

Prognostic Value of 6-Minute Walk Distance

in Patients Undergoing Percutaneous Coronary
Intervention: a Veterans Affairs Prospective Study

Tarun W. Dasari, MD, MPH
Bhavin Patel, MD
Siddharth A. Wayangankar,
MD, MPH
David Alexander, LPN
Yan D. Zhao, PhD
JoAnn Schlegel, PT, WCC
Cheuk Leung, MSc
Pedro Lozano, MD
Faisal Latif, MD
Udho Thadani, MD

Presented as an abstract at
the 19th Heart Failure Society
of America Annual Scientific
Meeting, Washington, DC,
27 September 2015.

Key words: Coronary artery
disease/physiopathology/
rehabilitation; exercise test/
methods; heart failure/
diagnosis/mortality/physio-
pathology; patient readmis-
sion; percutaneous coronary
intervention; predictive value
of tests; prospective studies;
risk assessment/methods;
walking

From: Cardiovascular Sec-
tion, Department of Internal
Medicine (Drs. Dasari, Latif,
Lozano, Patel, Thadani,
and Wayangankar, and Mr.
Alexander); Department of
Biostatistics and Epidemiol-
ogy; College of Public Health
(Dr. Zhao and Mr. Leung);
and Physical Therapy Section
(Ms Schlegel); University of
Oklahoma Health Sciences
Center and Veterans Affairs
Medical Center, Oklahoma
City, Oklahoma 73104

Address for reprints:
Tarun W. Dasari, MD,
Cardiovascular Section,
Department of Internal
Medicine, University of
Oklahoma HSC, 800 SL
Young Blvd., COM 5400,
Oklahoma City, OK 73104

E-mail:
tarun-dasari@ouhsc.edu

© 2020 by the Texas Heart®
Institute, Houston

The 6-minute walk distance (6MWD) test is a useful prognostic tool in chronic heart failure. Its usefulness after percutaneous coronary intervention is unknown.

In a prospective observational study, patients underwent a 6MWD test within 2 weeks after percutaneous coronary intervention. The primary endpoint was major adverse cardiovascular events (MACE) (death, acute coronary syndrome, and heart failure admission) at one year. Receiver operating characteristic curves and area under the curve were used to determine the 6MWD test's predictive power, and the Youden index was used to measure its effectiveness.

A total of 212 patients were enrolled (98% men; mean age, 65 ± 9 yr). Major comorbidities were hypertension in 187 patients (88%), dyslipidemia in 186 (88%), and diabetes mellitus in 95 (45%). Among the 176 patients (83%) who completed the 6MWD test, the incidence of MACE at one year was 22% (acute coronary syndrome in 17%; heart failure admission in 4%; and death in 3%). The area under the curve for MACE was 0.59, and 6MWD was shorter for patients with MACE than for those without (290 vs 326 m; P=0.03). For 39 patients with previous heart failure who completed the 6MWD test, the area under the curve was 0.64 for MACE and 0.78 for heart failure admission.

The 6MWD test predicted reasonably well the incidence of MACE one year after percutaneous coronary intervention. In a subgroup of patients with previous heart failure, it fared even better in predicting heart failure admission. Larger studies are needed to confirm these findings. (Tex Heart Inst J 2020;47(1):10-4)

The 6-minute walk distance (6MWD) test is a well-validated prognostic tool in patients with chronic heart failure (HF). This simple evaluation helps to predict peak exercise oxygen consumption (VO_2) and is a good predictor of cardiovascular morbidity and death and hospital admission in patients with HF.¹⁻⁶ Six-minute walk distance also has prognostic value in patients undergoing coronary artery bypass grafting (CABG). A 6MWD >300 m has been associated with lower mortality rates in elderly patients undergoing CABG.⁷ Other data suggest that 6MWD also helps predict outcomes in patients with aortic stenosis undergoing surgical or transcatheter aortic valve procedures.^{8,9} Before percutaneous coronary intervention (PCI) was introduced into clinical practice, 6MWD was also a useful predictor of major adverse cardiovascular events (MACE) in patients with ST-segment-elevation myocardial infarction undergoing fibrinolysis.¹⁰ The 6MWD test is easily reproducible and sensitive to changes in quality of life. It has also been suggested that the 6MWD test is prognostically comparable to the exercise stress test.¹¹ However, the usefulness of 6MWD in predicting outcomes in patients undergoing PCI is unknown. We therefore conducted this prospective observational study to evaluate the ability of 6MWD to predict MACE and HF admission one year after PCI.

