Using the 6-min Walk Test to Monitor Peak Oxygen Uptake Response to Cardiac Rehabilitation in Patients With Heart Failure

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Purpose: We examined the agreement between peak oxygen uptake ($\dot{V}O_{2peak}$), estimated using prediction equations from the 6-min Walk Test (6MWT), and $\dot{V}O_{2peak}$ measured using a cardiopulmonary exercise test (CPX) to estimate change in $\dot{V}O_{2peak}$ in patients with heart failure (HF) enrolled in cardiac rehabilitation (CR).

Methods: This was secondary analysis of 54 (including 9 women) patients with HF who completed a clinical CR program. Four previously published equations using 6MWT distance were used to estimate $\dot{V}O_{2peak}$ and were compared with a CPX at baseline, follow-up, and change using the standard and modified Bland-Altman method. Analyses were repeated for quartiles of cardiorespiratory fitness (CRF) based on measured $\dot{V}O_{2peak}$ from the CPX.

Results: Bland-Altman plots revealed proportional bias between all prediction equations and the measured $\dot{V}O_{2peak}$. The difference between methods varied by the level of CRF, with overestimation of prediction equations at greater levels of CRF and underestimation at lower levels of CRF. This poor agreement remained when comparisons were made between the estimated and measured $\dot{V}O_{2peak}$ values at quartiles of CRF, indicating prediction equations have limited ability to predict $\dot{V}O_{2peak}$ at any level of CRF.

Conclusion: Estimated $\dot{V}O_{2peak}$ using 6MWT distance demonstrated poor agreement with measured $\dot{V}O_{2peak}$ from a CPX. While distance ambulated on the 6MWT remains an important measure of physical performance in patients with HF, prediction equations using 6MWT distance are not appropriate to monitor changes in $\dot{V}O_{2peak}$ following CR in patients with HF.

Key Words: cardiac rehabilitation • cardiorespiratory fitness • functional capacity • heart failure • peak oxygen uptake • 6-min Walk Test

Exercise-based cardiac rehabilitation (CR) increases cardiorespiratory fitness (CRF) in patients with heart failure (HF), as measured by peak oxygen uptake ($\dot{V}O_{2peak}$) using a symptom-limited cardiopulmonary exercise test (CPX), which translates into reduced long-term risk of mortality and enhanced quality of life. Even a modest (i.e., 1.75 mL/kg/min) increase in $\dot{V}O_{2peak}$ following CR is clinically important, as this is strongly associated with lower morbidity and mortality. One quality indicator for CR is an increase in CRF by $\geq 0.5$ metabolic equivalents.

In many instances, a CPX is not feasible for clinical CR programs and a 6-min Walk Test (6MWT) is recommended instead. Distance walked during a 6MWT is a practical, non-invasive, and cost-effective method of assessing functional capacity that predicts short-term morbidity and mortality in patients with HF. There is a known positive correlation between 6MWT distance and $\dot{V}O_{2peak}$, which has led to the creation of several prediction equations to estimate CRF using the 6MWT distance. While evidence suggests that the 6MWT and prediction equations using the 6MWT are not valid measures for predicting $\dot{V}O_{2peak}$ in the HF population, no study has examined this relationship following CR participation. Therefore, the primary purpose of this report was to assess the agreement between $\dot{V}O_{2peak}$ predicted by equations using 6MWT distance and $\dot{V}O_{2peak}$ measured by CPX to estimate change in $\dot{V}O_{2peak}$ in patients with HF enrolled in CR.

METHODS

Participants

This was a secondary analysis of 54 patients with HF who completed baseline and follow-up measures in a previously published study. That study was conducted at the University of Ottawa Heart Institute (UOHI), a tertiary care cardiovascular institute, and received ethics approval from the UOHI Human Research Ethics Board (protocol #2011139-01H) and Ottawa Health Sciences Network Research Ethics Board (protocol #20130774-01H). All participants provided written informed consent before participating. Information on demographic, anthropometric, and CRF measures, as well as a detailed description of the CR program, can be found elsewhere.

