30 _____Moderate depression
31-40 _____Severe depression
Over 40 _____ Extreme depression

Godin Leisure-Time Exercise Questionnaire

Candidate number: Date;

1. During a typical 7-Day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time.

a) STRENUOUS EXERCISE
(e.g., running, jogging, playing football, etc). _____

b) MODERATE EXERCISE
(e.g., fast walking, baseball, tennis,
volleyball, badminton) _____

c) MILD EXERCISE
(e.g, yoga, easy walking) _____

2. Total score:

3. Grading:
I). 24 units or more/week = Active
II). 14-23 units/week = Moderately active
III). Less than 14 units/week = Insufficiently active

Appendix VII: Manuscript submission

CVJ SA submission Guidelines

Available online at http://www.cvja.co.za/authors.php

(Accessed on 22nd July 2019)

INFORMATION FOR AUTHORS

The Cardiovascular Journal of Africa is pleased to consider original articles, reviews, discussions on topical issues, case studies, meeting reports and other contributions relevant to the understanding, treatment and care of vascular disease. Original articles and reviews are sent for independent peer-review. Material is accepted for publication on the understanding that it has not been published elsewhere. Authors will be asked to confirm this in writing and transfer copyright to the Journal. Authors submitting papers to CVJA should also register as a reviewer as a quid pro quo for authors for reviewers reviewing your submission. If authors do not register as reviewers it may be taken in consideration when deciding on acceptance and rejection, and the time of publication. We do try not to call on a reviewer more than once a year but in rare circumstances it may be twice.

Important Notice to all Authors:

It has become necessary for the Cardiovascular Journal of Africa to charge a manuscripts submission fees for all articles submitted for publication (effective 13 December 2016). On acceptance of a manuscript an additional Article Processing Fee will apply before publishing.

- Manuscript Submission Fee: South African and International Authors: ZAR 1000.
  Paid on Submission of Manuscript.
- Article Processing/Publishing Fee: South African and International Authors: ZAR 6000.Paid on Article Acceptance for Publication in the CVJA.

This is normal for most, if not all, journals. We so far have been able to survive without charging authors for submissions and processing but can no longer do so. We regret that we have to implement this as from the 13 of December 2016. Payment will need to be made online and once payment has been received, the manuscript will be further processed for possible publication. The payment of the manuscript submission fee and does not guarantee publication of the article. The manuscript submission fee is not refundable in the event of rejection as processing cost will have been incurred. (Payment can be made online with a valid credit card)

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The Cardiovascular Journal of Africa (CVJA), which incorporates the Cardiovascular Journal of South Africa, is particularly concerned with publication of scientific articles related to Cardiac and Vascular conditions and situations, concerning adults and children, in Sub Saharan Africa. But will accept articles from all parts of the world.

Basic Science publications related to clinical aspects either for elucidation, in-depth understanding or therapeutic approaches are accommodated. The Journal functions as official medium for other related societies which do not as yet have own Journals such as, Hypertension, Stroke, Nuclear Medicine and Magnetic Resonance in Cardiology, Paediatrics, Molecular and Cellular Cardiology, and Vascular disease in Diabetes and Obesity.

Index Medicus / PubMed Central / Medline and Sabinet lists the Journal for indexing and electronic citation. A printed version and an electronic version for citation and publication of abstracts are produced. The abstracts of articles published appear on PubMed with a link out to Sabinet to give access to full text retrieval of published material. In order to improve visibility for our authors, the CVJAfrica is now also able to index articles for PubMed Central.

ARTICLE SUBMISSION

All categories of manuscripts for the Cardiovascular Journal of Africa must be submitted on-line to Editorial Manager. You will be assigned your own password and username. This will allow complete interaction between the editor and authors. Internally, reviewers will be approached to review material in their field of expertise and assigned with similar interaction. All information will be entirely protected and confidential. All submissions should be written in a clear and succinct manner, following the style of the Journal. Title page should include a descriptive title; authors' surname and forename, address of each author and full address, telephone, fax and e-mail contacts for the corresponding author. In text: tables and figures are either inserted as part of sentence, for example Table 1, or in parentheses, for example (Fig. 1). Each table should carry a descriptive heading.