Patients and Methods

Screened for participation in this study were all patients who underwent PCI either for stable angina—with or without an abnormal noninvasive functional study result—or for acute coronary syndrome (ACS) at the Oklahoma City Veterans Affairs Medical Center from June 2010 through December 2011. Excluded were patients who could not walk effectively because of chronic severe musculoskeletal issues, severe symptomatic peripheral artery disease, neurologic conditions such as disabling stroke or severe myoneuropathies, or severe obstructive pulmonary disease or advanced HF with New

York Heart Association functional class IV symptoms that limited exercise capacity. Informed consent for this study was obtained from each patient after PCI. The study was approved by the local institutional review board. Demographics, clinical characteristics, and procedural details about coronary interventions were documented at baseline.

Patients underwent a standard 6MWD test in our physical therapy department within 2 weeks after PCI. The 6MWD test was administered by a dedicated physical therapist and involved the patient walking at his or her own pace with opportunities to rest during the walk if needed. Total distance walked (in meters) over 6 minutes and symptoms during the test were documented. Follow-up in the clinic or by telephone occurred at one year (12 ± 2 mo) after PCI. Clinical outcome and medication use were documented at the time of follow-up. The primary endpoint was MACE, which included death, ACS, and admission for HF (left ventricular ejection fraction, <0.40).

Statistical Analysis

Continuous data are presented as mean \pm SD. Continuous variables were compared by using the Student t test or analysis of variance as appropriate. Categorical variables were compared by using the χ^2 test. A 2-tailed P value of ≤ 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves and areas under the curve (AUCs) were calculated and used to determine the ability of 6MWD to predict MACE. The Youden index, which maximizes a function of sensitivity and specificity, was calculated and used to determine the optimal cutoff point of 6MWD for classifying MACE outcome. The optimal cutoff point was defined as the maximum vertical distance between the ROC curve and the diagonal. A P value of ≤ 0.05 was considered statistically significant. Data were analyzed with SAS version 9.3 (SAS Institute Inc.).

Results

A total of 274 patients underwent PCI and were screened for participation in this study. Of those, 62 patients were excluded because they were unable to walk effectively. The remaining 212 patients were enrolled in this study (Fig. 1). Tables I and II summarize their baseline characteristics, indications for PCI, and procedural details of coronary intervention. The mean age of the patients was 65 ± 9 years, and 208 (98%) were men. Major comorbidities were hypertension in 187 patients (88%), dyslipidemia in 186 (88%), and diabetes mellitus in 95 (45%). A total of 118 patients (56%) with ACS underwent revascularization. Drug-eluting stents were used in 171 patients (81%).

Of the 212 patients who underwent PCI and were enrolled in this study, 176 (83%) completed the 6MWD

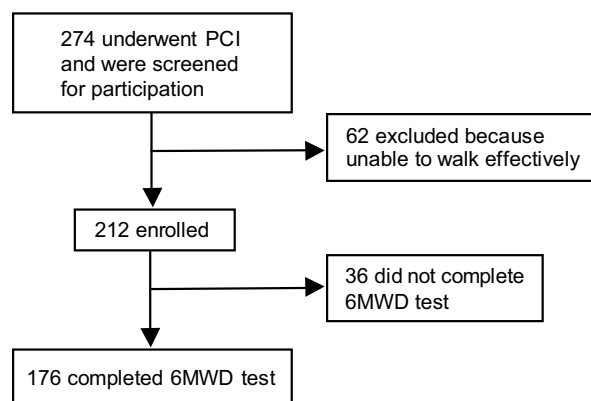


Fig. 1 Flow diagram shows selection of patients included in the study.

