To Correlate Ejection Fraction with 6 Minute Walked Distance and Quality of Life in Patients with Left Ventricular Heart Failure

Pramila S Kudtarkar*, Mariya P Jiandani*, Ashish Nabar**

Abstract

Purpose: 6 minute walk test (6MWT) is a reflection of activities of daily living [ADL]. Walking is an activity performed daily by all but the most severely impaired patients. Patients with left heart failure show decrease exercise tolerance. This study was developed to investigate the correlation of decreased ejection fraction (EF) on 6 minute walk distance (6 MWD) and Left ventricular dysfunction -36(LVD-36) score in patients with left ventricular heart failure (LVHF).

Material and Method: A prospective study of 30 patients with 15%-45% of EF on 2D echo was evaluated where they were randomly selected. NYHA class was assessed. 6 MWD was measured using AHA 2002 guidelines. Quality of life was assessed using LVD-36 Questionnaire.

Results: Intergroup comparison of LVHF patients with that of normal individuals of same age was done. It showed patients with LVF cover lesser distance (n= 30, mean walk distance= 384.66 ± 115.14 mts, mean age= 54.7 ± 10 yrs) as compared to normal individuals (n = 30, mean walk distance= 526.33 ± 54.6 mts, mean age= 50.7 ± 8.2 yrs) with p < 0.001. We found statistically significant positive correlation between 6MWD and EF (r = 0.6319; p < 0.001).

Statistically significant negative correlation was observed between 6MWD and LVD-36 score (r = -0.8, p < 0.001) and LVD-36 score and EF (r = -0.87, p < 0.001).

Conclusion: The result of this study showed that by performing 6 MWT we may predict the EF and quality of life of patients with LVHF. Patients with LVF cover less distance as compared to normal.

Introduction

Testing capacity to walk as far as possible for 6 minutes is a simple, reliable, objective and inexpensive tool. 6MWT assesses sub-maximal exercise capacity and functional activity. The 6 MWT may indicate the ability to carry out ADL and can be performed by elderly, heart failure and COPD patients. It is performed in a corridor without sophisticated equipment and doesn't require highly qualified staff. Contraindications for it include unstable angina and recent acute myocardial infarction. However, the intensity of the test is self determined. A recent review of functional walking test concluded that 6 MWT is easy to administer, better tolerated and more reflective of ADL than any other walk test. It is a better index to provide information about ability to perform ADL than is peak oxygen uptake. It evaluates global and integrated response of all systems involved during exercise like pulmonary, cardiovascular, musculoskeletal and neuromuscular. As described by Guyyat et al it carries prognostic information in patients with mild to moderate heart failure.
strong trend to predict cardiovascular mortality and morbidity. In patients with LVHF there is decrease in cardiac output, stroke volume and EF, because of this patient present with symptom of dyspnoea, fatigue and exercise intolerance. Investigations like 2D echo are one of the major tools of objective assessment of left ventricle performance. The LVD-36, disease specific questionnaire, is another tool for assessing health status and physical performance of LVHF patients. It measures the impact of left ventricle dysfunction on ADL and well being. Several modalities which assess left ventricle dysfunction are 2D echo, LVD-36 questionnaire, 6 MWT and NYHA class.

Hence, this study was conducted to observe if decrease EF has impact on 6 MWD and LVD-36 score, as walk distance and LVD-36 score reflects ADL.

Methods

30 patients of LVHF, NYHA class between II-III and EF between 15%-45% were evaluated. They were referred by Cardiologist for the study. The patients were made aware of the proposed study procedures and freely gave written informed consent. All procedures were approved by the Ethics Committee.

Ejection Fraction Evaluation: Ejection fraction was evaluated using Panasonic Video Cassette Recorder AG: 7360 by Cardiologist.

Quality of Life Evaluation: A version of Left Ventricular Dysfunction –36 used to evaluate patient quality of life.

6MWT: We conducted the 6MWT as per American thoracic Society guidelines 2002. Patients were instructed to walk, attempting to cover as much ground as possible within 6 min. A research assistant timed the walk, and standardized verbal encouragement was given to each patient. Before and after the test, data were obtained for heart rate, respiratory rate, Borg scale fatigue and dyspnoea score, and BP. The distance covered was measured in meters. Age match normal individuals were also made to walk and distance covered in 6MWT was recorded.