CARDIORESPIRATORY FITNESS

Peak oxygen uptake was measured using a symptom-limited CPX on a treadmill at the beginning and end of CR. Gas
exchange was monitored continuously using a metabolic cart (Sensormedics). A 12-lead electrocardiogram, blood pressure and heart rate measurements, and Borg ratings of perceived exertion were obtained throughout the CPX.

**FUNCTIONAL CAPACITY**

Functional capacity was measured using the 6MWT on a measured indoor track at the beginning and end of CR. Participants were instructed to walk as far as possible in 6 min without running or jogging. At 2, 3, and 4 min of the 6MWT, participants were provided with standardized verbal encouragement and informed of the time remaining. Total 6MWT distance was measured in meters.

**PEAK OXYGEN UPTAKE PREDICTION EQUATIONS**

We used 4 previously published equations to predict VO_{2peak} from 6MWT distance in patients with heart disease at baseline, follow-up, and change from baseline to follow-up. Our approach was similar to that of a recently published study. Prediction equations were as follows:

- Cahalin et al^{8} = 0.03 × 6MWT (m) + 3.98
- Ross et al^{9} = 4.9848 + 0.023 × 6MWT (m)
- Adedoyin et al^{10} = 0.0105 × 6MWT (m) + 0.0238 × age (yr) – 0.03085 × body mass (kg) + 5.598
- Mandic et al^{11} = 0.253 × 6MWT (m) − 2.324 (if female) – 0.281 × BMI + 15.377

**STATISTICAL ANALYSIS**

Descriptive data are reported as means ± SD for continuous variables and as proportions for categorical variables. Pearson correlation analyses were used to examine the associations between measured and predicted VO_{2peak} values at baseline, follow-up, and change from baseline to follow-up. Pairwise t-tests were performed to compare continuous variables between baseline and follow-up. Paired t-tests were also performed to examine whether systematic error existed between VO_{2peak} from CPX and predictive equations at baseline, follow-up, and changes over time. Linear regression analysis was used to examine whether proportional bias existed between the measured and predicted VO_{2peak} values. Standard and modified Bland-Altman plots were used for visual presentation of the agreement between the measured and predicted VO_{2peak} values. The statistical level of significance was set at P < .05. To adjust for multiple comparisons, significance was set to P < .004 for paired t-tests. All data were analyzed using SPSS for Windows version 24 (IBM Corp).

**RESULTS**

Participant characteristics are presented in Supplemental Digital Content (SDC) 1 (available at: http://links.lww.com/JCRP/A178). Most were male (83%), had a previous myocardial infarction (55%), had undergone a revascularization procedure (70%), and were prescribed β-blocker medications (98%).

**BASELINE ANALYSIS**

Mean values and correlations between VO_{2peak} measured by CPX and VO_{2peak} estimated by the prediction equations at baseline, follow-up, and their change are presented in the Table. Paired t-test analyses demonstrated that estimated VO_{2peak} values from the Cahalin et al^{8} (t_{53} = 1.125, P = .266) and Mandic et al^{11} (t_{53} = 0.809, P = .422) equations were not different from the measured VO_{2peak} values, but the estimates calculated using the Ross et al^{9} (t_{53} = 4.390, P < .001) and Adedoyin et al^{10} (t_{53} = 12.110, P < .001) equations were significantly different from the measured VO_{2peak} results. Bland-Altman plots are illustrated in the Figure and SDC 2 (available at: http://links.lww.com/JCRP/A179), SDC 3 (available at: http://links.lww.com/JCRP/A180), and SDC 4 (available at: http://links.lww.com/JCRP/A181). Results of the linear regression analyses revealed significant proportional bias between the measured and estimated VO_{2peak} values, indicating the differences between measured and predicted VO_{2peak} values were dependent on their average values.

**FOLLOW-UP ANALYSIS**

Paired t-tests (Table) demonstrated that estimated VO_{2peak} values from the Cahalin et al^{8} (t_{53} = −0.435, P = .665) and Mandic et al^{11} (t_{53} = −0.041, P = .967) equations were not significantly different from the measured VO_{2peak} but the Ross et al^{9} (t_{53} = 3.507, P = .001) and Adedoyin et al^{10} (t_{53} = 11.061, P < .001) equations were significantly different from the measured VO_{2peak}. Bland-Altman plots are illustrated in the Figure and SDC 2 (available at: http://links.lww.com/JCRP/A179), SDC 3 (available at: http://links.lww.com/JCRP/A180), and SDC 4 (available at: http://links.lww.com/JCRP/A181). Results of the linear regression analyses revealed significant proportional bias between the measured and estimated VO_{2peak} values; the difference between measured and predicted VO_{2peak} values was dependent on their average values.

