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PRO AND CON EDITORIALS

The case against inspiratory muscle training in COPD

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Despite maximal medical therapy, many chronic obstructive pulmonary disease (COPD) patients remain breathless and this has led to persistent and commendable efforts to reduce symptoms and improve exercise performance using nonpharmacological approaches; some of these, for example pulmonary rehabilitation (PR) [1], comprising general exercise and fitness training, are of proven benefit, while others remain controversial.

Inspiratory muscle training (IMT), being cheap and free of side-effects, is intuitively attractive, since improving the capacity of the inspiratory muscles should ''make breathing easier'' and so improve exercise performance. Enthusiasts do not allow the superficial attractiveness of this proposition to be clouded by aspects of the data. These are that the diaphragm is already working hard and well trained in emphysema, with a shift towards fatigue resistant type I fibres [2], that at a single fibre level it is energetically more efficient [3], that (allowing for hyperinflation) it is not actually weak [4, 5] and that diaphragm fatigue cannot be elicited in patients *in vivo* [6, 7], even when patients are sufficiently ill to require mechanical ventilation [8]. The question of whether the respiratory muscles are weak in COPD seems particularly important in the context of IMT. In the current issue of the *European Respiratory Journal*, GOSSELINK *et al.* [9] cite our paper [5] as evidence that the diaphragm is weak; in fact, we concluded that the major reason for the reduced transdiaphragmatic pressures observed in COPD was hyperinflation, which of course would not be expected to improve with IMT. They also state that inspiratory muscle weakness contributes to a range of poor outcomes in COPD, whereas in our view associations between reduced inspiratory pressures due to hyperinflation and poor outcomes may simply be epiphenomena. Thus, for example, in a recent survival analysis [10] we found that both inspiratory muscle strength and hyperinflation predicted death in a substantially similar way, probably because they measured different properties of the same thing. In fact, inspiratory muscle strength proved statistically, but not clinically, superior with an area under the curve on a receiver operating characteristic plot of 0.68 *versus* 0.62 compared with inspiratory capacity/total lung capacity ratio, but the possible technical factors, notably transmission of pressure within the emphysematous lung, underlying this are beyond the scope of this editorial.

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Inspiratory muscle training is usually considered to have its origins in the now classic paper by LEITH and BRADLEY [11], in which 12 normal subjects were randomised into three groups of four to receive no treatment, or training for strength or for endurance. The strength group increased their maximal inspiratory pressure ($P_{I,max}$) by an impressive 55% (more of this below). In the present issue, GOSSELINK *et al.* [9] conducted an exhaustive review of the English and non-English language literature in order to update their 2002 meta-analysis [12]. They conclude that statistically significant and clinically relevant improvements were observed for inspiratory muscle strength and endurance, functional exercise capacity, and dyspnoea and quality of life indices. However, this conclusion comes with some health warnings.

First, although we accept that IMT can be associated with structural changes in the inspiratory muscles [13], GOSSELINK *et al.* [9] did not exclude from their meta-analysis studies with other factors which might have biased the results. Of these the most important is lack of a sham control, without which the placebo effect might be particularly strong for measures of dyspnoea and quality of life indices. Patient assessed outcomes have been shown to improve following interventions without a known aetiological mechanism, including osteopathy (even though flow limitation also worsened in the treatment group) [14], listening to music for 30 min [15], singing [16], as well as a humour intervention by a clown which improved a ''cheerfulness index'' [17]. It is therefore plausible that outcomes might also improve through a placebo type mechanism after IMT. Consistent with this proposition the patients studied by RAMIREZ-SARMIENTO *et al.* [13] failed to improve their 6-min walk distance (6MWD) or maximal oxygen uptake despite a 12 cmH_2O increase in $P_{I,max}$ and histological improvement in their inspiratory muscles.

Secondly, the first two outcomes (strength and endurance) are not directly relevant to the patient experience, in the sense that patients do not present to their physicians with difficulty completing respiratory muscle assessments. Moreover, technique is critically important in performing voluntary tests of maximal strength and endurance. We explored this in detail in a (admittedly small) study in normal subjects who were allocated to receive either real or sham IMT [18]. Consistent with other reports the treatment group improved $P_{I,max}$ but their twitch transdiaphragmatic pressure failed to improve, leading us to infer that they had simply ''got better at doing the test'' [19]. We also found that they improved their inspiratory muscle endurance; however, when analysed using a technique which accounted for breathing pattern [20], it was found that their apparent improvement simply reflected a more efficient breathing pattern [21]. A further example of ''getting better at

doing the test'' is provided by one of us (M. Green) who was a (then) naïve subject in the 1976 LEITH and BRADLEY [11] study. He was randomised to strength training and showed an impressive improvement in strength. M. Green participated intermittently in studies requiring respiratory muscle strength measurement in our laboratory between that time and until his retirement from academic work in 2001. Over 25 years he found that the improvement in $P_{I,max}$ documented following ''strength training'' in 1976 never wore off, suggesting that the improvement recorded by LEITH and BRADLEY [11] was due to improved test technique rather than as a result of true increase in muscle strength!

The only outcomes currently accepted as valid for COPD by regulatory agencies in Europe and the USA are forced expiratory volume in 1 s, exacerbation and death; however, 6MWD is accepted in other diseases (such as pulmonary hypertension) and thus logically could in future be accepted for COPD. Until recently the minimal clinically important difference (MCID) for the 6MWD was considered to be 54 m [22]. More recently this has been reduced to either 35 m [23] or 25 m [24]. Only with the latter threshold does the improvement shown in the current meta-analysis (32 m) exceed the MCID, and then only by 7 m, scarcely clinically significant. Careful review of the data of HOLLAND *et al.* [24], who derived their figures by analysing the benefit conferred by a PR course, showed that patients who experienced no detectable benefit increased 6MWD by a mean of 17 m, while those who perceived a ''small'' benefit had a mean increase in 6MWD of 60 m. We also note that, in the current meta-analysis, the subanalysis of patients receiving PR alone compared to IMT in addition to PR failed to demonstrate significant improvement (fig. 4 of GOSSELINK *et al.* [9]). Since PR is a therapy of proven benefit these data would suggest that IMT has little additional to offer.

In conclusion, we congratulate GOSSELINK *et al.* [9] for their comprehensive review and analysis of the literature. We interpret their data as showing that when given alone IMT is of marginal clinical benefit in COPD, and that it offers no additional value to PR; indeed, by committing the time of both patients and their rehabilitation team, IMT may distract from PR itself. We suggest that future studies do not attempt to measure inspiratory muscle strength or endurance but that the primary measure should reflect a patient focused outcome, such as a field walking test or physical activity monitoring.

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STATEMENT OF INTEREST

None declared.

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