Statistical Analysis: To study the correlation between variables like walk distance, ejection fraction, LVD-36 score and NYHA class, Pearson correlation coefficients of was used. Receiver Operating Characteristic [ROC] curves was plotted for the same variables. Unpaired t-test was done to compare the walk distance of patients and normal individuals.

Results

Baseline Characteristics of the Study Population: Of the 30 patients (29 males and 1 female), 15 patients were diagnosed with dilated cardiomyopathy and 15 with Ischaemic heart disease. Mean age of the patient was 54.7 ± 10 yrs and normal population was 50.7 ± 8.2 yrs. 20 patients were in NYHA class was II and 9 in class III. The heart failure was moderate in 14 patients (46.62%), severe in 9 patients (30%) and very severe in 17 patients (23.33%). The mean EF of patient was 27.5 ± 9.62%. All the patients were on treatment with anti hypertensive, anti failure and anti platelet drugs. Mean BMI was 24.67 ± 3.68 kg/m². In all patients, the LVD-36 score for QOL were > 50% in domains (symptom and activities), indicating significant impairment of general health status.

6 MWT and Correlation Coefficient: Unpaired t-test of LVF patients and age matched normal individual showed, normal (mean WD 526.33 ± 54.67 mts) cover more distance as compared to LVHF patients (mean WD 385 ± 115 mts), with statistically highly significant difference.
The 6 MWD presented statistical significant positive correlation with EF. Conversely, LVD-36 score was found to correlate negatively to a statistical significant degree with EF and WD.

ROC Curve: ROC curve of WD and EF showed that patient covers distance of less than 532 mts show 100% [specificity] possibility of having EF less than 25%.

ROC curve of WD and LVD-36 score showed if distance is more than 325 mts then possibility of having LVD-36 score between 0-25 per cent is 93.33% (sensitivity).

ROC curve of LVD-36 and EF showed if score is less than 30% then 100% [specificity] possibility of having EF more than 25%.

Discussion
In this study we compared walk distance of patients with LVHF and age matched normal individuals (Fig. 1 and Table 1).

<table>
<thead>
<tr>
<th>Normal WD</th>
<th>Patient WD</th>
<th>Normal Age</th>
<th>Patient Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>526.33±54.6</td>
<td>384.66±115.14</td>
<td>50.7±8.2</td>
<td>54.7±10</td>
</tr>
<tr>
<td>t-value WD</td>
<td>t-value Age</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>-0.61887</td>
<td>1.67</td>
<td>&lt; 0.001***</td>
<td></td>
</tr>
</tbody>
</table>

Unpaired t-test showed the LVHF patients (n=30) covered less distance (mean WD = 384.66 ± 115.14 mts, mean age 54.7 ± 10 years) as compared to normal individuals (n=30, mean walk distance is 526.33 ± 54.6 mts, mean age 50.7 ± 8.2 years).

Fig. 1: 6 minute walked distance normals and patients with heart failure

<table>
<thead>
<tr>
<th>r-value</th>
<th>p-value</th>
<th>Mean EF</th>
<th>Mean WD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6319</td>
<td>0.001***</td>
<td>27.5 ± 9.62</td>
<td>384.66 ± 115.14</td>
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</tbody>
</table>

Positive correlation of EF (mean 27.5 ± 9.62%) and walk distance (mean 384.66 ± 115.14 mts) where as EF is decreasing, walk distance is also decreasing.
p<0.001. Heana et al7 enumerates cardiac causes for decrease functional capacity like left ventricular dilation, impaired left ventricular systolic function, decrease forward stroke volume and EF. As stated by Martin et al8 that the primary mechanism responsible for exercise intolerance in these patients is due to increased capillary wedge pressure which stimulated pulmonary J receptors causing dyspnoea. Study done by Mancini D and Xenon et al9 and study done by Guazzi et al10 have stated that reduced alveolar capillary membrane diffusing capacity in heart failure leading to impaired pulmonary gas transfer who correlates with exercise capacity and functional status. As per study done by Arslan S et al11 where they have evaluated prognostic value of 6MWT in patients with stable CHF (EF less than or equal to 40% and NYHA class II or III). They formed two groups where group I 6 MWD less than or equal to 300 mts (79%) than in patients with more than 300 mts (7%) (p < 0.001) they concluded that death risk is higher in patients with decreased walk distance and ejection fraction (P < 0.005 and < 0.02 respectively).

