Editorial Commentary

Prehabilitation in thoracic surgery: strong signal or surgical confounding?

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Preventing postoperative pulmonary complications (PPCs) following lung resection surgery is a key objective of perioperative care. PPCs are a leading cause of morbidity, with reported incidence of 15% to over 40%, depending on patient risk factors, surgical characteristics, and PPC definition (1,2). Despite advances in surgical techniques, anaesthetic management, and enhanced recovery after surgery pathways, PPCs continue to be associated with longer hospital stays, higher healthcare costs, and reduced quality of life (2,3).

Historically, efforts to prevent PPCs have primarily involved postoperative interventions such as respiratory physiotherapy and early mobilisation. More recently, preoperative exercise interventions that aim to improve respiratory muscle strength and physiological reserve are gaining traction as effective methods to prevent PPCs after lung resection (4). Preoperative exercise training can be enhanced with the addition of structured educational, nutritional and psychological interventions that aim to further improve physiological and psychological reserve before surgery (5). The multicentre randomised controlled trial conducted by Brat and colleagues provides a timely addition to the prehabilitation literature in this area (6).

This prospective multicentre randomised trial was conducted across three hospitals in the Czech Republic between 2021 and 2024. Adults scheduled for lung resection due to confirmed or suspected malignancy, who were able to undergo cardiopulmonary exercise testing (CPET) and were identified as having impaired ventilatory efficiency with a minute ventilation for carbon dioxide output (VE/VCO_2) slope ≥33 were considered at high risk of a PPC and were eligible for inclusion (7). Of 474 patients screened for eligibility, 150 (32%) met the inclusion criteria. Eighteen (12%) declined to participate in the trial, leaving 132 patients to be randomly allocated to usual care or a prehabilitation intervention comprising preoperative respiratory muscle training (RMT), smoking cessation advice, nutritional screening, and psychological support. Both groups received standard perioperative and postoperative care, including respiratory physiotherapy and early mobilisation. Ten patients (7.6%) were lost to follow-up with outcomes reported for 122 patients.

Several methodological issues warrant consideration, as they may influence the internal and external validity of the trial. First, the authors do not explicitly state whether group allocation was concealed from researchers who determined participant eligibility. Inadequate allocation concealment raises the possibility that knowledge of group assignment

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could influence enrolment decisions, potentially biasing randomisation. Second, participants were not blinded to group allocation by a sham intervention. High-quality prehabilitation trials have successfully employed sham RMT utilising the same training device set to the minimal loading possible, to blind participants for expectancy effects (8). Third, there was a higher proportion of open thoracotomies in the usual care group (45% *vs.* 33%). Open thoracotomy may be associated with higher rates of pulmonary complications and persistent air leak (PAL) compared with minimally invasive approaches (9). This imbalance raises concern that the observed difference in PPC incidence may, at least in part, reflect surgical approach rather than a true treatment effect.

Although randomisation was stratified by surgical approach, residual baseline differences between groups, such as in the proportions of patients having an open thoracotomy, may be a major confounder to observed outcomes. This highlights the importance of multivariable statistical models to manage possible confounders. The reliance of Brat *et al.*'s clinical trial on univariate analyses makes it challenging to definitively attribute observed reductions in complications and length of stay to the intervention itself, rather than differences in surgical invasiveness or other confounding variables.

RMT of both inspiratory and expiratory muscle training was delivered through supervised, face-to-face physiotherapy sessions three times per week, supplemented by a daily home-based programme. Training loads were set at 50–60% of measured maximal inspiratory and expiratory pressures, broadly aligning with established dosing principles in the literature (10). This has been shown to improve respiratory muscle strength, breathing control, and symptom burden in both surgical and non-surgical populations (11,12). The inclusion of expiratory muscle training in addition to inspiratory loading represents a particular strength, given its relevance to cough effectiveness and secretion clearance. Furthermore, the programme accurately reflects the real-world constraints of limited preoperative timeframes and respiratory muscle loading capped at levels prioritising tolerability over maximal physiological adaptation.

The authors report 100% attendance at supervised sessions and adherence to the home-based programme. While encouraging, these adherence rates substantially exceed those reported in most prehabilitation trials (13). This may imply that the intervention was delivered under highly controlled conditions, which may prove challenging to replicate into clinical practice outside well-resourced research environments.

