



# Prehabilitation in video-assisted thoracoscopic surgery lobectomy for lung cancer: current situation and future perspectives

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We thank Prof. Giles *et al.* from Canada for their thoughtful comments and suggestions about our recent article (1). Our group published a study in *Anesth Analg*, reporting that a 2-week, home-based, multimodal prehabilitation strategy could produce clinically relevant improvements of perioperative functional capacity assessed via the 6-minute walk distance (6MWD) in patients undergoing video-assisted thoracoscopic surgery (VATS) lobectomy for lung cancer (2). In this randomized controlled study, we enrolled 73 patients (37 in the prehabilitation group and 36 in the control group). The simple home-based, multimodal prehabilitation program includes aerobic and resistance exercises, respiratory training, nutrition counseling with whey protein supplementation, and psychological guidance utilizing a pictured instruction booklet, completion diaries, and regular visits to encourage adherence.

Many studies have been published regarding preoperative exercise for lung cancer. However, though positive conclusions are often reported, heterogeneity is extremely obvious from differences in interventions, and population and outcome measurements, especially preoperative training interventions (3). All exercise modes in the published literature focus mainly on aerobic exercise with or without resistance exercise and inspiratory muscle training (IMT) (4-12). However, our study contributed most to the innovation of patient-centered multimodal prehabilitation methods for patients undergoing VATS lobectomy by including respiratory training, nutritional supplements, and psychological optimization. Based on our limited clinical

practice experience, we also made improvements to exercise duration, modality, and place compared with other forms of preoperative training associated with pulmonary surgery. Instead of advocating fixed forms of exercise, our patients could choose any form of aerobic exercise at their discretion with restrained frequencies, durations, and intensities to improve acceptance (4-8,11,12). Considering that the urge to proceed with surgery requires shorter exercise interventions, the duration of prehabilitation was simplified to approximately 2 weeks, compared with 4-8 weeks in most published studies (4,8-11). We found that it was also more convenient for patients to perform the prehabilitation program at home under various types of guidance including telephone follow-up (8). We therefore tried to establish a more flexible, feasible, and economical way of benefitting the clinical wide-range application of prehabilitation programs that may occur in the near future.

As noted by Giles *et al.*, both intervention and control groups in our analysis were primarily fit and young (mean, 56 years old), with baseline pulmonary functions within normal levels (FEV<sub>1</sub> and FVC >90% predicted, FEV<sub>1</sub>/FVC >70%), although the inclusion criteria were not strictly restricted to age (adult patients <70 years old) or preoperative pulmonary function. Giles *et al.* commented that these factors might limit the generalizability and practical significance of this study, which we also mentioned in our publication. However, we noted a rising trend of lung cancer incidence in females and in the younger population in China (13,14), and the fact that increasing numbers of

patients undergoing lobectomy for lung cancer have normal pulmonary functions, given that fewer patients have tobacco exposure or a history of chronic pulmonary obstructive disease (COPD) (15). For patients with impaired pulmonary function or COPD undergoing lung cancer resection, the role of preoperative exercise is still uncertain because of limited data (10). Nevertheless, it had been indicated that patients with a lower baseline walking capacity were more likely to gain meaningful improvements in physical function from prehabilitation (16). Furthermore, a recent randomized controlled trial in elderly patients (aged  $\geq 70$  years) scheduled for lung cancer surgery demonstrated that short-term pulmonary prehabilitation combined with aerobic endurance and IMT was a feasible strategy with positive physical and psychological effects (6). Therefore, we consider the benefits of prehabilitation strategy to be more prominent in patients of an advanced age and pre-existing impaired lung function or COPD, such that routine exercise plans should be carefully tailored for this group.

What outcomes are important to patients? For randomized controlled trials, the outcomes that highly related with clinical relevance should be used as the primary outcome, such as length of stay (LOS), morbidity, and mortality. While patients always equate recovery with a return to their normal activities (17). Obviously, LOS, morbidity, mortality, and quality of life deserved higher priority in our context, but 6MWD as the patient-centered outcomes was used as the primary end point in our trial. The 6-minute walk test as a measurement of the functional performance of physically demanding activities of daily living was previously shown to be a simple and sensitive assessment to estimate postoperative patient-reported outcomes (18). In addition, considering the relatively low incidence of complications and short LOS of VATS lobectomy for lung cancer (19), the sample size will need to be very large with corresponding high research costs and a long study duration if the classical prognostic indicators are evaluated as the primary outcome. The overall study was not powered based on these outcomes, hence, it is not surprised that null effects were observed in clinically relevant outcomes possibly due to the lack of statistical power.

We consider our article to be an exploration of the prehabilitation program and an attempt to provide clinical evidence for the feasibility and effectiveness of a 2-week home-based multimodal prehabilitation protocol for VATS lobectomy for lung cancer. However, details of the program such as the exercise content, duration, frequency,

intensity, and methods to improve compliance should be further optimized. Additionally, it is necessary to carry out a multicenter prospective study with LOS, morbidity, mortality, or even long-term outcomes as the primary end point to determine the possible influence on current “standard medical care”, or as guideline recommendations. Advanced age, COPD, a high body mass index, cardiovascular morbidity, low cardiorespiratory fitness, and a positive smoking status are well-established risk factors for postoperative complications (9). Therefore, it would be advisable to include high-risk patients as the first research subjects to explore the impact of a short-term family multimodal prehabilitation strategy on clinically relevant outcomes after VATS lobectomy.

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### Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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