Editorial Commentary

# Prehabilitation prior to lung cancer surgery: a small step forward

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Ever since the National Emphysema Treatment Trial (1), it has been clear that preoperative pulmonary rehabilitation improves function in patients preparing to undergo lung resection. However, the ensuing supporting comparative literature has consisted of small randomized trials and moderately sized cohort studies with a variety of limitations (2). We are left with mixed impressions as to the role of prehabilitation in patients awaiting lung cancer surgery.

In response, Liu and colleagues (3) conducted a randomized controlled trial of unselected patients undergoing thoracoscopic lobectomy at a university hospital in Beijing for non-small cell lung cancer (NSCLC). Patients were randomized to usual medical care or to a home-administered trimodality prehabilitation program (aerobic/resistance/pulmonary exercises, nutrition, and psychological support) for two weeks prior to surgery. The primary endpoint was improvement in the six-minute walk distance (6MWD). Secondary outcomes were pulmonary function tests, quality of recovery, and physical and mental well-being. Concealment of allocation and blinding of outcome assessors both appeared to be satisfactory.

They show that after a median of 15 days of prehabilitation, patients walked 60 meters further on the 6MWD as compared to the control group at 30 days after surgery. Those in the experimental group had a 45-meter increase from baseline at the end of the program, just prior to surgery, compared to only 3.8 meters in the control arm. There were no differences in any of the secondary outcomes.

A previous systematic review (2) showed that improvement in recovery (reduced length of stay and overall complications) is possible after a prehabilitation program, albeit with high heterogeneity. While the present study achieved the minimum clinically important difference threshold of 30 meters [as determined among COPD patients undergoing rehab; (4)], it did not show a difference in clinically meaningful endpoints. Why this discrepancy? Certainly one answer is that it was not powered to do so, and with only 73 patients the likelihood of type II error is high.

It is also useful to note that the patient population differed substantially from that of other reports. Patients in this trial were young (mean 56 years old), female (70%), with a normal-range BMI (mean BMI of 23). Baseline pulmonary function tests were near normal and 90% had never smoked. Only one patient had COPD, and few patient (11%) were classified as ASA III or IV. Baseline 6MWD measured 560 m, similar to healthy population averages (5).

So, what have they demonstrated? Primarily that a short but rigorous multimodal prehabilitation program can result in a measurable improvement in cardiopulmonary performance in generally young and fit patients. It is questionable whether this result will be replicated in a more heterogeneous population of patients with lung cancer, especially those seen in Europe and North America. It is possible that if a wider range of patients experience this degree of improvement, they may indeed have improved clinical outcomes. Alternatively, the typical patient may not be fit enough to begin with to benefit from this particular

intervention.

The authors merit acknowledgement on several fronts. First, they addressed many of the methodologic issues of prior studies, such as concealment, adequate randomization and blinding of assessors. While not totally novel, the prehabilitation program was well considered, although quite demanding. The interventions were comprehensive, the course was abbreviated to 2 weeks to eliminate concerns associated with delay to oncologic resection (6), and home administration makes this widely applicable and potentially more affordable.

Thus, while their results do not provide further guidance regarding whether prehabilitation should be standard therapy for patients undergoing lobectomy for NSCLC, they do show us that methodologically sound studies on prehabilitation are possible. Second, that not all patients with lung cancer are comparable in terms of baseline function and comorbidity. A large-scale multinational RCT would be necessary to address the scope of this question and to ascertain which patients truly stand to benefit from prehabilitation. As to how this should be conducted, those designing such a trial would do well to consider the methods used here as a starting point.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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