Is There Really A Controversy Surrounding the Effectiveness of Respiratory Rehabilitation in COPD?

We have recently witnessed an unfortunate debate regarding the effectiveness of respiratory rehabilitation in COPD.1-2 Some of the views expressed reflected views held some years ago that exercise in patients with COPD was of no value since these patients were so limited by their irreversible airflow obstruction. The debate was also limited by an incomplete appreciation of the modern literature on rehabilitation in which randomized controlled trials have shown clinically important changes in health-related quality of life. Given the commitment required from the patients, their families, and the professionals who assist in their care, it is incumbent on those involved with respiratory rehabilitation to provide the necessary information to satisfy all parties of the value in promoting this treatment modality. Such information is also important for organizations that endorse respiratory rehabilitation in their practice guidelines and for health-care administrators who decide on funding and reimbursement.

Ongoing discussions of the effectiveness of rehabilitation resulted in a meta-analysis3 of clinical trials of respiratory rehabilitation in COPD. The objectives of this meta-analysis were (1) to resolve uncertainty when reports disagreed; (2) to increase the statistical power for primary end points and for subgroups; and (3) to improve the estimates of effect size.4 The analysis included 14 randomized controlled trials comparing rehabilitation with usual community care in a total of more than 400 patients.

A useful way to interpret the results of this meta-analysis is in relation to the minimal clinically important difference (MCID), defined as the smallest difference perceived by the average patient. An intervention for which the magnitude of the treatment effect equals or exceeds the MCID should mandate a change in patient management, unless there are troublesome side effects or excessive cost.5 If the magnitude of the treatment effect is greater than the MCID, then there are strong arguments to recommend it. If the treatment effect comes from a meta-analysis of randomized controlled trials in which the results are homogeneous, the recommendation is even stronger6 (Table 1).

From this meta-analysis, it was noted that respiratory rehabilitation improved important domains of health-related quality of life in patients with COPD.7 It relieved dyspnea and enhanced the patients’ sense of control (mastery) over their disease. These clinically important effects (Table 2) compare well with other important modalities of care in COPD, such as bronchodilators or oral theophyllines.9,10 In fact, rehabilitation resulted in greater improvements in health-related quality of life and functional exercise capacity. Since the publication of this meta-analysis, data supporting the effectiveness of respiratory rehabilitation have continued to accumulate.11,12 The high level of evidence attached to the effect of rehabilitation on dyspnea and mastery is an important measure of the strength of the data supporting it. Few interventions in pulmonary medicine have reached such levels of evidence.

We believe that much of the controversy regarding the effectiveness of respiratory rehabilitation in COPD stems from the choice of clinical outcomes. Physical deconditioning and the emotional responses to chronic dyspnea contribute greatly to the resulting morbidity.13,14 Therefore, when selecting outcome measures, it is important to address the complaints most frequently identified by the patients.7,15 These complaints usually relate to health-related quality of life rather than FEV1 or oxygen consumption. Quality of life reflects a change in at least one of the following four domains: (1) physical and occupational function; (2) psychological state; (3) social interaction; and (4) somatic sensation.13,16,17

Initial measures of quality of life relied on semistructured interviews, questionnaires related to fixed personality traits, or measures borrowed from the psychosocial sciences.18,19 Such instruments were often limited by their validity (the capacity of an instrument to measure what it claims to measure20). Some investigators preferred to develop their own questionnaires or to adapt
existing instruments.21 The disadvantage of this approach was all too evident in trials of theophylline in COPD in which nonvalidated diary questionnaires failed to show significant improvements,22 yet trials in which valid, responsive, and interpretable questionnaires were used noted important improvements in quality of life.9,10,23

A variety of disease-specific quality-of-life measures have now been developed to assist in discriminating between groups of subjects and in evaluating changes in individuals or among groups over time.20,24-28 Such instruments should be valid, responsive (the ability of an evaluative instrument to detect real change, even when it is small), and interpretable (the ability to identify whether a change in score represents a small, moderate, or large clinical improvement or deterioration).29 A disease-specific instrument is more likely to be responsive to change than a generic instrument,29 as it contains questions regarding symptoms, activities, and participation most likely to relate to a particular diagnostic category.

