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A Review on Six-Minutes' Walk Test and Health Related Quality of Life in Heart Failure Patients

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Introduction

Heart Failure is typically characterized by difficulty in breathing, leg swelling and easy fatigability due to a structural or functional cardiac abnormality resulting in abnormal haemodynamic indices. Heart failure is classified haemodynamically as: heart failure with preserved ejection fraction (EF≥50%), heart failure with reduced ejection fraction (EF≤40%) and heart failure with mildly reduced ejection fraction (EF 41% - 49%). From a time, course perspective, it can be acute where it can occur de novo or on the background of chronic heart failure [1].

It is a global disease with high morbidity and mortality [2]. In Africa about 3% - 7% of all hospital admissions are due to heart failure [3,4]. It is one of the most common cardiovascular disorders in Nigeria (Ansa et al., 2008). Hospital prevalence studies in Sub Saharan Africa show that heart failure accounts for 9.4% to 42.5% of all medical admissions and 25.6% to 30% of all admissions into the cardiac unit [5], another study reported in-hospital mortality rate of decompensated heart failure of up to 8.3% [6]. About 25% of cases of heart failure in Nigeria have advanced heart failure with a high mortality [7]. Though advances in medicine have improved survival in Heart failure patients, there is a steady increase in mortality with the projected 5-year survival rate of 50%, with 25% of patients dying within the first year [8].

Common causes of heart failure include hypertension, coronary artery disease, myocardial infarction, valvular heart diseases, diabetes mellitus, thyrotoxicosis, and lung diseases [9,10]. Management includes specific investigations such as electrocardiography, echocardiography, brain natriuretic peptides, cardiac enzymes, and use of drugs such as angiotensin converting enzyme inhibitor (ACEIs), beta-blockers, diuretics, angiotensin receptor blockers (ARBs), lipid lowering drugs, lifestyle modifications such as quitting smoking and reduction in alcohol intake and in some instances surgery and use of devices may be indicated [11].

Heart Failure and Exercise Capacity

Due to a decrease in supply of blood to meet metabolic demands of tissues in heart failure, there is impairment of physical function [12], hence assessment of exercise capacity should be an important modality in patient's evaluation and management. This assessment also may give insights on prognosis, severity of the condition, disabilities, and quality of life of affected patients [13].

Functional Capacity

This is the ability of an individual to perform aerobic work as defined by the maximal oxygen uptake (V02 Max) which is the product of cardiac output and arteriovenous oxygen difference at physical exhaustion [14]. Methods used in assessment of functional capacity include New York Heart Association (NYHA) classification, Goldman Specific Activity scale, six-minute Walk Test (6MWT), measurement of maximal oxygen consumption during exercise stress test [15,16].

Types of Exercise Test

a. Six-minute Walk Test (6MWT): This is a simple test that requires a 100 ft (30m) flat surfaced walkway, no exercise or advanced training is required. The patient walks for six-minutes and distance covered is recorded [17].

b. Shuttle Walk Test (SWT): Patient walks without stopping for rest with the pace of walking increased incrementally after a set time until patients cannot keep up anymore [18].

c. Cardiopulmonary Stress Test: The patients use a treadmill or bicycle ergometer connected to 12 lead ECG, breathes only from the mouth and oxygen consumption is derived with incremental load [19] or estimated from the duration of exercise [20]. Balogun et al carried out a study which looked at cardiovascular response to treadmill exercise among Nigerian hypertensive with echocardiographically proven left ventricular hypertrophy and found out that there was significant and progressive reduction in exercise capacity from normotensive to hypertensive left ventricular hypertrophy and to hypertensive heart failure [20].

Six-minute Walk Test

The six-minute walk test is a sub maximal exercise test that is simple to carry out and has been shown to predict outcomes in patients with chronic heart failure [21,22]. Cahalin et al. [23] studied 45 patients with advanced heart failure and Roul et al. [24] looked at 121 patients with either class 2 or 3 heart failure patients with systolic dysfunction found out that the six-minute walk test was significantly able to predict likelihood of death or poorer outcome in patients who walked <300m [24,10], on the contrary Green et al in their study find out that there was no significant correlation of the distance walked and Peak O2 consumption or functional capacity, also the distance walked did not predict mortality but the shuttle walk had better correlation [25,26].

A significant correlation has been noted however when the 6MWT and other measures of functional capacity were analyzed. Guyatt et al studied 18 patients with chronic heart failure and found significant correlation between the 6MWT and cycle ergometer test, they also found significant correlation between the 6MWT and use of questionnaire (MLHFQ) as patients who had poorer quality of life also were noted to walk shorter distances in six-minute walk test [27]. Lucas et al. [28] carried out the 6MWT and symptom limited cycle ergometry on 307 patients with advanced heart failure and found out that correlation between Peak Oxygen consumption and 6MWT varied depending on the level of Peak VO2 consumption, they also noted that peak VO2 of (10-20ml/kg/min) correlated poorly with 6MWT (r=0.28) while patients with higher VO2 (>20ml/kg/min) and low VO2 (<10ml/kg/min) showed moderate correlation (r=0.57). They therefore inferred that the 6MWT did not predict VO2 in patients with advanced Heart Failure (Ejection Fraction <35%) [28].

