

# 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

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**Question:** Does the distance covered during a 6-minute walk test predict risk of death or hospitalisation for cardiovascular reasons in men with stable heart failure over three years of follow-up? **Design:** Prospective observational study. **Participants:** 243 men with stable systolic heart failure, with a mean age of 60 yr (SD 11) and left ventricular ejection fraction of 29% (SD 8). According to the New York Heart Association (NYHA) classification, 15% of the participants were in Class I, 44% in Class II, 37% in Class III, and 4% in class IV. **Outcome measures:** The exercise capacity of participants was measured using the 6-minute walk test. The participants were followed up for at least three years in the case of survivors. The primary end-points of the survival analyses included cardiovascular death or urgent cardiovascular hospitalisation. **Results:** During the 3-year follow-up, 44% of the participants died, and 69% died or required hospitalisation for cardiovascular reasons. A multivariate analysis showed that the shorter the distance covered in the 6-minute walk test, the greater the 1-year and 3-year mortality risk. Participants with a 6-minute walk test  $\leq 468$  m had a mortality hazard ratio of 3.22 (95% CI 1.17 to 8.86) at one year and 2.18 (95% CI 1.18 to 4.03) at three years. Multivariate analysis also showed that higher risk mortality or hospitalisation for cardiovascular reasons was predicted by a 6-minute walk distance  $\leq 468$  m, with a hazard ratio of 2.77 (95% CI 1.30 to 5.88) at one year and 1.71 (95% CI 1.08 to 2.72) at three years. **Conclusion:** The 6-minute walk test distance constitutes an independent predictor of mortality and mortality or hospitalisation for cardiovascular reasons in men with stable systolic heart failure. [Wegrzynowska-Teodorczyk K, Rudzinska E, Lazorczyk M, Nowakowska K, Banasiak W, Ponikowski P, Wozniwski M, Jankowska EA (2013) 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. *Journal of Physiotherapy* 59: 177–187]

**Key words:** Heart failure, 6-minute walk test, Cardiovascular mortality, Re-hospitalization

## Introduction

Heart failure places a major burden on the healthcare system in the western world (Bleumink et al 2004). The prevalence of heart failure is predicted to increase in the coming decades (Stewart et al 2003). However, the healthcare burden of heart failure does not pertain solely to the constantly increasing number of patients. Recurrent exacerbation periods impair the physical and psychological condition of the patient, require frequent re-hospitalisation, and are associated with poorer prognosis (Stewart et al 2003, Bleumink et al 2004). The risks of mortality and re-hospitalisation are difficult to predict with precision in the population of people with heart failure. Most tests aimed at determining factors that could be used as predictors of morbidity and mortality in this group of patients are complicated and expensive, which prevent them from being cost effective.

A marked reduction in the capacity to undertake physical activity is one of the principal symptoms of heart failure. Therefore, potential associations have been investigated between various methods of assessing physical exercise capacity and prognosis (Sarullo et al 2010, Poggio et al 2010).

Many predictor variables from formal cardiopulmonary exercise testing have been proposed, including peak oxygen consumption as a percentage of the predicted value, the chronotropic index, and ventilatory efficiency (Poggio et al 2010). When multiple predictors are available, conflicting predictions can make interpretation difficult (Poggi et al 2010).

The 6-minute walk test is a simple and inexpensive method of indirectly assessing physical capacity that is widely available and commonly used (Bellet et al 2011, Rostagno et al 2008, Faggiano et al 2004). Most previous studies have

**What is already known on this topic:** The 6-minute walk test is a simple and inexpensive method of indirectly assessing exercise tolerance. The distance covered by hospitalised patients during the test is predictive of the 1-year risk of cardiovascular death.

**What this study adds:** Among men with chronic heart failure, the 1- and 3-year mortality risk are greater among those who cover less than 468 m on the 6-minute walk test.

demonstrated that the distance covered by hospitalised patients during a 6-minute walk test is predictive of the one-year risk of cardiovascular death (Cahalin et al 1996, Opasich et al 2001, Shah et al 2001). However, few studies have examined the predictive ability of the 6-minute walk test distance beyond one year.

The specific research questions for this study were:

1. Are there relationships between the distance covered during the 6-minute walk test and the clinical characteristics of men with stable heart failure?
2. What are the 1-year and 3-year mortality and hospitalisation rates among men with stable heart failure?
3. Is the distance covered in the 6-minute walk test associated with mortality and hospitalisation for cardiovascular reasons at one and three years?

