Challenging the Evidence for Pulmonary Rehabilitation in Pulmonary Fibrosis Is Good, Enough?

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Pulmonary rehabilitation (PR) is a comprehensive, multifaceted treatment of undisputed importance for people who live with chronic lung diseases. Evidence of clinical effectiveness is strong for people with COPD, and maturing for diseases such as interstitial lung disease (ILD), bronchiectasis, chronic asthma, and pulmonary hypertension. The PR “package” promotes a variety of physiological and behavioral adaptations capable of addressing various mechanisms known to contribute to common respiratory issues, such as breathlessness and exercise intolerance (eg, limitations of ventilatory capacity, energy supply, or peripheral muscle function). One might therefore presume PR confers equal benefits across different diseases. We accept, however, that differences in pathophysiology, comorbidities, phenotypes/endotypes, and therapeutic options between diseases mean disease-specific evidence is essential to inform clinical decision-making. In this issue of CHEST, Nolan and colleagues asked, “how do treatment responses to PR compare between people with IPF and people with COPD?” This was justified on the grounds that PR is considered a standard of care for people with IPF in the United Kingdom (weak recommendation), and conducting the ideal RCT would entail the ethical dilemma of withholding (or denying) treatment that may be underused and underresearched, but is not necessarily “under-effective.” Weak recommendations for PR in IPF in international guidelines may seem surprising to some readers, because PR is associated with greater benefits across more outcomes than disease-modifying antifibrotic agents. Nolan et al’s3 approach involved comparisons of “real life” data from 163 propensity-matched pairs of IPF or COPD participants who undertook usual PR care (8 weeks’ supervised program) at an established outpatient hospital department.

Propensity matching has gained popularity in recent years in the field of PR research, including studies examining its role for people with bronchiectasis as well as comparisons between various types of PR models (examples noted as originating from within the same author group). The technique can be applied in different ways, with interesting commentary regarding its use in respiratory medicine previously described in this journal and more detailed information available via other sources. Propensity matching helps reduce sources of variability between groups to mimic more robust experimental conditions such as RCTs in which randomization would typically limit the key difference between groups to treatment exposure. Variable selection and the sequence in which they are applied during matching can influence study findings and introduce issues of selection bias to comparator groups but can also be overcome via strategies such as randomization and sensitivity analyses exploring different candidate predictors (not described in this study). Nolan et al used propensity matching to control for covariate influences on outcomes (eg, baseline age, sex, BMI, dyspnea [Medical Research Council], self-
reported Chronic Respiratory Questionnaire-total score (CRQ-T) and exercise tolerance (incremental shuttle walk test distance, ISWT)), with both groups exposed to the same treatment. This resulted in two groups satisfactorily matched across these important baseline characteristics. Their main findings demonstrated clear benefits from PR, on average, across outcomes of ISWT, MRC (Medical Research Council dyspnoea scale), and CRQ-T within both the COPD and IPF groups, with no appreciable difference in responses between groups ($P > .05$ for all).

The authors also explored the potential impact of PR on mortality, with a greater proportion of noncompleters (failure to complete $\geq 8$ sessions) and nonresponders (attendees at post-PR reassessment who completed $\geq 8$ sessions but did not achieve clinically important improvements in ISWT) dying in the year following PR compared with responders (attendees at post-PR reassessment who completed $\geq 8$ supervised sessions and achieved clinically meaningful benefits in ISWT) (40%, 24%, 10%, respectively; $P < .01$), presenting a 3.5- to 4.5-fold increased risk in Cox proportional hazards regression modeling (adjusted for age, smoking status, FVC % predicted, MRC, prescription of anti-fibrotic therapy, and frailty status). The potential impact of PR training gains on mortality has been previously shown in people (nondirective)(3) and frailty status). The potential impact of PR training gains on mortality has been previously shown in people (nondirective)(3) and frailty status). The potential impact of PR training gains on mortality has been previously shown in people (nondirective)(3) and frailty status). The potential impact of PR training gains on mortality has been previously shown in people (nondirective)(3) and frailty status). The potential impact of PR training gains on mortality has been previously shown in people (nondirective)(3) and frailty status).

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So what should we make of these findings? The data from Nolan and colleagues(3) do not provide definitive cause and effect evidence of PR effectiveness in ILDs (nor did it aspire to). However, it does add to a rapidly growing evidence base currently represented via “weak” clinical recommendations. Guidelines are typically informed by processes that rate the certainty or trustworthiness of evidence, with RCTs usually sitting at the top of evidence hierarchies. No one would deny that treatment decisions need to be evidence-informed, and that robust data from high-quality RCTs constitute ideal evidence for such purposes. However, practical and ethical challenges now inhibit our ability to rely solely on RCT-informed decision-making in this space. What other types of evidence might be considered “good enough” to improve clinical practice? And how specific must evidence be for individual lung diseases, considering there are more than 100 different ILDs? People with ILD do not likely have the time to wait until ideal evidence emerges. In the meantime, policymakers may need to consider whether “best available” evidence is good enough to inform evidence-based practice.

References