The primary outcome was a composite of PPC diagnoses within 30 days of surgery, including pneumonia, atelectasis, respiratory failure, acute respiratory distress syndrome, and a PAL. PPCs occurred in 35 (55%) of the usual care group patients and 20 (34%) in the prehabilitation group [odds ratio (OR) 0.44, 95% confidence interval (CI): 0.21 to 0.91, P=0.029]. However, the observed reduction in PPCs was largely attributable to a between-group difference in PAL incidence, which has also been highlighted as a possible concern by others (14). This concern may be justified, given the control group in the study had a higher proportion of patients having open thoracotomy. Increased rates of PAL has been associated with open thoracotomy (9,15), although recent evidence has found similar rates of PAL with minimally invasive thorax surgeries (16). Regardless, the inclusion of PAL as a PPC within the Brat *et al.*'s study does not align with current consensus PPC diagnostic frameworks, which specifically exclude diagnoses such as PAL, pneumothorax and pulmonary embolus PPC definitions (17). If PAL is excluded from the study's composite PPC outcome, the difference between groups is no longer statistically significant [23/64 *vs.* 14/58, OR 0.57, (95% CI: 0.26 to 1.25), P > not significant (NS)].

Beyond uncertainty regarding the reported results, several factors should be considered when applying findings to everyday clinical practice. Replicating this approach requires access to preoperative CPET to identify patients exceeding a VE/VCO_2 threshold. The use of VE/VCO_2 slope as an inclusion criterion is physiologically sound; it provides a precise, objective measure of ventilatory efficiency that is a robust predictor of postoperative mortality in this population (7) yet in practice, access to CPET is limited in many centres. Recent international survey data suggest that just 10–15% of centres actively engaged in prehabilitation routinely provide CPET as part of thoracic surgical pathways (18). The trial also relied on a 2-week preoperative window to deliver a relatively resource-intensive, supervised RMT programme. In many healthcare systems surgical timelines following a decision to operate are shorter, and delaying surgery to accommodate prehabilitation is neither feasible nor acceptable (13). Shorter periods of RMT may be feasible and worthwhile (8) but this has not yet been explored in this cohort.

Face-to-face attendance requirements are also associated with reduced compliance in real-world settings (19). The burden placed on patients to attend frequent in-

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person sessions should also be considered, particularly considering the likely financial and psychological barriers to prehabilitation participation among cancer patients and their families (20). This raises the question of whether similar benefits could be achieved using less resource-intensive approaches. Systematic reviews of RMT suggest that improvements in postoperative outcomes are achievable across a range of dosages and that highly supervised protocols may not be necessary (21). It also remains unknown in this population whether other interventions, such as a single preoperative physiotherapy session focused on education and teaching of breathing exercises, could deliver comparable benefits with lower patient and healthcare resource burden. Such approaches have demonstrated efficacy and improvements in health care costs in other surgical populations and may be more amenable to widespread implementation (22-24).

In Brat *et al.*'s study, both groups received postoperative physiotherapy described as 'standard care'. However, the specifics of this were not described in detail. Postoperative physiotherapy interventions may influence outcomes such as atelectasis, secretion retention, or length of stay. Future trials should explicitly report all components of interventions, including postoperative physiotherapy care, using frameworks such as the Template for Intervention Description and Replication (TIDieR) checklist. This underscores the complexity of isolating the effects of preoperative interventions within dynamic perioperative care pathways. Despite the identified methodological limitations of the Brat *et al.* study and questions about its external generalisability, viewed alongside the broader literature, their findings add to a growing body of randomised evidence reporting the impact of preoperative RMT on reducing the risk of PPCs after major surgery (25). Cumulative evidence and sequential analyses now suggest that further trials designed solely to establish efficacy are unlikely to change this conclusion (26). The preoperative period can serve as an active therapeutic window rather than a passive waiting phase.

Future research should focus on cost-effectiveness and identifying the minimum training windows required to impact PPC risk. Emerging evidence from a large, multicentre trial in cardiac surgery suggests that even a few days of training could be effective, with significant PPC reductions observed following a median of just three days of preoperative inspiratory muscle training (8). While such findings require replication in lung resection cohorts, they suggest that even a short preoperative window may be effectively utilised. Replication in other surgical cohorts, including lung resection, is needed. It is also vital to consider how to minimise the risk of PPC in all patients awaiting lung resection, not just those considered high-risk. Simple, low-cost, once-off preoperative education and breathing exercise training demonstrated to halve the risk of PPC in all patients awaiting major abdominal surgery (24) is yet to be rigorously assessed in the thoracic surgery population. Lastly, implementation science methods are needed to develop strategies that align with real-world surgical pathways to determine how such programmes can be adapted to local health systems and to rethink how respiratory prehabilitation can be delivered efficiently, equitably, and at scale within physiotherapy service constraints, ensuring that physiotherapy-led interventions move beyond efficacy trials toward sustainable integration within routine thoracic surgical care.

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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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