Though exercise stress test is a more objective assessment of functional capacity, it is more technical and demanding and may be a more difficult test for patients to take as noted by Lipkin et al who looked at 26 patients with NYHA (II - III) and 10 normal subjects, maximal exercise capacity test and 6MWT were done [29], they found that the 6MWT can objectively assess exercise capacity and that patients preferred the 6MWT to the maximal exercise test. They further stated that the 6MWT could usefully supplant history and physical examination [29]. Adedoyin et al studied 35 patients with congestive heart failure; the patients performed the 6MWTand the bicycle ergometer test (Adedoyin et al., 2010), they also found high positive correlation between distance walked and Peak VO2 (r=0.65, p<0.01). The average distance walked was 327m±12.03m, they also noted that the peak VO2 was higher during the bicycle ergometer test (13.7±1.9L). They inferred that the 6MWT could be useful to evaluate exercise tolerance and the stress test more appropriate in assessing maximal functional Capacity.

When Morales et al (1999) looked at 6MWT and shuttle walk test with respect to peak VO2 consumption, 6MWT correlated moderately when peak VO2 [11] was <14ml/kg/min. The 6MWT significantly predicted peak VO2 with an accuracy of 83% (< - 0.02) with best cut-off distance of 450m (sensitivity 80%, specificity 83%). When the distance walked was <450M the 6MWT lost its ability to predict peak VO2, the 6WT however was an independent predictor of peak VO2. Morales et al further stated that the reason for the stronger correlation of the 6MWT with peak VO2 was due to the fact that the 6MWT is symptom limited while the shuttle walk is time limited, in essence patients are sub-maximally exercised [15]. Studies by Pulz et al. [18] and Zugck et al. [30] had similar results to Guyat et al. [27] and Lipkin et al. [29] as discussed above. A systematic review of 14 publications on determination of functional capacity using the 6MWT was carried out and the researchers noted that inconsistencies in the results from the 6MWT was due to various factors like if encouragement was given to the participants, the amount of experience and reliability of the administrators and whether the administrator was blinded to other tests and previous 6MWT [10].

The 6MWT is also highly reproducible (stability of a test when no important change has occurred) and responsive (the sensitivity of a measure to a clinically relevant change in health status) [23]. Several factors are known to affect six-minute walk test such as age, sex, high, BMI, parity [31,32]. In this study the 6MWT will be used to assess functional capacity since it is simple to carry out, inexpensive, patients would prefer it and it also mimics the activity of daily living of the patients.

Heart Failure and Health Related Quality of Life (HRQoL) of Heart failure Patients

The patients' personal experiences, response to treatment and perceptions are presently regarded as an important aspect of management that should not be neglected. Clinicians are

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giving more attention to this aspect of patient's day to day life challenges [25], this is termed Patient Reported Outcome (PRO). Health status refers to perceived changes in a patient's activities when compared to normal life, it takes into consideration the patient's physical and mental functioning [28]. Functional status on the other hand takes into consideration the ability of patients to carry out activities of daily living at home or work, in essence it focuses on physical functioning mainly [33]. Health status, functional status, and quality of life or HRQOL are terms which are used interchangeably though some researchers do not agree with this practice [33], these terms come under PRO [34]. Health related quality of life is defined by the WHO as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns [29].

Primary treatment goals for the clinician in Heart failure are to improve symptoms, decrease morbidity and mortality, also important is the degree of impact of the disease condition on the patient's functional capabilities, and quality of life the patient has to enjoy alongside the ailment [30,35], this latter aspect is usually not given the attention it deserves but it is of more importance to the patient than physiological and laboratory parameters which the clinician needs [36]. When patients were asked to define QOL, it was viewed as their ability to perform desired physical and social activities to meet their needs and their family's needs, maintain happiness and engage in fulfilling relationships with others. Heart failure impairs quality of life [37-39].

Importance of Assessing the HRQOL of Heart Failure Patients

Physiological and laboratory parameters do not correlate with patient functional capabilities, also an illness may affect different domains with varying severity in different patients. Assessment of these domains may aid diagnosis of other co-morbidities which may worsen prognosis, for example depression in a patient with heart failure [36]. Ola et al. [40] looked at the relationship between depression and QOL in heart failure patients and found out that depression impairs quality of life and recommended that assessment of QOL should be incorporated early in management of heart failure patients [40].

Adebayo et al. [41] noted that QOL was a successful predictor of adverse outcome in heart failure; they also noted it's reliability and usefulness in determining outcome was at par with markers such as LVEF, 6MWT, B-type naturetic peptide and NYHA [41]. QOL should be a primary outcome measure in clinical trials [42-45]. It helps clinicians to measure the impact of diseases on the lives of patients, enabling health care professionals to know which domain of HRQOL is most important to the patient and the treatment that would provide the patient with maximum benefits [46]. Evaluation of new health policies as they affect patients can be monitored through HRQOL measures [47].

