ORIGINAL ARTICLE

Can the Six-Minute Walk Test Predict Peak Oxygen Uptake in Men With Heart Transplant?

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ABSTRACT. Doutreleau S, Di Marco P, Talha S, Charloux A, Piquard F, Geny B. Can the six-minute walk test predict peak oxygen uptake in men with heart transplant? Arch Phys Med Rehabil 2009;90:51-7.

Objective: To determine whether the six-minute walk test (6MWT) might predict peak oxygen consumption ($\dot{V}O_2$peak) after heart transplantation.

Design: Case-control prospective study.

Setting: Public hospital.

Participants: Patients with heart transplant (n=22) and age-matched sedentary male subjects (n=13).

Interventions: Not applicable.

Main Outcome Measures: Exercise performance using a maximal exercise test, distance walked using the 6MWT, heart rate, and $\dot{V}O_2$peak.

Results: Compared with controls, exercise performance was decreased in patients with heart transplant with less distance ambulated (516±13m vs 592±13m; $P<.001$) and a decrease in mean $\dot{V}O_2$peak (23.3±1.3 vs 29.6±1mL·min^{-1}·kg^{-1}; $P<.001$). Patients with heart transplant showed an increased resting heart rate, a response delayed both at the onset of exercise and during recovery. However, the patient's heart rate at the end of the 6MWT was similar to that obtained at the ventilatory threshold. The formula did not predict measured $\dot{V}O_2$, with a weak correlation observed between the six-minute walk distance and both $\dot{V}O_2$peak ($r=.53$; $P<.01$) and ventilatory threshold ($r=.53$; $P<.01$) after heart transplantation. Interestingly, when body weight was considered, correlations coefficient increased to .74 and .77, respectively ($P<.001$).

Conclusions: In heart transplant recipients, the 6MWT is a safe, practical, and submaximal functional test. The distance-weight product can be used as an alternative method for assessing the functional capacity after heart transplantation but cannot totally replace maximal $\dot{V}O_2$ determination.

Key Words: Exercise; Functional residual capacity; Rehabilitation; Transplantation.

ALTHOUGH BOTH FUNCTIONAL status and exercise performance progressively increase during the first 2 years after surgery,[1,2] patients with heart transplant still present low activity level and exercise capacity compared with matched sedentary subjects.[3-7] This can be, in part, explained by both central and peripheral limitation, leading to a reduced quality of life in patients with heart transplant.[8-12] Thus, cardiac diastolic dysfunction[6] and chronotropic insufficiency[10,13] on the one hand and muscular[11,14] and endothelial dysfunction[15] on the other hand appear to be the main limiting factors of exercise capacity after heart transplantation.

Standardized laboratory maximal exercise test with oxygen uptake measurement can, noninvasively and objectively, quantify this limitation by measuring VT and $\dot{V}O_2$peak. Thus, a maximal cardiopulmonary exercise test is considered a criterion standard, used in order to prescribe appropriate and individualized physical rehabilitation, allowing a complete assessment of all systems involved in exercise performance.[16] However, laboratory tests of maximal exercise performance require sophisticated equipment and specially trained people. They are costly and time-consuming. Furthermore, these tests are not always well accepted, and some participants may have difficulties achieving a maximal exercise test.

Therefore, easier modalities to assess exercise capacities have been developed. Particularly, the 6MWT is the most popular and commonly used submaximal exercise test. Indeed, it is easy to perform, is well tolerated, and better reflects daily life activities of the subjects than other walk tests.[17] The 6MWT can predict functional change resulting from disease progression or therapeutic intervention, morbidity and mortality in heart[18] or lung disease,[19] and capacity in older, healthy, sedentary people.[20] The 6MWT can also be used to assess functional exercise performance across various subjects like young[21] or older, sedentary people,[22] patients with heart failure,[18,23,24] and patients with a wide variety of pulmonary alterations.[25,26]

The 6MWT performance has previously been shown to be reduced in kidney transplant recipients.[27] Interestingly, a weak but significant correlation between the 6MWD and the $\dot{V}O_2$peak has been reported in patients with heart[18,28,29] or lung failure.[19] But curiously, whereas this test is commonly used in patients with heart failure needing cardiac transplantation,[30] data on the 6MWT characteristics and usefulness in heart transplant recipients are lacking.

The main objective of the present investigation was therefore to determine whether the 6MWT could predict $\dot{V}O_2$peak in patients with heart transplant. Other objectives were to determine whether the 6MWT is a submaximal or a maximal exercise test, and to compare the $\dot{V}O_2$peak predicted by formula with the measured $\dot{V}O_2$peak after heart transplantation.

List of Abbreviations

6MWD	six-minute walk distance
6MWT	six-minute walk test
SEM	standard error of the mean
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_2$peak	peak oxygen uptake
VT	ventilatory threshold

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Table 1: Resting Clinical, Hemodynamic, and Echocardiographic Characteristics of Both the Control Subjects and the Subjects With Heart Transplant

Characteristics	Control (n=13)	Heart Transplant (n=22)
Age (y)	57.70±1.50	56.00±1.70
Height (cm)	179.20±1.10	174.50±1.30
BMI, ($kg.m^{-2}$)	25.80±0.50	26.00±0.70
Heart rate ($b.min^{-1}$)	73.00±3.20	95.10±2.40*
Blood pressure (mmHg)		
Systolic	125.00±2.30	143.00±2.80*
Diastolic	81.00±1.50	88.00±1.70†
EF (%)	65.00±3.00	64.00±2.00
E/A ratio	1.55±0.08	1.49±0.09

Abbreviations: BMI, body mass index; E/A, ratio of peak early (E) and late (A) transmitral filling velocities; EF, ejection fraction.
Differences between groups: *$P<.001$; †$P=.01$.