6MWD = 6-minute walk distance; PCI = percutaneous coronary intervention

TABLE I. Demographic and Clinical Characteristics for All Patients and for Those Who Completed the 6-Minute Walk Distance Test

Variable	Total (N=212)	6MWD (n=176)
Age (yr)	64.9 \pm 8.8	64.7 \pm 9.1
Male	208 (98)	172 (98)
Body mass index (kg/m ²)	30.2 \pm 5.75	30 \pm 6
Weight (kg)	97.4 \pm 41.4	94 \pm 19
Race		
White	165 (78)	138 (78)
Black	13 (6)	12 (7)
Hispanic	3 (1)	3 (2)
Other or missing	31 (15)	23 (13)
Hypertension	187 (88)	153 (87)
Diabetes mellitus	95 (45)	78 (44)
Dyslipidemia	186 (88)	152 (86)
COPD	52 (25)	44 (25)
Heart failure	50 (24)	39 (22)
Myocardial infarction	72 (34)	58 (33)
Previous PCI	90 (42)	72 (41)
Previous CABG	55 (26)	46 (26)
Peripheral artery disease	25 (12)	16 (9)
Stroke	20 (9)	13 (7)
Atrial fibrillation or flutter	19 (9)	17 (10)
Smoking status (n=211)*		
Current	66 (31)	56 (32)
Former	102 (48)	78 (45)
Never	43 (20)	41 (23)

6MWD = 6-minute walk distance; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention

*Smoking status for one patient was unknown.

Data are presented as mean \pm SD or as number and percentage.

test after PCI and had returned for a follow-up visit or had been contacted by telephone at one year. The remaining 36 patients (17%) did not return to complete the 6MWD test after PCI, for reasons such as ride availability, lack of interest, inability to be contacted during the required pretest time frame, illness, or forgetting to keep the test appointment.

Of the 176 patients who completed the 6MWD test, 39 (22%) experienced MACE within one year after PCI (Table III). Overall, the AUC was 0.59 for MACE and 0.69 for HF admission (Fig. 2A–B). Optimal cutoff points of 225 m for MACE and 286 m for HF admission were calculated by using the Youden index. The odds ratio (OR) for MACE was 0.26 (95% CI, 0.11–0.62; $P=0.002$) among patients who walked >225 m as compared with those who walked ≤225 m. The mean 6MWD was shorter for patients who had MACE than for those who did not (290 vs 326 m; $P=0.03$).

A subset of 50 enrolled patients (24%) had a baseline diagnosis of HF, 39 of whom completed the 6MWD

evaluation. Of those 39 patients, 8 (21%) experienced MACE within one year after PCI (Table IV). For this subset of patients, the AUC was 0.64 for MACE and 0.78 for HF admission (Fig. 2C–D).¹² Optimal cutoff points of 195 m for MACE and 335 m for HF admission were determined by using the Youden index. The OR for MACE was 0.25 (95% CI, 0.04–1.46; $P=0.12$) among patients who walked >195 m as compared with those who walked ≤195 m. The OR for HF admission was 0.81 (95% CI, 0.037–5.38, $P=0.52$) among patients who walked >335 m as compared with those who walked ≤335 m.

Discussion

Our findings suggest that 6MWD is a reasonably good predictor of MACE and HF admission in patients undergoing PCI and an even better predictor of HF admission in a subset of patients with previous HF. The 6MWD test is an inexpensive, easily available noninvasive test that has been well validated in patients with both cardiac and noncardiac disease. In patients with chronic HF, 6MWD predicts death and recurrent hospitalization.^{1,6} Therefore, this test is quite often used in routine HF follow-up. Unlike other functional tests such as the exercise stress test, the 6MWD test can be administered to a wider population of patients who have cardiovascular disease and very limited functional capacity but who can walk short distances. Although 6MWD has been proved useful in the HF population, evidence of its usefulness in patients after PCI is lacking. Our study evaluated the prognostic value of 6MWD in a sample of such patients and showed that

TABLE II. Indications and Procedural Details for All Patients and for Those Who Completed the 6-Minute Walk Distance Test

