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Reply to Cavalheri *et al.*

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We appreciate Cavalheri *et al.*'s [1] comments on the strengths and limitations of our study. Indeed, we included a majority of relatively physically fit patients with low-grade chronic obstructive lung disease (COPD), and the high-intensity interval training was solely performed within 2–3 weeks preceding lung cancer surgery [2, 3]. These conditions prevail in most reference centres and, in the current trial, patients with low aerobic fitness or severe comorbid conditions were not excluded.

Importantly, regardless of the presence of COPD and the degree of aerobic fitness ($\text{VO}_2\text{peak} < 16$ or ≥ 16 ml/kg/min), we observed a functional improvement (increase in VO_2peak , peak WorkRate and 6-min walk distance) and a reduction in postoperative pulmonary complications (PPCs) when the target physiological end-points were achieved ($+10\%$ VO_2peak and/or $+30$ m 6-min walk test). Low preoperative VO_2peak and COPD were independent predictors of PPCs, and subsequent analysis of our data indicates that the occurrence of PPCs is associated with reduced survival at 2 years following surgery (log-rank test, $P = 0.009$), whereas the development of cardiovascular complications was not associated with a poorer outcome. Two recent cohort studies confirmed these findings regarding the negative prognostic implications for PPCs in lung cancer surgery [4, 5]. In contrast to COPD, poor aerobic fitness is a potentially modifiable risk factor. Therefore, preoperative physical training should be considered a cost-effective approach to minimize the risk of PPCs, in association with other interventions (e.g. restrictive fluid management, protective lung ventilation and minimally invasive surgery) that are included in modern enhanced perioperative recovery protocols.

We agree also that further studies should be conducted to evaluate the long-term functional changes and clinical outcome following initiation/continuation of a rehabilitation programme particularly in the postoperative period. In a similar surgical population, Edvardsen *et al.* [6] reported marked functional improvement when a high-intensity interval training protocol was initiated 5–7 weeks after lung cancer resection and continued over 20 weeks

(60 min, 3 times a week). Compared with the control group, the exercise group presented significant increase in aerobic capacity ($+3.4$ ml/kg/min of mean VO_2peak , $+4.3$ steps in stair run), in carbon dioxide diffusion capacity ($+5.2\%$ predicted) and in muscle mass ($+1.36$ kg).

Ultimately, the perioperative period represents a window of therapeutic opportunity, the patient being more receptive to adopt a healthier lifestyle. Using an interdisciplinary approach, rehabilitation programmes including physical training coupled with nutritional and psychological support are aimed to empower patients for 'taking control' and improving their survival and quality of life.

Conflict of interest: none declared.

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