METHODS

Participants

The study was carried out between January 2005 and May 2006. During this period, the chirurgical team transplanted 8 patients. Eight heart transplant recipients were excluded: 3 refused to perform a maximal exercise test, and 5 were enrolled in exercise rehabilitation or in sport. Twenty-two male sedentary patients with heart transplant, at least 6 months since transplant, in sinus rhythm, and clinically stable (free of rejection with no sign of heart failure and without cardiac allograft vasculopathy on the coronary arteriography) participated in the study. Thirteen healthy sedentary age-matched people served as controls. Patients with diabetes, pulmonary dysfunction, or conditions that might impair a successful completion of the 6MWT or of the maximal exercise test, such as orthopedic or muscular problems, were excluded. All patients with heart transplant took their usual immunosuppressive therapy composed of cyclosporine (189±12mg/d), prednisolone (6.9±0.8mg/d), and mycophenolate mofetil (909±170mg/d). All of them had a systemic hypertension treated with angiotensin-converting enzyme inhibitor (n=15) and/or calcium antagonist (n=9), but none of them took beta-blockers.

Clinical, hemodynamic, and echocardiographic characteristics of the subjects are presented in table 1. Systolic and diastolic left heart functions were obtained through the left ventricular ejection fraction and the mitral ratio of peak early and late transmitral filling velocities, respectively, following the recommendations of the American Society of Echocardiography.[31] All patients gave written informed consent, and the study was approved by the hospital and university review board for human studies.

Interventions

Both patients with heart transplant and control groups performed, 1 hour after a standardized meal, a 6MWT followed after a 2-hour resting period by a maximal upright bicycle cardiopulmonary exercise test in a quiet air-conditioned room (21°C). To avoid circadian variation, all exercise tests were performed between 2 PM and 4 PM.

Exercise Testing Protocol

Six-minute walk test. The 6MWT was coached by the same physicians, according to the American Thoracic Society recommendations.[32] Briefly, patients were instructed to walk the most distance possible in 6 minutes in a 13-m straight calibrated track. Standardized encouragements were given every minute. Before the test, patients rested in a chair, located near the starting position, for 10 minutes. After 6 minutes, the distance walked was recorded to the nearest meter. Results are expressed as actual distance walked in meters.

Heart rate ($b.min^{-1}$) and pulse oxygen saturation (%) were continuously measured before the walk, during the test, and during the first 5 minutes of recovery by using a lightweight pulse oximeter[a] on the finger.

A reference equation for healthy adults[33] was used to compute the percent predicted of 6MWD for individual adult patients with the following formula:

$$6MWD\ (m) = [7.57 \times height_{(cm)}] - [1.76 \times weight_{(kg)}] - [5.02 \times age_{(y)}] - 309$$

Predicted Vo_2peak from the 6MWT was calculated by using the following formula from Cahalin et al:[18]

$$Vo_2peak\ (mL \cdot min^{-1}) = [0.03 \times 6MWD\ (m) + 3.98]$$

Because the body weight of the patient directly affects the work/energy required to perform the walk, whereas it is of minor importance during cycling exercise, we used the body weight-walking distance (body weight × walking distance) product to assess the walking capacity of the subject (6-minute walk work = kg.m).[34-36]

We also compared the 6MWD × body weight product to the maximal workload (maximal power tolerated), the oxygen uptake on the VT, and the Vo_2peak reached during the maximal bicycle exercise test.

Maximal cardiopulmonary bicycle exercise test. All patients performed a symptom-limited exercise test in the upright position using an electronically braked bicycle ergometer.[b] The protocol was the same for all patients, and after a warm-up on the bicycle for 3 minutes at 30W, exercise workload was increased by 15W every minute. Exhaustion was defined as the inability to maintain the pedal frequency above 50rev/min because of leg fatigue and/or dyspnea.

Breath-by-breath $\dot{V}o_2$ ($mL.min^{-1}$), carbon dioxide output ($mL.min^{-1}$), and minute ventilation ($L.min^{-1}$) were measured throughout using a Vmax 229.[c] The system was calibrated before each test using known gas concentrations, and a 3-L calibrated syringe was used to ensure the accuracy of the pneumotach.

Peak values of Vo_2 were averaged on the last 30 seconds of the exercise test (Vo_2peak). The VT was manually determined by 2 blinded examiners, using the V-slope and ventilatory equivalents methods.[37] The interobserver variability for VT determination was 4.8±1.64%. Vo_2peak was compared with age/sex-adjusted peak oxygen uptake (peak % Vo_2).[38]

Electrocardiographic activity was monitored continuously using a standard 12-lead configuration,[d] and systemic arterial blood pressure was registered every 2 minutes using a sphygmomanometer. Maximal exercise heart rate was defined as the maximal value reach at the end of the test.

Statistical Analysis

Sigma-Stat Software[e] was used for statistical analysis. All data are presented as mean ± standard error of the mean. Differences between predicted $\dot{V}o_2$, 6MWD, and measured values were evaluated using paired t tests. For comparison of chronotropic response between groups, a 2-way analysis of variance with repeated measures was performed. When the F value indicated significant differences between means at different time, a Student-Neman-Keuls test for multiple compar-