**CHANGE BETWEEN BASELINE AND FOLLOW-UP ANALYSIS**

Paired t-tests (Table) demonstrated that the estimated VO_{2peak} value did not differ from the measured VO_{2peak} value for the Cahalin et al^{8} (t_{53} = −2.047, P = .046), Ross et al^{9} (t_{53} = −0.924, P = .360), Adedoyin et al^{10} (t_{53} = 1.373, P = .176), and Mandic et al^{11} (t_{53} = −1.133, P = .262) equations. Bland-Altman plots are illustrated in the Figure and SDC 2 (available at: http://links.lww.com/JCRP/A179), SDC 3 (available at: http://links.lww.com/JCRP/A180), and

| Table | Measured and Predicted VO_{2peak} at Baseline and Follow-up* |
|-------|------------------------------------------------------------|
|       | Baseline | Correlation With CPX | Follow-up | Correlation With CPX | Change | Correlation With CPX |
|       | CPX, mL/kg/min | 18.7 ± 6.3 | ... | 20.2 ± 7.8 | ... | 1.4 ± 3.6 | ... |
| Cahalin et al^{8} | 18.0 ± 2.9 | 0.696, < .001 | 20.4 ± 4.1 | 0.841, < .001 | 2.4 ± 2.2 | 0.277, 0.043 |
| Ross et al^{9} | 15.7 ± 2.2 | 0.696, < .001 | 17.6 ± 3.2 | 0.841, < .001 | 1.9 ± 1.7 | 0.277, 0.043 |
| Adedoyin et al^{10} | 9.2 ± 1.2 | 0.530, < .001 | 10.1 ± 1.6 | 0.773, < .001 | 0.9 ± 0.8 | 0.306, 0.026 |
| Mandic et al^{11} | 18.1 ± 3.8 | 0.637, < .001 | 20.2 ± 4.8 | 0.796, < .001 | 2.0 ± 1.9 | 0.307, 0.025 |

Abbreviations: CPX, cardiopulmonary exercise test; VO_{2peak}, peak oxygen uptake.

*Data are expressed as mean ± SD (baseline, follow-up, and change) and r, P value (correlations), n = 53 for Eq. 3 and Eq. 4 for follow-up and change.

Paired t-test P < .001 compared with CPX at baseline.

Paired t-test P ≤ .001 compared with CPX at follow-up.
DISCUSSION
This was the first study to examine the agreement between measured and estimated $V\dot{O}_{2\text{peak}}$ values in response to CR. The major novel findings were that mean $V\dot{O}_{2\text{peak}}$ values estimated from the Cahalin et al\textsuperscript{8} and Mandic et al\textsuperscript{7} equations showed significant proportional bias between the measured and estimated $V\dot{O}_{2\text{peak}}$ values; the difference between measured and predicted $V\dot{O}_{2\text{peak}}$ values was dependent on their average values.

**Figure.** Bland-Altman plots for (A) baseline, (B) follow-up, and (C) change peak oxygen uptake between values measured using the cardiopulmonary exercise test and those estimated using the Cahalin et al\textsuperscript{8} equation.
were similar to measured VO$_{2peak}$ values from the CPX at baseline and following CR; however, proportional bias existed in both equations—the difference increased with average VO$_{2peak}$ values. Therefore, the ability of the prediction equations to accurately estimate VO$_{2peak}$ varies with CRF level and may be amplified by the improvements in CRF following CR. This was supported by the weak correlation and lack of agreement between predicted and actual VO$_{2peak}$ change values. Comparisons between measured and estimated VO$_{2peak}$ values were also made between quartiles of measured VO$_{2peak}$ but did not change the results (data not shown). This suggests that prediction equations do not lose their ability to predict VO$_{2peak}$ at a given level of CRF; rather, they have a limited ability to predict VO$_{2peak}$. These data suggest that the 6MWT is not appropriate to predict VO$_{2peak}$ in patients with HF participating in CR.