Receiver Operating Characteristic (ROC) curve of ejection fraction and walk distance where we split data of ejection fraction below 25% and above 25%. We observed that patient covering less than 532 mts distance have 100% possibility (specificity) of having EF less than 25% and if he is covering distance more than 532 then 21.4% possibility (sensitivity) of having EF more than 25%. Area under curve is 0.884 ranging from 0.76 to 1 with confidence interval of 95% and is highly statistically significant.

Opasich C et al12 have correlated walk test performance with standard indices of cardiac function i.e. EF and exercise capacity. Patients in this study covered distance of 396 ± 92 mts on 6MWT and it was not significantly correlated with ejection fraction. Muller et al13 have evaluated patients with heart failure subjected to symptom limited treadmill/bicycle ergometer test and their regional blood flow and cardiac output was measured. They concluded that to determine the exercise capacity blood flow to skeletal muscles is more important than cardiac output as it is responsible for patient’s symptom. Hence central haemodynamic variable do not correlated with exercise tolerance.

As per Fig. 3a and Table 3a, WD and LVD-36 scores were correlated. It showed negative correlation where lesser the walk distance more are the % of LVD-36 score. ROC curve and Table 3b where it is observed that if patient is walking more than 325 mts then
93.33% [sensitivity] possibility of having LVD-36 score between 0-25% (CI 95% and p < 0.001). This correlation can be attributed to, when we perform ADL we work at our sub-maximal capacity. Studies have shown that 6MWD is an indicator of ADL. Patients with LVF show decreased EF and stroke volume. They perform low in ADL and hence may show poor performance on 6 MWT. As per studies, LVD-36 is an indicator of ADL and functional capacity (6, 12 and 16). It is useful to predict aerobic capacity of patients and those undergoing treadmill tests.4 When it is compared with Minnesota Living with Heart Failure and SF-36 questionnaire, they concluded that LVD-36 scores are strongly related to patient’s perception overall health and functional status.

Table 3a

<table>
<thead>
<tr>
<th>r-value</th>
<th>p-value</th>
<th>Mean LVD</th>
<th>Mean WD</th>
</tr>
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<tr>
<td>-0.806</td>
<td>&lt;0.001***</td>
<td>0.3295967</td>
<td>384.66 ± 115.14</td>
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</tbody>
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Negative correlation of LVD-36 and walk distance where lesser the walk distance more are the % of LVD-36 score.

Table 3b

<table>
<thead>
<tr>
<th>Area Under the Curve</th>
<th>Test Result</th>
<th>Variable(s): WalkDist</th>
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</thead>
<tbody>
<tr>
<td>Area</td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>Lower Bound</td>
<td>0.933</td>
<td>.847</td>
</tr>
<tr>
<td>Upper Bound</td>
<td>1.008</td>
<td></td>
</tr>
</tbody>
</table>

P value < 0.001

ROC curve of walk distances and LVD-36 score, we split data of LVD-36 score below 25% and above 25%. It is observed that if patient is walking more than 325 mts distance then possibility of having LVD-36 score between 0-25% is 93.33% (sensitivity) and if patient is covering distance less than 325 mts then 80% possibility (specificity) LVD-36 score is more than 0-25%. Area under curve is 0.933 ranging from 0.847 to 1 with 95% confidence interval and it is statistically highly significant.