Domains which HRQOL focuses on include physical health effects, such as energy level, pain, physical activity, and sleep; psychological functioning such as emotions, self-esteem, learning, memory and concentration, social relations which include aspects of sexual activity and social support, environmental factors like financial capabilities, transport, and security. The Spiritual/ Religious belief is also assessed [47]. Various demographic profiles of patients have been found to either positively, negatively, or inconsistently affect QoL, these include level of education, age, gender, marital status, duration and severity of illness, socio-economic status, and recurrent admissions [39,48].

Minnesota Living with Heart Failure Questionnaire (MLHFQ)

It was developed at the University of Minnesota, USA [49] as a specific tool to measure the QoL of patients with chronic heart failure. It is well validated [25,39]. It can be self-administered or used with an interviewer. It uses Likert – type size point scale which ranges from 0 (no effect on QoL) to 105 (maximum effect on QoL). Higher scores mean poorer QoL. It is made up of 21 item Questions. Three scores can be determined, a total score (21-items) range 0 - 105, the physical dimension (8-items) range 0 - 40, and the emotional dimension (5-items) range 0 - 25. The questions range from symptoms and signs relevant to Heart Failure e.g., physical activity, social interaction, sexual activity, work, and emotions [50].

Cut-off to distinguish good moderate and poor QoL will be set at < 24 to mean a good QoL, 24 - 45 a moderate QoL and >45 a poor QoL, these cut-offs have been shown to correlate with survival status NYHA functional class and six-minutes' walk test [51]. It has a Cronbach's alpha rating for internal consistency of 0.92 and Test retest/reproducibility r = 0.87 [43]. A study done in Nigeria recommended that the MLWHF should be used regularly in patient evaluation as it is reliable and valid [52].

Relationship between HRQoL and Echocardiographic parameters in Heart Failure

Left ventricular systolic and diastolic dysfunctions are important clinical prognostic factors for outcomes in heart failure [42], in evaluating heart failure patients with echocardiography the common abnormalities are reduced left ventricular ejection fraction (LVEF) indicating poor systolic function, in other cases, the LVEF is normal, but mitral inflow patterns are abnormal denoting diastolic dysfunction [4]. Behlouli et al. [51] studied 758 patients with coronary artery disease and found that HRQol was weakly associated with left ventricular function parameters in patients in NYHA I– II but a stronger association was observed in patients in NYHA III between LVEF and physical functioning. This finding was also highlighted by Wu et al. [53]. In the VIDA-IC study 1037 patients with HFREF were evaluated and the authors concluded that there was no association between LVEF and other

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clinical parameters such as Haemoglobin and renal function with HRQoL [54].

In the survival and ventricular enlargement (SAVE) trial, 184 patients who had compromised left ventricular function but not in overt heart failure were enrolled, the authors did not find any correlation between HRQoL parameter and left ventricular echocardiographic features [55], a similar finding to that of Staniūtė et al in patients in NYHA I – II. Some studies which did not show any relationship between LVEF and HRQoL, were performed in patients who were without significant reduction in LVEF like the study of Sjöland [56] where participants with LVEF less than 40% were 9% of the total population [56] and the study by Mattera et al. [57] where only a small percentage had abnormal LVEF [57]. Some studies have observed an association between HRQoL and diastolic dysfunction [55,56]. Mehani et al. [58] in their study of patients with dilated cardiomyopathy found out that improvement in diastolic function translated also to improvement in HRQoL [58].

Factors Affecting HRQoL in Chronic Heart Failure

Both clinical and non-clinical variables are known to influence HRQoL [37]. Iqbal et al. [59] studied 179 patients over a 3-year period. The study highlighted that NYHA class, socio-economic deprivation and presence of an informal caregiver are 3 independent predictors of HRQoL. The study also showed that chronic heart failure patients who did not have an informal caregiver had a poorer quality of life. In the HRQoL arm of the CHARM trial, independent clinical determinants associated with a worse HRQoL included younger age, higher BMI, lower systolic blood pressure, female gender, worse NYHA, PND, rest dyspnoea and lack of ACE-inhibitor use [60] and Iron deficiency anemia in chronic heart failure [61].

The relationship between age and HRQoL is not clear-cut, some authors have reported worsening HRQoL with increasing age [62] and other studies have shown improvement in HRQoL results [63,64]. Women were also found to have lower HRQoL than men [65]; however other studies did not find any significant difference between both genders, suggested reasons were that women had less social support and were more likely to have depression [66,67]. Higher education level, patients who are employed and were residing in a country capital had worse quality of life, and also those who had been admitted 3 times or more [68]. Low socio-economic status has been pointed out as one of the major factors associated with HRQoL [69]. Social support has been noticed to improve HRQoL [70].

A systematic literature review by Hawkins et al concluded that low socioeconomic status was a powerful independent predictor of heart failure development and poor outcomes [71]. Expenses on medication, possible job loss due to severe illness and financial difficulty experienced by these patients affect their quality of life negatively and may even lead to poor compliance with medication [35,69,72,73].

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