whether COVID-19 respiratory failure was truly ARDS; however, there is no indication that the COVID-19 group did not receive evidence-based ARDS care on the basis of the similar driving pressures and high rates of proning in the COVID-19 group. In summary, this important work highlights both the severity of COVID-19 and the limited range of specific therapies, particularly early in the pandemic, while also confirming the overall similarity in the presentation of COVID-19 ARDS to other etiologies. It remains to be seen if the experience and therapeutics we have gained since those early days will improve outcomes in COVID-19, or if to quote Muddy Waters, the times don't get no better. ■

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Is Preoperative Exercise Training the New Holy Grail for Patients Undergoing Major Surgery?

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Surgical advances and postoperative care have improved recovery from most major surgeries. However, despite advances in perioperative care that have improved safety and accessibility for patients potentially at risk, there remains a group of patients who still have suboptimal recovery. Approximately 20–50% of patients undergoing surgery develop a postoperative complication with resulting increases in hospital length of stay and subsequent increases in overall healthcare costs. After surgery, patients also experience physical fatigue and periods of physical inactivity–induced loss of muscle mass, deconditioning, and poor quality of life (1). These complications occur predominantly in moderate- to high-risk patients who often present with modifiable risk factors.

An emerging body of evidence reports that the preoperative status of the patient has a critical impact on postoperative recovery (2, 3). Prehabilitation describes the process of enhancing preoperative functional capacity to enable patients to withstand the stress associated with a pending major procedure. Prehabilitation intervention may involve a single mode or be multimodal in addition to offering medical optimization concentrating on patient nutritional, psychological, and/or physical preoperative status, with the main aim of improving readiness for impending surgery.

In this issue of *AnnalsATS*, Assouline and colleagues (pp. 678–688) contribute to the growing body of evidence on the role of preoperative exercise (4). The authors report results of a systematic review with

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meta-analyses examining the effectiveness of preoperative exercise training in reducing postoperative pulmonary complication rates in patients undergoing cardiac, lung, esophageal, or abdominal surgery, when compared with usual care. Secondary outcomes included change in preoperative functional status, postoperative mortality, cardiovascular complications, and hospital length of stay.

Twenty-nine trials with sample sizes ranging from 15 to 276 (median, 44) were included (involving 2,070 patients). Most of the included trials presented low risk of bias. Data from 1,864 patients demonstrated a moderate quality of evidence, favoring preoperative exercise training in reducing postoperative pulmonary complications by 48% (47% cardiac, 55% lung, and 50% abdominal surgery), when compared with usual care. Length of hospital stay, postoperative pneumonia, and atelectasis were also significantly reduced in the preoperative exercise training group across all surgeries. These results are consistent with those of previously published systematic reviews in individual surgical populations (2, 5–7).

A unique aspect of this systematic review was the subgroup analysis involving different training modalities and durations. Interestingly, trials including endurance exercises or combined endurance and respiratory exercises were conclusively demonstrating a significant reduction on postoperative pulmonary complications. Certainly, breathing exercises and inspiratory muscle training are increasingly being advocated in prehabilitation, although it is not clear from the results in this review whether the higher proportion of lung cancer trials influenced this result. The type and intensity of exercise training that provides best outcomes is a hot topic in prehabiltation, with more recent trials comparing continuous with intermittent and high- and lower-intensity interventions (8).

Assouline and colleagues (4) report that preoperative exercise training interventions of $\geqslant$1 week in duration were equally effective in reducing postoperative pulmonary complications across all major surgeries. This is an important result because in many countries, there is a short time workup period between diagnosis and surgery, for example, in lung cancer. It was previously considered that 1 week of training is not long enough to impact postoperative outcomes (5).

In the study conducted by Assouline and colleagues (4), patients receiving preoperative exercise training were discharged from the hospital more than 2 days earlier. Interestingly, in some of the included trials, even a brief exercise intervention provided significant results. This evidence, in addition to evidence of lowering postoperative pulmonary complications, is by far the most appealing evidence for the effectiveness of preoperative exercise training. Reducing these two end points impacts both the patient and the health-system costs. However, caution should be exercised, as larger trials are needed to reduce the heterogeneity evident for length of hospital stay.

Limitations of the current evidence, including the current systematic review, are the heterogeneity among the studies. The patient population enrolled varies greatly, and it is unclear whether all patients benefit or whether only those deemed at higher risk for surgery benefit. The effect of risk stratification was not included in this review. Furthermore, identification of responders to preoperative exercise training has not been investigated thoroughly (9). Identification of responders will assist in reducing trial heterogeneity and allow recruitment smaller sample sizes to achieve separation between groups. The variety of outcome measures that exist in current literature make comparisons between studies difficult and meta-analyses less reliable. For postoperative pulmonary complications, a recent report sought to provide definitions of complications to move the field forward (10).

We still face several challenges in generalizing, interpreting, and scaling the preoperative exercise interventions reported in the current literature. The main reasons for this are that, despite the promising results from Assouline and colleagues (4), we remain unsure which elements included in a preoperative training program are most effective; we do not have a standardize exercise intervention outlining intensity, duration, and frequency. It is clear from this review and others that current trials include a wide range of preoperative exercises, including aerobic, resistance, and respiratory-muscle training. The intensity ranges from moderate to high and is measured in different ways. The frequency of the preoperative exercise sessions is also variable, with studies reporting from three times a day to twice a week. The duration of the preoperative exercise programs is also inconsistent, ranging from 1 to several weeks before surgery. Assouline and colleagues (4) have reported improvements in 1 week of training, but would 1 week be sufficient for a higher-risk patient with sarcopenia or frailty? In addition, because of the unprecedented circumstances of the coronavirus disease (COVID-19) pandemic, the setting of preoperative exercise training is now being discussed more often. Supervised training is clearly superior, but does this need to be conducted in large centers? Can we provide different approaches to training for patients presenting with different needs?

Is it still a long and perhaps winding road to ultimately reach the holy grail? We do not yet have enough specific evidence that allows prehabiltation implementation at scale, despite the positive outcomes from this well-presented systematic review with meta-analyses. The future of prehabiltation before major surgery should involve multicenter, international trials with adequate sample size and appropriate power. However, the intervention needs to be able to be implemented in different healthcare settings, including those serving rural and remote individuals, so further research investigating home- or community-based prehabilitation using telehealth-, app-, or web-supported exercise training is warranted, as is understanding the role of the different prehabilitation elements and the type, timing, intensity, setting, and frequency of their application. Deciding on validated core outcomes will assist interpretation of studies. The cost benefit of prehabilitation must also be explored alongside any clinical trial. Understanding the answers to these questions will most definitely establish preoperative exercise training as the most recent holy grail of perioperative medicine. ■

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