Variable	Total (N=212)	6MWD (n=176)
Indication		
Abnormal stress study	80 (38)	61 (35)
Stable angina	79 (37)	62 (35)
Stable angina and abnormal stress study	55 (26)	42 (24)
Stable angina and normal stress study	24 (11)	20 (11)
Unstable angina or NSTEMI	105 (50)	91 (52)
STEMI	12 (6)	10 (6)
Acute coronary syndrome	118 (56)	91 (52)
PCI location		
Left main coronary artery	9 (4)	7 (4)
Left anterior descending	92 (43)	78 (44)
Right coronary artery	78 (37)	62 (35)
Left circumflex	75 (35)	64 (36)
Ramus intermedius	9 (4)	6 (3)
Venous graft	30 (14)	23 (13)
Drug-eluting stent	171 (81)	141 (80)

6MWD = 6-minute walk distance; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment-elevation myocardial infarction

Data are presented as number and percentage.

TABLE III. Clinical Outcomes at One Year in the 176 Patients Who Completed the 6-Minute Walk Distance Test

Outcome	No. (%)
Major adverse cardiovascular events*	39 (22)
Death	6 (3)
Acute coronary syndrome	30 (17)
Heart failure admission	7 (4)

*Five patients had multiple events.

TABLE IV. Clinical Outcomes at One Year in the 39 Patients Who Had Heart Failure at Baseline and Who Completed the 6-Minute Walk Distance Test

Outcome	No. (%)
Major acute cardiovascular events*	8 (21)
Death	1 (3)
Acute coronary syndrome	5 (13)
Heart failure admission	3 (8)

*One patient had multiple events.

6MWD may help to identify high-risk patients after PCI, especially those with a previous history of HF.

The predictive value of 6MWD in our study was much more robust in terms of predicting HF admission after index PCI, as evidenced by a C statistic (AUC) of 0.69 overall (Fig. 2B) and 0.78 in patients with a previous history of HF with reduced left ventricular ejection fraction (Fig. 2D). Although 6MWD was relatively weaker at predicting MACE than it was at predicting HF admission, this difference needs validation in a larger population. Our study sample included not only patients with ACS, but also patients who underwent elective revascularization because of an abnormal

functional or stress test result. Moreover, our study was not large enough to compare the predictive capability of 6MWD in each subset of the sample. Thus, it would be interesting to determine if the ability of 6MWD to predict MACE and HF admission in patients with ACS is superior to its ability to do so in patients with stable angina or abnormal functional or stress test results who then undergo elective revascularization.

In our study, we determined different cutoff points for the 6MWD in subsets of patients. As noted in our results, the optimal 6MWD cutoff point for predicting HF admission after PCI was 286 m overall and 335 m in the HF subset. We also calculated cutoff points for