The 6MWT is a well-established tool to assess functional capacity in patients with HF, which provides an overall assessment of performing everyday activities. A pioneering study by Cahalin et al. demonstrated that ambulating a distance below or above 300 m can discriminate between low versus high likelihood of short-term survival, respectively. The 6MWT also demonstrates good reliability (ICC = 0.90), with wide limits of agreement and a learning effect of 31 m in patients with HF. While the most commonly reported minimal clinically important difference on the 6MWT is 54 m, a recent study in patients with chronic HF has reported a minimal clinically important difference of 36 m. The collective findings from the literature to date underscore the important use of the 6MWT as an evaluation of the functional capacity of patients with HF that enables practitioners to determine disease severity and prognosis, with good construct validation. Several researchers have utilized the 6MWT to develop prediction equations to estimate VO$_{2peak}$. The use of an alternative assessment tool to estimate VO$_{2peak}$ that is both time- and cost-efficient is desirable and perhaps preferred in a clinical setting where resources are limited. However, a vast majority of studies developing prediction equations to estimate VO$_{2peak}$ have examined the association but not the agreement between these measures. In addition, none have evaluated the ability of prediction equations to estimate change in VO$_{2peak}$ following CR.

Our findings are supported by a recent study evaluating the agreement of VO$_{2peak}$ prediction equations derived from the 6MWT in patients with HF at a single time point. This study found the Cahalin et al. prediction to be the most accurate at predicting measured VO$_{2peak}$, as compared with the Ross et al. and Adedoyin et al. equations; however, all equations demonstrated proportional bias according to their Bland-Altman plots. We have extended this finding to a larger sample of patients with HF (n = 54) completing a CR program. The proportional bias and lack of agreement limit the use of prediction equations derived from the 6MWT to estimate actual VO$_{2peak}$. An important finding from the present study was that the average distance walked on the 6MWT increased by 56 m following CR, meeting the commonly reported clinically important difference of 54 m. This improvement greatly exceeds the recently reported minimal important difference of 36 m that was identified in patients with chronic HF. It is speculated that physiological mechanisms associated with improved CRF may decrease oxygen consumption for a given submaximal workload. In fact, additional analysis demonstrated a significant positive correlation between change in distance walked on the 6MWT and VO$_{2peak}$ ($r = 0.277$, $P = .043$).

The 6MWT remains a fundamental measure of functional capacity, which in many settings is the foundation of approaches intended to increase well-being and quality of life. The ability of the 6MWT to predict morbidity and mortality, the ease of its administration, the ability to identify a clinically meaningful result, and the comorbidities present in many with HF are substantial arguments for recognizing the advantages of such functional testing. The 6MWT allows a straightforward assessment of functional capacity while serving to provide self-evident feedback and reinforcement to CR participants. The focus of future research should incorporate clinicians, CR specialists, and researchers and be directed toward determining whether improvements in VO$_{2peak}$ or distance ambulated is a more clinically relevant outcome in patients with HF following CR. Future work should also focus on developing appropriate submaximal testing procedures that better predict CRF changes in CRF in patients with HF.

There are limitations to the current study that are necessary to identify. First, this was secondary analysis of data from a quasi-experimental study, which limits the generalizability. Second, the majority of the study participants were males. This is an important limitation in all studies, as mortality and hospitalization rates due to HF are greater in women. Future work examining sex differences is urgently required. Third, because of the nature of this clinical CR program, we were not able to account for a potential learning effect on the 6MWT, which has been demonstrated. In addition, we did not screen participants for comorbidities, such as chronic obstructive pulmonary disease, which could have influenced their 6MWT and VO$_{2peak}$ results.

CONCLUSION

While the 6MWT is an established tool to assess functional capacity in the form of one’s ability to perform daily activities and to identify those at high risk of short-term mortality and hospitalization, it demonstrated less utility in estimating VO$_{2peak}$ in patients with HF. Such limitations must be appreciated by clinicians and practitioners when using the 6MWT.

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