93.33% [sensitivity] possibility of having LVD-36 score between 0-25% (CI 95% and p < 0.001). This correlation can be attributed to, when we perform ADL we work at our sub-maximal capacity. Studies have shown that 6MWD is an indicator of ADL. Patients with LVF show decreased EF and stroke volume. They perform low in ADL and hence may show poor performance on 6 MWT. As per studies, LVD-36 is an indicator of ADL and functional capacity (6, 12 and 16). It is useful to predict aerobic capacity of patients and those undergoing treadmill tests.4 When it is compared with Minnesota Living with Heart Failure and SF-36 questionnaire, they concluded that LVD-36 scores are strongly related to patient’s perception overall health and functional status.

Fig. 3a: Correlation of walked distance and LVD-36

Fig. 3b: ROC of walk distance and LVD-36

This study also shows negative correlation between LVD-36 and EF. As seen in Graph D and Table 4a, lesser the EF higher the LVD-36 scores. As per ROC curve and Table 4b, if LVD-36 score is less than 30% then 100% [specificity] possibility of having EF more than 25% (CI 95%, p < 0.001). LVD-36 includes question of ADL like bathing, dressing, household and social activities. It also includes questions on fatigue and dyspnoea. In our data the patients [n = 15] gave true answer (mean 59.26 ± 10.84) for the questions regarding ADL, perception of dyspnoea, physical health, social activity, etc. And 21 patients gave true answer (mean 45.50 ± 24.06) for question on psychological and social
Table 4a

<table>
<thead>
<tr>
<th>r-value</th>
<th>p-value</th>
<th>Mean LVD</th>
<th>Mean EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.87</td>
<td>&lt;0.001***</td>
<td>329.59</td>
<td>27.5±9.62</td>
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</table>

Negative correlation of LVD-36 and Ejection fraction where lesser the ejection fraction higher the LVD-36 score.

Table 4b

<table>
<thead>
<tr>
<th>Area Under the Curve</th>
<th>Test Result Variable(s): LVD-36 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area</td>
<td>Asymptomatic 95% Confidence Interval</td>
</tr>
<tr>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>.989</td>
<td>.96</td>
</tr>
</tbody>
</table>

P value < 0.001

ROC curve of LVD-36 score and ejection fraction. We split data of LVD-36 score below 25% and above 25% then, if LVD-36 score is less than 30% then 100% (specificity) possibility of having EF more than 25%. And if LVD-36 score is more than 30% then 93.8% (sensitivity) possibility of having EF less than 25%. Area under curve is 0.98 ranging from 0.96 to 1 with 95% confidence interval and it is statistically highly significant. (0-25% mild dysfunction 25-50% moderated dysfunction, 50-75% severe dysfunction and > 75% is very severe dysfunction of LVD-36 score).

...activities. Patients with LVHF have decreased cardiac output and decreased EF. These shows changes in musculoskeletal and cardio respiratory system and hence decreased capacity perform ADL.4

Hence to conclude, the relationship of 6MWD to EF and QOL is seen in our study does not necessarily imply a causal relationship. Further studies will be required in order to evaluate the influence of EF on 6MWD. 6 Minute walk test is simple, inexpensive and time saving test which can be performed on OPD basis and does not require any specialized equipment. It assesses functional capacity of patients with left ventricular heart failure. By performing this test we may predict the Quality of Life and ejection fraction of the patient. If patient covers less than 532 mts distance then has 100% possibility (specificity) of having EF less than 25%. If patient covers distance more than 325 mts, then 93.33% possibility of having LVD-36 score between 0-25%. Also, LVD-36 score may predict ejection of these patients. If patient’s LVD-36 score is less than 30% then 100% possibility of having ejection fraction more than 25%.

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enriched my endeavour during the creation of this project. I would also like to thank the Biostatistician whose expertise and invaluable assistance enriched the study itself. Last but far from the least I thank my subjects, the departmental staff, all my colleagues and my parents for extending full co-operation during the course of my study.

References
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INTERLEUKIN-2 IN PATIENTS WITH HIV INFECTION

In patients infected with human immunodeficiency virus (HIV), an increase in the CD4+ cell count through control of the HIV virus with antiretroviral therapy has emerged as an important surrogate marker of improved health. In two prospective, randomized studies, the addition of interleukin-2 to antiretroviral therapy to increase the CD4+ cell count was not associated with clinical benefit.