Response to pulmonary rehabilitation: toward personalised programmes?

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Personalised pulmonary rehabilitation with multidimensional response profiling could aid efficiency and effectiveness <http://ow.ly/TouTt>

Clinical practice should be based on the best scientific evidence, which does not always correspond to evidence-based medicine, involving guidelines, meta-analyses and protocols as a basis for clinical approach [1, 2]. There is no need of further randomised controlled trials (RCTs) for evidence that pulmonary rehabilitation (PR) improves daily symptoms, exercise performance and health status in patients with chronic obstructive pulmonary disease (COPD), independently of disease stage and complexity [3]. Although the direct demonstration of a clear benefit in survival is lacking (as is also true for most therapies used in COPD), PR is well recognised as a fundamental part of the integrated care of these patients and it has been incorporated in most guidelines for their management [4].

Due to the current restraints in healthcare resources and the different opportunities in healthcare policies all over the world [5], we need solid outcomes to decide how to optimally invest money in this field. Clinical observations have attempted to define predictors of PR success, evaluating outcome measures able to discriminate responders from nonresponders to treatment [6–8]. Nevertheless, the improvement of a single outcome measure like exercise tolerance in an RCT may not be enough to catch the real and/or perceived benefit that the individual patient may achieve, just like the glycaemia control might not be a perfect or unique index of control of diabetes and related complications in different environments and stages along the natural history of this disease [9].

As reported in this issue of the *European Respiratory Journal*, SPRUIT *et al.* [10] looked for a profile of multidimensional response to PR in >2000 COPD patients based on eight different outcome measures, including symptoms, exercise performance, health and mood status, and activities of daily life. Analysis led to clustering of patients into four groups with different response profiles and different prevalence: “very good responder” (18.3%), “good responder” (35.9%), “moderate responder” (35.4%) and “poor responder” (10.5%). The “very good responder” had more severe dyspnoea, more hospitalisations per year, worse exercise tolerance, worse performance and satisfaction scores for activities of daily life, more severe anxiety and depression, worse health status, and was more likely to follow an inpatient PR programme compared with the other three categories. Interestingly, even the “poor responder” may show that PR is a therapy of clinical value in those COPD patients who are symptomatic despite optimal medical therapy.

Overall, it seems that the best responders are the most severe patients, as probably expected. The authors conclude that a multidimensional response outcome needs to be considered to study the effectiveness of PR in COPD patients, as responses of usual outcome measures for a given programme are different between COPD patients with different clinical and functional characteristics. Moreover, these findings emphasise that key performance measures to evaluate effectiveness of PR programmes have to be selected within multiple domains, also related to what a patient perceives in his/her daily life [11]. In addition, although

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clinical complexity associated with number and severity of comorbidities is not a contraindication for PR [12], we cannot exclude that this complexity may lead to interference with outcomes [13].

In a previous study [8], response to PR improvement was assessed by a pre-defined cut-off threshold level of both exercise tolerance and perceived quality of life: the proportion of “responders” declined when severity of dyspnoea increased. However, those findings were not able to catch the global complexity of different patients with COPD, as that study only referred to symptoms following different degrees of exercise. Previous observational studies had already demonstrated that the more severe the patients in a single functional outcome measure, the more likely he/she may gain benefits after PR programmes [7, 14]. The other problem is that most studies have focused on non-individualised PR programmes, usually including exercise training protocols based on general principles, rather than on individually tailored (personalised) programmes. However, physicians should be focused on the individual patient, with his/her present global health condition, within a specific time and circumstantial frame. This might also provide true transparency and give the policy makers more detailed insights into the effectiveness and possibly into the efficiency of PR, in terms of both the individual and the composite outcome measures. Clinicians should be able to recognise which general principles of a scientific theory are relevant and applicable to the individual, given his/her condition here and now [15].

Recently, the term “personalised medicine” has been used to describe the use of genomics, proteomics and biomarkers to precisely tailor therapy according to phenotypic characteristics of an individual patient [15]. Although PR is still far from this level of knowledge, we can try to plan personalised PR programmes taking into account individual patients’ clinical, functional, environmental and social factors. We believe that this would be a useful field of research, and that enough time has been spent reviewing RCTs of clinical effectiveness. Recent development of PR tools, like noninvasive ventilation-aided exercise training and neuromuscular electrical stimulation, may allow us to propose sequential levels of intervention as suggested and displayed in figure 1. This approach would allow resource savings for poor responders or first-stage patients and optimal treatment for responders and more severe patients.

FIGURE 1 Possible representation of personalised pulmonary rehabilitation programmes. As the abnormalities on initial assessment become more complex and severe (on the left axis), the programme and activities are progressively and specifically adapted to the patient's characteristics. Outcome measures are recorded throughout the programme. ADL: activities of daily life; NIV: noninvasive ventilation; NMES: neuromuscular electrical stimulation.

The study of Spruit *et al.* [10] may be a basis for further research aimed at personalised PR and may help healthcare professionals and funders to realise that one size does not fit all in the vast population of COPD patients. The multidimensional profiling of response to therapies, including PR, might provide several useful pieces of information, such as the overall priority of intervention, the type of response in each single outcome, and suggestions of how to personalise activities and/or motivate subjects to achieve the goals they perceive as the most important in their daily life.

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