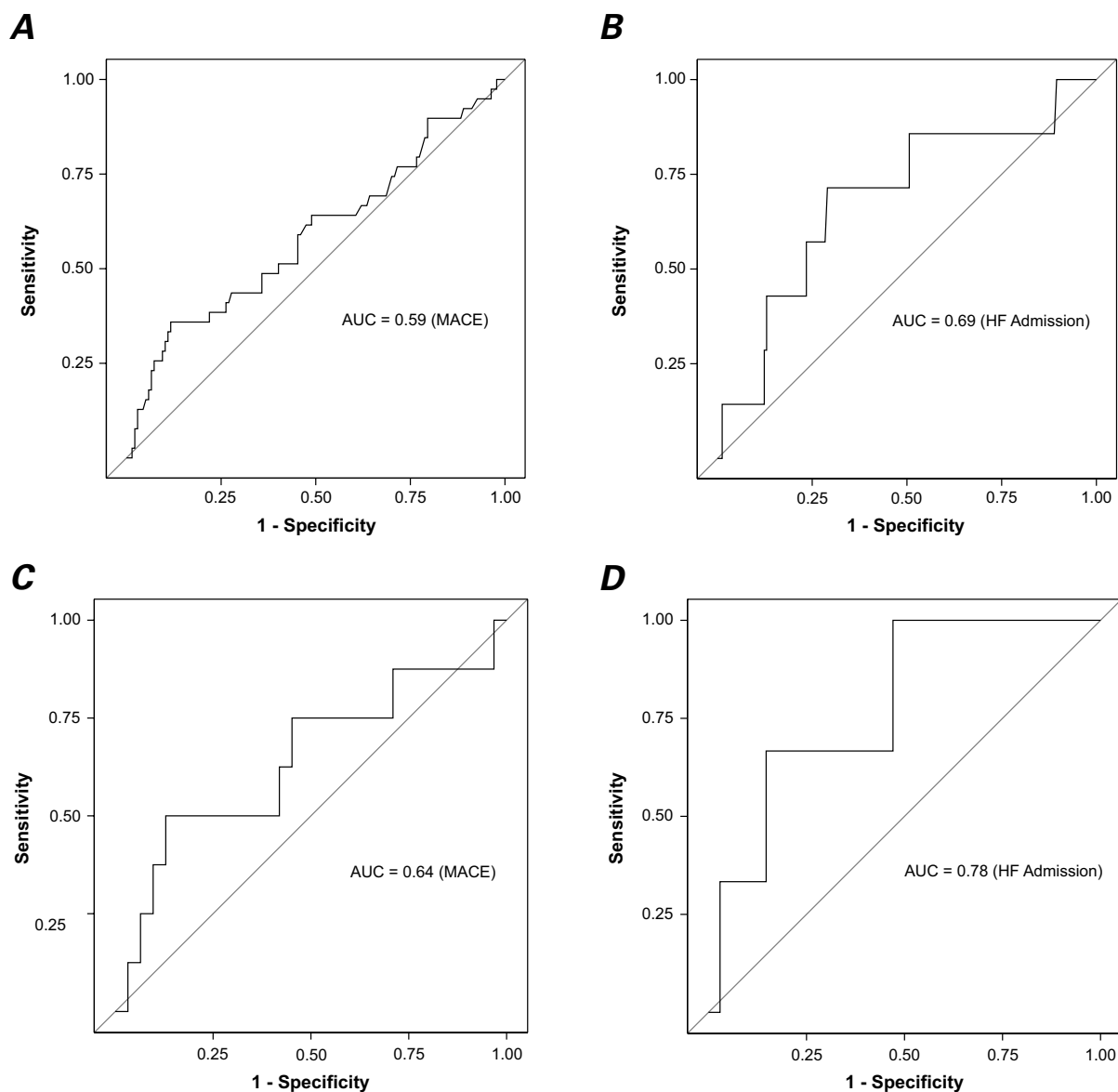


Fig. 2 Graphs show the receiver operating characteristic curves and areas under the curve (AUC) for **A**) major acute coronary events (MACE) and **B**) heart failure admission among the 176 patients who completed the 6-minute walk distance (6MWD) test; and for **C**) MACE and **D**) heart failure admission among the 39 patients with heart failure at baseline.

Figures 2C and 2D are adapted from *J Card Fail* 2015;21(8 Suppl):S127, with permission from Elsevier.¹²

predicting MACE after PCI. The resulting ORs were probably clinically insignificant, except when predicting MACE in the overall sample at a 6MWD cutoff of 225 m, because of the small sample size. These findings warrant further study in a larger group of patients undergoing PCI to define more precisely the optimal cutoffs for different subsets of these patients.

The 6MWD test can be used to estimate peak O₂ consumption indirectly without the need for an exercise stress test.¹³ Unlike the exercise stress test, the 6MWD test is inexpensive, easily administered, highly reproducible, and available at all centers. The only conditions are a level, premeasured hallway; a stopwatch; and a set of instructions. If optimal cutoffs are established for patients undergoing PCI (whether for ACS or for elective revascularization), then using a tool as simple as the 6MWD test will enhance the ability to predict MACE and HF admission during the first year after PCI. This may in turn enable earlier identification and triage and closer follow-up of patients who perform poorly on the 6MWD test, most of whom are likely to have a history of HF. The 6MWD may also be a useful quality-of-life variable and a good surrogate endpoint for PCI procedures. A 6MWD obtained before PCI, and another 6MWD obtained 6 months to one year after PCI, may then become one of several quality-of-life variables that reflect a patient's functional status.

