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# Six-minute walk test: independent prognostic marker?

Carlo Rostagno

In heart failure prognosis is related to the severity of impairment of functional capacity.<sup>1</sup> The peak oxygen consumption ( $\text{VO}_2$ ) at cardiopulmonary exercise test (CPET) is considered the gold standard for the evaluation of exercise tolerance; nevertheless, its clinical application is limited. The 6-minute walk test (6MWT) has been proposed as a simple, inexpensive, reproducible alternative to the CPET. The 6MWT reproduces the activity of daily life and this is particularly relevant in elderly patients who usually develop symptoms below their theoretical maximal exercise capacity.<sup>2</sup> The test showed a good reproducibility and is largely independent from aetiology of heart failure, NYHA class and indices of left ventricular systolic or diastolic function measured at rest.<sup>3</sup>

Peak  $\text{VO}_2$  and distance walked at 6MWT have been demonstrated to have a non-linear relation and, in particular, a wide variation has been shown for  $\text{pVO}_2$  values between 10 ml/min/kg and 20 ml/min/kg. A closer relation exists in more severe heart failure. The incremental workload nature of CPET may result in an earlier muscular exhaustion in patients with more severe disease, who otherwise may better perform in a stable workload test such as the 6MWT.

In this issue of *Heart* two papers deal with different aspects of the usefulness and prognostic value of 6MWT in patients undergoing aortic valve replacement (AVR) (see pages 113 and 118).

In patients from the ASSERT study, in which stentless versus stented AVR was compared, 208 subjects with severe aortic stenosis underwent 6MWT before surgery and then were followed for 12 months.<sup>4</sup> Composite endpoint of death, myocardial infarction and stroke was 13% in patients who walked  $\leq 300$  metres in comparison to 4% in those walking  $>300$  metres. Distance walked at 6MWT provided further prognostic information to additive Euroscore risk calculation and was the only independent variable related to increased risk of composite endpoint.

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Rimington *et al* evaluated the baseline predictors of improvement of functional capacity and health-related quality of life at 12-month follow-up in 225 patients undergoing their first AVR.<sup>5</sup> Distance walked at 6MWT after AVR significantly increased. The improvement in distance walked was independently related to preoperative walking distance, age and IPQ-R treatment control. Preoperative walking distance contributed to 36% of the overall 44% change of variance. Also quality of life significantly improved after AVR and preoperative PCS and walking distance were the only independent variables at 12-month follow-up.

Results of previous investigations evaluating the independent prognostic value of 6MWT in heart failure as in other different clinical conditions (aortic stenosis, primary pulmonary hypertension, various pulmonary diseases) gave contrasting results. The wide differences in examined populations may in part account for reported differences.

In patients with heart failure the prognostic value of 6MWT was first reported from a substudy of SOLVD investigation.<sup>6</sup> Mortality was threefold in patients who walked  $<350$  metres in comparison to those walking  $>450$  metres. Ejection fraction and the distance walked resulted independent predictors of mortality or hospitalisation. Roul *et al*<sup>7</sup> in mild to moderate heart failure did not find significant differences in distances at 6MWT between those who reached the endpoint of death or hospitalisation for heart failure in comparison to the event-free group, while  $\text{pVO}_2$  was significantly higher in event-free patients. Nevertheless the subgroup walking  $<300$  metres had an higher rate of death and hospitalisation. The relation between  $\text{pVO}_2$  and distance at 6MWT was closer ( $r = 0.65$ ) in these patients than in the whole group ( $r = 0.21$ ), suggesting that in more severe disease 6MWT approached maximal exercise capacity. In a similar population walking a distance of  $<350$  metres levels of brain natriuretic peptide (BNP), ischaemic aetiology and atrial fibrillation were reported to be independently related to prognosis.<sup>8</sup>

Opasich *et al* followed 270 patients with chronic heart failure (CHF) for a

minimum of 6 months: 21% died or underwent transplantation.<sup>9</sup> Although distance at 6MWT was significantly associated with survival at univariate analysis, predictive value was lost at multivariate analysis. The absence of a statistical significance of  $\text{pVO}_2$  and categorised distance at 6MWT when they are considered together in a bivariate model suggested that these two variables give similar diagnostic information.

Rostagno *et al* investigated a group of patients with mild to moderate heart failure: event-free (death or heart transplantation) survival at 36 months was significantly lower, 62%, in patients walking  $<300$  metres in comparison to 82% of those with intermediate (300–450 metres) or high performance ( $>450$  metres).<sup>10</sup> Peak  $\text{VO}_2$  did not show a predictive value. Only the 6MWT and left ventricular ejection fraction (LVEF) were independent prognostic factors.

In severe heart failure a distance below the median (210 metres) was associated with a 6-month mortality of 50% vs 20% in patients who covered a longer distance,<sup>11</sup> while a distance  $<300$  metres predicted an increased likelihood of death or hospitalisation for inotropic or mechanical support within 6 months but failed to predict overall or event-free survival at 62 weeks.<sup>12</sup> The predictive value of 6MWT in patients with advanced heart failure was questioned by other authors.<sup>13</sup> Six-minute walk strata ( $<350$  metres, 350–450 metres,  $>450$  metres) were significantly associated with  $\text{pVO}_2$  strata ( $<$  or  $>14$  ml/kg/min;  $\chi^2 = 29.5$ ); however,  $\text{pVO}_2$  was related to mortality whereas the 6MWT was not.

It is difficult to assess that distance walked at the 6MWT may be considered an independent risk factor when another objective test of functional capacity such as CPET is used in the same population. In fact, despite clear differences between the two tests, the relation between  $\text{pVO}_2$  and distance walked at 6MWT was found by most authors to be unreliable or that they may not be independently related prognostic factors at all. Most interesting is the application of the 6MWT as a test of functional cardiovascular capacity in several clinical contexts, including the preoperative evaluation of surgical risk in different valvular surgery and heart surgery that was not involving the valves. Euroscore, as with other preoperative score systems for surgical risk assessment, is often relatively inaccurate, in particular in patients with valvular heart disease. Functional evaluation has been

demonstrated to be more sensitive than haemodynamic and echocardiographic indexes in the prognostic evaluation of heart failure from different aetiologies. The inclusion in a preoperative clinical evaluation of a simple and reproducible test allowing assessment of cardiovascular performance should be investigated in a large study with the aim of assessing if it should be routinely employed not only to evaluate immediate surgical risk but also postoperative results in term of mortality, expected exercise and improvement of quality of life.

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