9 Polkey MI, Spruit MA, Edwards LD, *et al.* Six-minute-walk test in chronic obstructive pulmonary disease: minimal clinically important difference for death or hospitalization. *Am J Respir Crit Care Med* 2013; 187: 382–386.
10 Ringbaek T, Martinez G, Brondum E, *et al.* Shuttle walking test as predictor of survival in chronic obstructive pulmonary disease patients enrolled in a rehabilitation program. *J Cardiopulm Rehabil Prev* 2010; 30: 409–414.

Eur Respir J 2014; 43: 1820–1822 | DOI: 10.1183/09031936.00222013 | Copyright ©ERS 2014

6-minute walk distance as a predictor of outcome in idiopathic pulmonary fibrosis

To the Editor:

The interesting manuscript by DU BOIS *et al.* [1] states in the discussion section that "only two previous studies have demonstrated an independent association between 6MWD and the risk of mortality in patients with IPF", quoting the studies of CAMINATI *et al.* [2] and of LEDERER *et al.* [3].

It should be noted that in 2012 the *European Respiratory Journal* published a study demonstrating the significant and independent association between 6-min walk distance (6MWD) and outcome in patients newly diagnosed with idiopathic pulmonary fibrosis (IPF) [4]. In this prospective study, patients were followed for at least 3 years from the time of diagnosis. Baseline 6MWD and 6-month changes were assessed. Both 6MWD metres and 6MWD % predicted, according to the reference equations of ENRIGHT and SHERRILL [5], were considered.

As a continuous variable, 6MWD % predicted, but not 6MWD metres, was significantly and independently associated with 3-year mortality (HR 0.97 (95% CI 0.96–0.99), p=0.0193 Cox proportional hazards analysis), together with the Medical Research Council dyspnoea score and the composite physiologic index [6]. With a cut-off of 72% pred, based on receiver operating characteristic analysis, 6MWD % predicted was also significantly and independently associated with 3-year mortality (HR 3.27 (95% CI 1.25–8.82), p=0.0162 Cox proportional hazards analysis) together with Medical Research Council dyspnoea score and composite physiologic index. 6MWD metres with a cut-off of 350 m was not a significant predictor. These results were confirmed in an independent, retrospective cohort from another centre (HR 5.43 (95% CI 1.35–36.17), p=0.0160). In patients with relatively preserved exercise capacity at the time of diagnosis (6MWD >350 m or 6MWD >72% pred), a 6-month decline of either 6MWD meters or 6MWD % predicted was also associated with significantly increased risk of mortality at 3 years after diagnosis (p=0.038 and p=0.012, respectively; log rank test) [4].

The study of DU BOIS *et al.* [1], selectively conducted on patients with mild-to-moderate IPF (forced vital capacity ⩾55% pred, diffusing capacity of the lung for carbon monoxide ⩾35% pred and 6MWD ⩾150 m) with data from the GIPF-007 (Interferon-γ-1b in patients with IPF) trial, provides further evidence supporting the use of 6MWD as a reliable and independent predictor of survival in IPF. It would certainly be interesting to learn about the predictive power of 6MWD % predicted *versus* 6MWD metres in their study, although better reference equations are needed.

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Both baseline 6MWD and its 6-month changes are independent predictors of survival in newly diagnosed IPF http://ow.ly/tinC6

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Received: Dec 08 2013 | Accepted: Dec 22 2013

Conflict of interest: None declared.

References

1 du Bois RM, Albera C, Bradford WZ, *et al.* 6-minute walk distance is an independent predictor of mortality in patients with idiopathic pulmonary fibrosis. *Eur Respir J* 2014; 43: 1421–1429.

2 Caminati AA, Bianchi R, Cassandro R, *et al.* Walking distance on 6-MWT is a prognostic factor in idiopathic pulmonary fibrosis. *Respir Med* 2009; 103: 117–123.
3 Lederer DJ, Arcasoy SM, Wilt JS, *et al.* Six-minute-walk distance predicts waiting list survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2006; 174: 659–664.
4 Mura M, Porretta MA, Bargagli E, *et al.* Predicting survival in newly diagnosed idiopathic pulmonary fibrosis: a 3-year prospective study. *Eur Respir J* 2012; 40: 101–109.
5 Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998; 158: 1384–1387.
6 Wells AU, Desai SR, Rubens MB, *et al.* Idiopathic pulmonary fibrosis: a composite physiologic index derived from disease extent observed by computed tomography. *Am J Respir Crit Care Med* 2003; 167: 962–969.

Eur Respir J 2014; 43: 1822–1823 | DOI: 10.1183/09031936.00213313 | Copyright ©ERS 2014

From the authors:

We thank M. Mura for reminding us of the study published in the *European Respiratory Journal* (*ERJ*) in 2012 that confirmed the increasing importance of the 6-min walk test (6MWT) in the evaluation and prediction of outcome in patients suffering from idiopathic pulmonary fibrosis (IPF) [1]. In this prospective study by MURA *et al.* [1], of factors that predicted survival in 70 patients with newly diagnosed IPF, the major 6MWT findings were that the 6-min walk distance (6MWD) % predicted, but not 6MWD defined as metres walked, was independently associated with 3-year survival, and that a receiver operating characteristic-based cut-off of 72% pred 6MWD best differentiated probable outcome.

By contrast, our data recently reported in the *ERJ* showed that both baseline and especially 24-week change in 6MWD, defined as metres walked, were independent predictors of outcome [2]. In our study we did not explore 6MWD % predicted because of the reference equation concerns, referred to by M. Mura. Reference equations from healthy population-based samples using standardised 6MWT methods are not yet available [3]. The study by MURA *et al.* [1] used the equations that were derived from a study of 173 healthy females and 117 healthy males from Tuscon, AZ, USA [4] and, therefore, are possibly not representative of the Italian individuals who participated in their study. Given that our study included 748 patients who had enrolled in a clinical trial in 81 centres in seven European countries, the USA and Canada, we felt that it would not be appropriate to derive percent predicted values based on data from a single state in the USA. The highlights of our study were that 6MWD provided a prediction of mortality that was independent of other indices previously reported by us [5], and that the addition of 6MWD to the clinical prediction model improves model discrimination compared with the original model [2].

The findings of the study reported by MURA *et al.* [1], combined with those of our own recent study [2], provide compelling evidence supporting the utility of 6MWD in both clinical practise and in designing end-points for clinical trials of novel therapy, and reinforce the data from several earlier studies that showed favourable performance characteristics of 6MWD in patients with IPF [6–8]. Recently, this index of evaluation has appeared to have fallen out of favour but the complementary positive data provided by our study and that of MURA *et al.* [1] support the use of the 6MWT as a future end-point. To abandon an index prematurely would do a disservice to our patients if added value due to its continued use to predict probable outcome accrued, which would in turn be of value when considering the initiation of, or change in, therapy and the timing of referral for lung transplantation.

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6MWD provides prediction of mortality in IPF independent of other indices previously reported to predict IPF outcome http://ow.ly/tirmb

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Received: Jan 04 2014 | Accepted: Jan 07 2014

Conflict of interest: Disclosures can be found alongside the online version of this article at www.erj.ersjournals.com

References

1 Mura M, Porretta MA, Bargagli E, *et al.* Predicting survival in newly diagnosed idiopathic pulmonary fibrosis: a 3-year prospective study. *Eur Respir J* 2012; 40: 101–109.
2 du Bois RM, Albera C, Bradford WZ, *et al.* 6-minute walk distance is an independent predictor of mortality in patients with idiopathic pulmonary fibrosis. *Eur Respir J* 2014; 43: 1421–1429.