## Method

### Design

This was a prospective, longitudinal, observational study in which the predictive ability of the 6-minute walk test distance was assessed in men with stable heart failure. Participants were followed up for a minimum of three years. The clinical outcomes assessed were mortality and hospitalisation for cardiovascular reasons.

### Participants

Participants were recruited from the Heart Failure Outpatient Clinic of the Center for Heart Disease in Wroclaw, Poland. Male clinic attendees with stable systolic heart failure were approached consecutively and informed about what participation in the study would entail. Those who expressed interest in participation underwent a cardiac evaluation and this was used to assess whether they met the eligibility criteria.

The inclusion criteria were: male aged over 18 years, a documented history of heart failure of six months or longer, a left ventricular ejection fraction (LVEF) of 45% or lower as assessed by echocardiography (performed at the time of screening using a Simpson's planimetric method), and clinical stability indicated by unchanged medications for at least one month prior to enrolment. The exclusion criteria were: acute coronary syndrome, coronary revascularisation and/or major surgery within the three months prior to enrolment, unplanned hospitalisation due to heart failure deterioration or any other cardiovascular reason within one month prior to enrolment, any condition precluding the independent performance of a walk test, and unwillingness or inability to provide written informed consent.

### Outcome measures

**Laboratory tests.** Venous blood samples were taken in the morning following an overnight fast and after resting for at least 15 min. Standard laboratory tests, including complete blood count, serum levels of haemoglobin, creatinine, and uric acid, were performed using the standardised laboratory methods in our institution. Plasma levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured in pg/mL using the enzyme-linked immunosorbent assay method<sup>a</sup>, and C-reactive protein (hsCRP) serum levels were determined by an immunonephelometric high sensitivity method<sup>b</sup>. Renal function was assessed via the estimated glomerular filtration rate (eGFR) using the Modification in

Diet in Renal Disease calculator, ie,  $186 \times (\text{serum creatinine levels})^{-1.154} \times (\text{age})^{-0.203}$ .

**6-minute walk test.** The 6-minute walk test was performed in a long, straight hospital corridor, over a 30-m distance. Each participant was asked to walk (not run) back and forth along the corridor as briskly as possible, so that the longest possible distance was covered in six minutes. The participant was allowed to slow down or stop and rest if necessary, particularly in the case of symptoms such as severe dyspnoea or fatigue. During any rest period, the participant was informed of the elapsed time and encouraged to recommence walking when the symptoms attenuated enough to allow walking. However, the test was discontinued if the symptoms persisted. The participant was also allowed to discontinue the test at will at any time. Moreover, the test was interrupted by the investigator immediately one of the following symptoms appeared: chest pain that did not resolve at rest, dyspnoea precluding continuation of walking, cramps of the lower limb muscles, balance difficulty, severe sweating, pallor, or cyanosis. Otherwise, every two minutes during the test, an investigator informed the participant of the amount of time left and encouraged him to continue the test. At six minutes, the participant was advised to stop and be seated. An investigator immediately measured post-exercise arterial blood pressure and pulse rate. The participant assessed subjective fatigue and dyspnoea levels with the modified Borg scale from 0 (none) to 10 (maximal). The distance walked was measured to the nearest whole metre.

**Long-term clinical outcomes.** Information regarding survival and hospitalisation was obtained directly from the participant, over the phone from the participant or their relatives, from the hospital system, or from the heart failure clinic database. The participants who survived were followed up for at least three years. The first end-point of this study was cardiovascular death. The second end-point of this study was a composite outcome: death or urgent hospitalisation for cardiovascular reasons.

### Data analysis

Continuous variables with a normal distribution (ie, age, 6-minute walk test distance, LVEF, eGFR, haemoglobin, and uric acid) were presented as means and standard deviations. The between-group differences were tested using Student's t-test. The remaining continuous variables (ie, plasma NT-proBNP and serum hs-CRP) had a skewed distribution and were expressed as medians with lower and upper quartiles. These between-group differences were tested using the Mann Whitney U-test. For further analyses, these variables were log transformed in order to normalise their distribution. The categorical variables were expressed as numbers with percentages. The between-group differences were tested using the chi-squared test.

The relationship between the 6-minute walk test and the long-term clinical outcomes was assessed by using univariate and multivariate regression models. The associations between the analysed parameters and survival were established using Cox proportional hazards analysis. The number of variables included in the multivariable models was dependent on the number of events (ie, 1 predictor for 10 events). The following parameters were included in the analyses as potential predictors of death, and death or hospitalisation: age, heart failure aetiology,

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