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Lower-limb muscle function and exercise performance in lung cancer

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Reduced exercise performance is a common consequence of lung cancer and its treatment.\(^1\) It is apparent in across all stages of disease, and is associated with poorer functional independence, worse cancer treatment tolerability, and higher all-cause mortality.\(^2\) In patients with early stage lung cancer amenable to surgical resection, the main focus of exercise testing is on cardiorespiratory fitness; the capacity to deliver oxygen from the air to the skeletal muscles for energy production. Prior to surgery this focus is entirely appropriate as poor cardiorespiratory fitness is a risk factor for peri- and post-surgical complications including post-operative pulmonary complications (PPCs) and mortality.\(^3, 4\) Repeat testing following curative treatment is also of value, as the surgery itself will have further reduced lung diffusion capacity, and side effects of adjuvant treatment such as anaemia might have added detrimental impact.

Exercise performance is arguably a broader concept than cardiorespiratory fitness in that it is also influenced by muscular fitness; what skeletal muscle can do with oxygen once it is delivered; and the patient’s tolerance for exercise-induced symptoms, such as breathlessness and fatigue, which will eventually become limiting.\(^5\) Muscular fitness can be reduced at the point of lung cancer diagnosis owing to the natural older age, poor lifestyle and comorbidities in this patient group. It generally continues to decline unless the cancer
can be eradicated due to the cachexia syndrome, a heavy symptom burden leading to physical inactivity and disuse atrophy. With regards to limiting symptoms, about one-third of patients report muscle fatigue (an indicator of low aerobic muscle metabolism) as the factor that stopped them during an exercise test, in keeping with observations among other cardiorespiratory diseases.

In this issue of Respirology, Burtin et al. provide important and novel data on this topic. Among 64 patients following resection surgery for non-small cell lung cancer, both lung diffusion capacity and quadriceps muscle function were consistent independent determinants of exercise performance. A key strength of the work is that assessments included multiple tests of both dependant and independent variables of interest. Exercise performance was assessed using laboratory-based cardiopulmonary exercise testing on a cycle ergometer, and by the 6-min walk test. Whilst cardiopulmonary exercise testing provides the physiological gold standard and access to continuous metabolic data, field walk tests offer a more familiar and potentially relevant assessment to everyday living. The 6-min walk test is however self-paced, and can result in sub-maximal effort as reflected in the lower Borg scores for both breathlessness and leg fatigue observed at breakpoint in the study. Nonetheless, the two types of exercise stress the respiratory, cardiovascular and muscular systems differently, offering complementary information. Muscle testing employed an assessment of both quadriceps strength (the ability to exert a force) and endurance (the ability to continue to perform without fatigue). Although interlinked properties, quadriceps strength was more closely related to peak oxygen uptake whilst
quadriceps endurance was more closely related to peak work rate and walking distance. Lower limb muscle power (the ability to perform work in a time period) was not explicitly tested, but has previously been associated with walking distance among patients with advanced lung cancer,\textsuperscript{10} highlighting the merits of complete muscle testing for a comprehensive understanding of exercise determinants.

As Burtin et al.\textsuperscript{8} describe, such thorough profiling could be used to effectively guide exercise prescription so it targets the factors affecting each individual’s performance. Whilst the current evidence base regarding optimal exercise prescription for patients with lung cancer is limited, a combined approach with both resistance and aerobic training is likely to be most effective. Indeed most physical activity guidelines for patients with cancer recommended this approach.\textsuperscript{11} Recent trials in patients with lung cancer listed for or following surgery have shown benefits from combined exercise resistance and aerobic training. Licker et al. found pre-operative high intensity interval training and resistance training improved exercise performance, as compared to an exercise and lifestyle advice group who experienced deterioration in peak oxygen consumption during the pre-operative waiting period.\textsuperscript{12} Similarly, Edvardsen et al. found a 20 week high intensity endurance and resistance training programme, starting 5-7 weeks post-operatively improved peak oxygen uptake, quadriceps mass and strength, and physical function as compared to a usual care control group.\textsuperscript{13} In the exercise group, the magnitude of change in peak oxygen uptake and muscle strength was such that it improved beyond baseline pre-operative values.
Burtin et al’s findings also beg the question, if lower limb muscle function can be specifically targeted, will this translate into enhanced exercise performance? The effects of isolated resistance training in this patient group are not well understood, however the ongoing LUNGEVITY trial (comparing aerobic training, resistance training, or combined training, to attention control on peak oxygen uptake, NCT01068210) should provide some answers. There is some evidence supporting this concept from trials of neuromuscular electrical stimulation though no current data specific to this patient group or setting.\textsuperscript{14}

To continue building this evidence base and to ensure the successful translation of findings into practice, we must acknowledge the barriers to exercise in lung cancer. Current barriers impeding translation include limited access to exercise services for patients with lung cancer (cancer rehabilitation programs are scarce, and not all pulmonary rehabilitation programmes accept lung cancer diagnoses); limited knowledge, confidence, prioritisation and time for physicians or surgeons to discuss exercise in clinic appointments; and lack of resources including funding and staffing to help embed exercise into usual care.\textsuperscript{15,16} As further evidence supporting exercise training emerges, efforts must be drawn to effectively translating this to maximise effect to those accessing clinical services worldwide.

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