Editorial Manager will clearly indicate which aspects of the submission that must be supplied off-line (download off-line document). This must be provided to the Journal by mail (PO Box 1013, Durbanville, South Africa, 7551) or e-mail to info@clinicscardive.com

All images MUST be at or above intended display size, with the following image resolutions: Line Art 800 dpi, Combination (Line Art + Halftone) 600 dpi, Halftone 300 dpi Image files also must be cropped as close to the actual image as possible.

Preferred Image Format

Image Format: . tif

Image Width: Greater than or equal to intended display size

Colorspace: RGB

DPI: 500+

Alpha Channels: None

Layers: Flattened

Image Format: .jpg

Image Width: Greater than or equal to intended display size

Compression Quality: Maximum

References must be numbered in the order of appearance in the text, according to Vancouver style. For articles: Author AB, Author C, Author M. The title of the article. Abbreviated journal title 1999; 14: 172–183. For book chapters: Author AB, Author CD. The title of the chapter. In: Editor A, Editor BC, ed. Title of the book, 2nd edn. Location: Publisher, 1999: 133 –139. DOI Numbers / PMID (Pubmed ID / PMC ID) must be added to all references to facilitate tagging for PubMed Central.

Original articles: Title page as above. Abstract (150 words) a short inclusive statement suitable for direct electronic abstracting, identifying the purpose of the study, key methods, the main results and the main conclusion. Keywords: maximum of six keywords for indexing. Introduction: concise description of background, sufficient for the non-specialist to appreciate the context of the work. Clear statement of the purpose of the study. Methods: a brief description of study design, procedures, analytical techniques and statistical evaluation. Results: a clear account of the study findings using quantitative language where possible and cross-referenced to tables and figures. Discussion: an interpretation of the study placed within the context of current knowledge, leading to specific conclusions where possible. Acknowledgements. References, figures and tables as above.

Reviews

Title page as above. Abstract (150 words) setting out the scope, key messages and conclusions of the review. Body of text liberally partitioned with headings and subheadings leading to a synopsis with conclusions at the end. Key messages in a separate box itemizing two to five short principal statements. Acknowledgements, references, tables and figures as above.

Other articles should adopt a concise style consistent with similar articles previously published in the journal. Manuscripts should include a title page, and appropriate subheadings for text. Style of tables, figures and references as above.

Figures be sent to us in a high-resolution JPEG format, but they MUST be sent separately from the Word document. If not in high resolution JPEG, then PowerPoint will do.

Editorial Manager will clearly indicate which aspects of the submission must be supplied off-line (download off-line document). This must be provided to the Journal by mail (PO Box 1013, Durbanville, South Africa, 7551) or e-mail to info@clinicscardive.com

The status of progression of the peer-review system will be directly accessible by authors. The Editorial Manager system is particularly useful to authors and reviewers as there is a direct link to PubMed for viewing all related articles on the subject matter.

Submitted manuscripts must be supplied with a covering letter with any additional information that may be helpful to the editor, such as the type or format of article that the manuscript represents. If the manuscript has been submitted previously to another journal, it is helpful to include the previous editor's and reviewers' comments with the submitted manuscript, along with the authors' responses to those comments. Copies of any permission to reproduce published material, to use illustrations or report information about identifiable people, or to name people for their contributions must accompany the manuscript.

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Authors submitting papers to CVJA should also register as a reviewer as a quid pro quo for authors for reviewers reviewing your submission. If authors do not register as reviewers it may be taken in consideration when deciding on acceptance and rejection, and the time of publication. We do try not to call on a reviewer more than once a year but in rare circumstances it may be twice.

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ZAR 4000 for Authors outside of Africa

ZAR 1500 for African Authors (including South Africa)

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