


Nutritional supplementation during pulmonary rehabilitation in COPD: Do not expect an elixir of life but keep the hunger for more robust evidence

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Pulmonary rehabilitation (PR) is a complex interdisciplinary intervention based on a thorough patient assessment, followed by patient-tailored therapies.¹ These include, but are not limited to, exercise training, dietary counseling, education, and behavior change to improve the physical and psychological condition of people with chronic respiratory disease. Promoting long-term adherence to health-enhancing behaviors is at the essence. PR for patients with chronic obstructive pulmonary disease (COPD) has proved its merits in terms of improving many domains including dyspnea, fatigue, exercise capacity, self-management, and health status.² Also, studies have suggested lower exacerbation frequency³ and health-care utilization⁴ after completion of PR. Further optimizing components of the intervention is an important focus of current research in the field of PR.

In the interpretation of (synthesized) data from different PR programs, it is important to bear in mind that a large heterogeneity exists in many aspects of PR programs around the globe, as illustrated by Spruit et al. in a survey among representatives of 430 centers from 40 countries.⁵ Programs vary particularly in setting (home-based, outpatient, inpatient, or combinations), duration, and composition of the multidisciplinary team. However, with respect to the latter, a commonality in this survey is that the dietician is the most represented discipline in PR teams after the chest physician. This underscores the global recognition of the importance of nutritional management in patients undergoing PR. Indeed, in COPD, common clinically relevant nutritional traits include involuntary weight and muscle mass loss, decreased skeletal muscle oxidative capacity, (central and sarcopenic) obesity, and bone decalcification.^{6,7}

While nutritional management in COPD should not be delayed until inclusion in a PR program, it follows a careful assessment consisting of a dietary history, anthropometric and body composition measurements, and calculations of energy and protein requirements. Goals are formulated to optimize dietary quality and habits, supplement nutritional deficiencies, and potentially nutritional interventions may be installed to enhance PR outcomes. Exercise training, alone or as part of PR, may contribute to improving some of the nutritional traits. However, ventilatory constraints during exercise in patients with COPD may limit the level of improvement. It is therefore that the appealing concept of nutrition as an ergogenic aid to enhance the effect of exercise training in COPD has attracted the attention of researchers for many years. In 2012, this specific topic was reviewed by Van de Bool et al.⁸ narratively summarizing the evidence for supplementation of carbohydrates, protein and amino acids, polyunsaturated fatty acids (PUFAs), vitamin D, creatine, and antioxidants. At that time, it was concluded that although among investigated nutritional supplements PUFAs appear promising to improve exercise capacity, possibly through improving mitochondrial function,⁹ solid evidence to support a performance-enhancing effect of nutritional supplementation in COPD was lacking. As it was commented later in a European Respiratory

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Society task force report by Schols et al.,¹⁰ this particular body of literature is characterized by many underpowered and single-center studies with large heterogeneity.


In this issue of the *Journal*, Aldhahir et al. publish a systematic review synthesizing the results of 17 randomized controlled trials and 5 cohort studies that investigated effects of nutritional supplementation during PR in COPD. It was hypothesized that nutritional supplementation in the context of interdisciplinary PR would be the optimal condition to seek functional improvements. The authors should be applauded for their efforts to systematically search the literature and provide the readership with this overview. These 22 studies applied either macronutrients, micronutrients, or varying mixtures of supplements in varying COPD subgroups (e.g. those with recent weight loss, those with low muscle mass, those without comorbidity, those without obesity, and those with recent exacerbation). As expected when summarizing PR studies from 11 countries on 4 continents, settings and intensities of PR programs varied significantly. Clearly, as the authors rightfully concluded, there were too many levels of heterogeneity to allow for a meta-analysis.

Aldhahir et al. prespecified five domains in which they presented findings from the 22 studies: body composition, muscle function, exercise performance, quality of life, and lung function. While these are clinically important domains, one should acknowledge the methodological designs of individual studies and rationales as to why specific nutritional supplements may be beneficial for specific domains in subgroups of COPD patients. Whereas some of these studies had a clear rationale for potential benefit with good design and low risk of bias, others rather performed explorative analyses without prespecifying primary outcomes. Concurring with the meta-analysis by Ferreira et al.¹¹ on nutritional supplementation in stable COPD, PR studies in depleted COPD patients generally managed to increase body weight and some also muscle mass, particularly through multi-nutrient supplements. Outcomes in all other domains were either highly variable or have not been sufficiently replicated. Consequently, indeed, there is not one overarching conclusion to draw, and studies should be judged on their individual qualities.

Considering that nutritional factors have been implicated in COPD risk and progression,¹² that nutritional status is significantly affected by the common erratic disease course with exacerbations preceding

(and sometimes during) PR, and that the duration of PR is relatively short, one may question what level of surplus multidomain improvement is realistic to expect from nutritional supplementation during PR. On top of optimizing dietary quality, and possibly on the longer term, targeted and integrated nutraceutical intervention, however, remains of high interest in COPD considering the deleterious but potentially reversible nutritional traits like for example muscle mass loss, impaired mitochondrial function, and adverse adipose tissue distribution. We should aim for more personalized, adequately powered, and preferably multicenter studies in comparable PR settings. We owe it to our patients that emerging knowledge on nutritional targets is followed by robustly designed intervention studies so that we can further improve outcomes of PR and beyond.

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