Study Limitations

Our study had several limitations. First, it excluded patients who had severely limited functional capacity and could not walk. This in turn may have undermined the ability of 6MWD to specifically predict MACE, because many noncardiac conditions (such as severe pulmonary, neurologic, and musculoskeletal diseases) can also limit functional capacity and 6MWD. Second, the study was conducted in the Veterans Affairs system, where most patients are men. Thus, our findings may not be readily and generally applicable to women. Third, our study's relatively small sample size may have adversely affected the AUC-based predictive value of 6MWD. Larger, more adequately powered studies are needed to confirm our current findings.

Conclusion

Six-minute walk distance was reasonably good at predicting MACE and even better at predicting HF admission within one year after PCI. These findings warrant larger confirmatory studies, especially in patients with HF.

References

1. Tabata M, Shimizu R, Kamekawa D, Kato M, Kamiya K, Akiyama A, et al. Six-minute walk distance is an independent predictor of hospital readmission in patients with chronic heart failure. *Int Heart J* 2014;55(4):331-6.
2. La Rovere MT, Maestri R, Caporotondi A, Corbellini D, Guazzotti G, Pinna GD, Febo O. Pre-discharge evaluation in heart failure – additive predictive value of the 6-minute walking test to clinical scores. *Circ J* 2015;79(8):1756-63.
3. Bittner V, Weiner DH, Yusuf S, Rogers WJ, McIntyre KM, Bangdiwala SI, et al. Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. SOLVD Investigators. *JAMA* 1993;270(14):1702-7.
4. Cahalin LP, Mathier MA, Semigran MJ, Dec GW, DiSalvo TG. The six-minute walk test predicts peak oxygen uptake and survival in patients with advanced heart failure. *Chest* 1996;110(2):325-32.
5. Zugck C, Kruger C, Durr S, Gerber SH, Haunstetter A, Hornig K, et al. Is the 6-minute walk test a reliable substitute for peak oxygen uptake in patients with dilated cardiomyopathy? *Eur Heart J* 2000;21(7):540-9.
6. Węgrzynowska-Teodorczyk K, Rudzińska E, Lazorzyc M, Nowakowska K, Banasiak W, Ponikowski P, et al. Distance covered during a six-minute walk test predicts long-term cardiovascular mortality and hospitalisation rates in men with systolic heart failure: an observational study. *J Physiother* 2013;59(3):177-87.
7. Cacciatore F, Abete P, Mazzella F, Furgi G, Nicolino A, Longobardi G, et al. Six-minute walking test but not ejection fraction predicts mortality in elderly patients undergoing cardiac rehabilitation following coronary artery bypass grafting. *Eur J Prev Cardiol* 2012;19(6):1401-9.
8. de Arenaza DP, Pepper J, Lees B, Rubinstein F, Nugara F, Roughton M, et al. Preoperative 6-minute walk test adds prognostic information to Euroscore in patients undergoing aortic valve replacement. *Heart* 2010;96(2):113-7.
9. Mok M, Nombela-Franco L, Urena M, DeLarocheliere R, Doyle D, Ribeiro HB, et al. Prognostic value of exercise capacity as evaluated by the 6-minute walk test in patients undergoing transcatheter aortic valve implantation. *J Am Coll Cardiol* 2013;61(8):897-8.
10. Hassan AK, Dimitry SR, Agban GW. Can exercise capacity assessed by the 6-minute walk test predict the development of major adverse cardiac events in patients with STEMI after fibrinolysis? *PLoS One* 2014;9(6):e99035.
11. Forman DE, Fleg JL, Kitzman DW, Brawner CA, Swank AM, McKelvie RS, et al. 6-min walk test provides prognostic utility comparable to cardiopulmonary exercise testing in ambulatory outpatients with systolic heart failure. *J Am Coll Cardiol* 2012;60(25):2653-61.
12. Patel BC, Wayangankar SA, Thadani U, Lozano P, Latif F, Zhao D, et al. Prognostic value of a 6-minute walk test in patients undergoing percutaneous coronary intervention: a prospective study [abstract]. *J Card Fail* 2015;21(8 Suppl):S127.
13. Ross RM, Murthy JN, Wollak ID, Jackson AS. The six-minute walk test accurately estimates mean peak oxygen uptake. *BMC Pulm Med* 2010;10:31.