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Nutritional targets to enhance pulmonary rehabilitation efficacy in COPD

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Valorisation

Valorisation is "the process of creating value from knowledge, by making this knowledge available and suitable for economic and social exploitation and to translate this knowledge into products, services, processes and new business."

This chapter will discuss the current findings in the light of the impact as well as innovative concepts for future health care.

RELEVANCE

COPD is a highly prevalent chronic disease, which is projected to further increase in the coming decades. Worldwide COPD is a leading cause of morbidity and mortality, resulting in a substantial and increasing economic and social burden. While COPD is characterized by airflow limitation, the degree of airflow limitation poorly correlates with actual disease burden. In fact, the COPD patient's health status is largely determined by extrapulmonary manifestations and comorbidities including skeletal muscle dysfunction, osteoporosis, cardiovascular disease, metabolic syndrome, and psychological disorders. These comorbidities contribute to common symptoms (breathlessness, fatigue), but also to reduced physical activity, disease exacerbations, hospital admissions and mortality.

This thesis highlights the importance of skeletal muscle dysfunction and in particular, low muscle mass as screening and therapeutic target for COPD:

Sarcopenia is defined as low appendicular muscle mass together with low muscle function (strength or performance) by the European Working Group on Sarcopenia. Recently, sarcopenia has been recognized as a disease entity with an ICD-10-CM (M62.84) code. Our findings indicate that assessment of 3-compartimental body composition (appendicular muscle mass, abdominal obesity and bone mineral content) might be favourable over 2-compartimental distinction between fat and fat-free mass, indicated by 1) the high persisting prevalence's of sarcopenia and abdominal obesity in all BMI categories; 2) it's discrimination for impaired muscle strength and endurance; 3) the higher predictive value of the 3-compartment prediction model compared to the 1 (BMI) or 2-compartment models. Dual Energy X-ray absorptiometry (DEXA) scans were originally designed for measurement of bone mineral density. This assessment is very relevant In COPD because of the high prevalence of osteoporosis in these patients (Chapter 2). Nowadays most hospitals are also able to use a DEXA scan for measurement of body composition according to the 3-compartmentmodel.

Next to low muscle mass, COPD patients often show structural alterations in muscle fiber type composition. Previous studies have already demonstrated a muscle fiber type I→II shift, and selective atrophy of the type IIx fibers in patients with COPD resulting in a loss of muscle oxidative phenotype. In an outpatient COPD population we revealed an even more pronounced decrease in type I muscle fibers in patients with sarcopenia,

compared with non-sarcopenic patients and healthy controls. Moreover, sarcopenic patients were characterized by selective atrophy of the type I fibers, independent of the more generalized type II atrophy in COPD as a whole. These findings could reflect a cross-talk between muscle mass and oxidative phenotype regulation, which might accelerate the muscle wasting process in COPD. Future research in this presumed cross-talk may provide new leads for targeted intervention. This study also indicates that sarcopenic patients with COPD seem extra vulnerable as not only their muscle mass but also muscle metabolism is affected.

The cause of abnormalities in body composition and structural changes within muscle in COPD not only involve disease specific factors (e.g. hypoxia, systemic inflammation, oxidative stress and use of corticosteroids) but also lifestyle factors. Lifestyle factors mainly concern smoking and physical activity, but also dietary behaviour. A poor dietary quality may accelerate disturbances in body composition in COPD, but only limited studies have investigated dietary intake from this perspective. We demonstrated differences in the quality of dietary intake between COPD patients with different body composition profiles. Patients with a low muscle mass had a low dietary quality reflected by low intake of micronutrients, especially vitamin D, and a lower intake of protein. Patients with both low muscle mass and abdominal obesity appeared most susceptible for a poor dietary quality. Therefore more attention and guidance is required for COPD patients in order to respect recommendations regarding healthy nutrition. This is presently undervalued relative to modifying sedentary behaviour and smoking cessation.

Exercise training is known to be effective in improving muscle function as well as exercise tolerance in patients with advanced COPD and is considered to be the cornerstone of pulmonary rehabilitation. The COPD guidelines recommend nutritional supplementation to prevent weight loss and promote weight gain in undernourished patients with COPD. However, the potential of nutritional strategies to enhance the efficacy of exercise training in COPD is not yet well established. The randomised placebo-controlled NUTRAIN-trial that we performed, investigated the additional effects of nutritional supplementation on top of exercise training in patients with low muscle mass, as integral part of an out-patient pulmonary rehabilitation program. The nutritional intervention was therefore easily implementable.

The results confirmed a good response to exercise training in COPD patients characterized by moderate airflow imitation and low muscle mass. New insights provided by this thesis include that, while targeted nutritional supplementation did not enhance muscle regain and improvements in lower limb muscle performance in these patients, beneficial effects were observed on nutritional status and inspiratory muscle strength. An unexpected finding was the decline in daily physical activity after exercise training in the control group, which was prevented by nutritional supplementation. These results of the NUTRAIN-trial provide new leads for optimisation of medical nutrition. Furthermore

the trial highlights the necessity in nutritional therapy to distinguish between supplementation of calories and protein and supplementation of specific nutrients. Moreover, the observed dissociation between physical performance and daily physical activity provides new leads for improvement of daily physical activity.

HEALTH CARE PROVIDERS

The present thesis gives important insights for health care providers. In order to develop and evaluate effective treatment strategies, individual assessment is required. Body composition needs to be assessed to distinguish not only muscle mass, but also to take body compositional shifts into account. These shifts include both the mass and distribution of muscle, fat and bone mineral density, which are able to serve as a stronger predictor of physical impairment. DEXA is the most appropriate tool for measurement of body composition, as it simultaneously allows for screening of highly prevalent osteoporosis in COPD. Assessment of dietary intake by dieticians is required not only to estimate total intake of calories, but also to identify possible nutrient deficiencies by comparing these with daily recommended intakes by the national Health Council. Daily intake of macro- and micronutrients is often below recommendations in COPD patients. An inadequate dietary intake might accelerate body compositional shifts, as reflected by differences in quality of dietary intake between patients with different body composition profiles.

This thesis therefore underlines the need to further tailor and accentuate nutritional guidelines for specific metabolic phenotypes. Moreover, nutritional and pharmaceutical industries are challenged to develop and optimize medical nutrition and supplements for patients with COPD distinguishing in providing high energy and/or protein or specific nutrients (e.g. vitamin D, poly-unsaturated fatty acids, resveratrol, and nitrate).

SCIENCE: FUTURE RESEARCH QUESTIONS

The findings in the current thesis might be important for researchers in the field. Meanwhile several new questions were revealed, which are presented in the discussion chapter. Nonetheless the presented findings create new opportunities. Future studies are needed to investigate the efficacy of tailored nutritional interventions for carefully selected COPD patient subgroups defined according to distinct clinical phenotypes. Furthermore, the challenge for future studies is to disentangle the mechanism behind the observed dissociation between physical performance and daily physical activity resulting from nutritional supplementation. Identification and measurement of outcome measures beyond muscle are required to unravel a broader potential of nutritional modulation in COPD.