If the properties of the measuring instruments have not been ascertained beforehand, they may fail to detect clinically important changes and lead to the erroneous conclusion that quality of life does not change. This recently occurred in an excellent, well-designed trial of rehabilitation in which significant differences in exercise capacity, self-efficacy for walking, and shortness of breath scores were not accompanied by changes in a general quality-of-life scale.30

Unfortunately, reports evaluating the efficacy of respiratory rehabilitation still focus too often on laboratory measures of exercise. In a recent update on pulmonary rehabilitation in the United States,31 235 programs reported using a treadmill (37% of programs), a cycle ergometer (23%), or both (40%). Graded exercise tests are useful in

### Table 1—Levels of Evidence and Grades of Recommendations for Therapy*

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Grade of Recommendation</th>
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<tbody>
<tr>
<td>Level I</td>
<td>Grade A</td>
</tr>
<tr>
<td>Level I+</td>
<td>Results come from a single RCT in which the lower limit of the CI for the treatment effect exceeds the minimal clinically important benefit</td>
</tr>
<tr>
<td>Level I−</td>
<td>Results come from a meta-analysis of RCTs in which the treatment effects from individual studies are consistent, and the lower limit of the CI for the treatment effect exceeds the minimal clinically important benefit</td>
</tr>
<tr>
<td>Level II</td>
<td>Grade B</td>
</tr>
<tr>
<td>Level II+</td>
<td>Results come from a meta-analysis of RCTs in which the treatment effects from individual studies are consistent, and the lower limit of the CI for the treatment effect overlaps the minimal clinically important benefit</td>
</tr>
<tr>
<td>Level II−</td>
<td>Results come from a meta-analysis of RCTs in which the treatment effects from individual studies are widely disparate, and the lower limit of the CI for the treatment effect still exceeds the minimal clinically important benefit</td>
</tr>
<tr>
<td>Level III</td>
<td>Grade C</td>
</tr>
<tr>
<td>Level IV</td>
<td>Results come from nonrandomized concurrent cohort studies</td>
</tr>
<tr>
<td>Level V</td>
<td>Grade C</td>
</tr>
<tr>
<td></td>
<td>Results come from nonrandomized historic cohort studies</td>
</tr>
<tr>
<td></td>
<td>Results come from case series</td>
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</tbody>
</table>

*RCT = randomized controlled trial; CI = confidence interval. From Cook et al.6

### Table 2—Primary Results of the Meta-Analysis*

<table>
<thead>
<tr>
<th>Outcome Measure†</th>
<th>MCID5,6,6*</th>
<th>Common Effect</th>
<th>95% CI</th>
<th>p Value for Homogeneity</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>CRQf</td>
<td>0.5</td>
<td>1.0</td>
<td>0.6-1.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Fatigue</td>
<td>CRQf</td>
<td>0.5</td>
<td>0.8</td>
<td>0.4-1.0</td>
<td>0.36</td>
</tr>
<tr>
<td>Emotional function</td>
<td>CRQf</td>
<td>0.5</td>
<td>0.6</td>
<td>0.2-1.0</td>
<td>0.68</td>
</tr>
<tr>
<td>Mastery</td>
<td>CRQf</td>
<td>0.5</td>
<td>0.8</td>
<td>0.5-1.2</td>
<td>0.77</td>
</tr>
<tr>
<td>Maximal exercise capacity</td>
<td>Incremental cycle ergometer test</td>
<td>?*</td>
<td>8.3W</td>
<td>2.8-16.5</td>
<td>0.85</td>
</tr>
<tr>
<td>Functional exercise capacity</td>
<td>6-min walk test</td>
<td>54 m</td>
<td>55.7 m</td>
<td>27.8-92.8</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

*Modified from Laeasse et al with permission.3 MCID = minimal clinically important difference. ? = unknown.
†Natural units are those of individual items (seven-point scale) of the Chronic Respiratory Disease Questionnaire (CRQ).
rehabilitation for measuring the physiologic limitations of exercise,32 identifying associated conditions, or formulating training prescriptions. Simple timed walk tests33 are also useful as they are easy to learn, reproducible, valid, inexpensive, and may more closely reflect the type of disability associated with chronic respiratory or cardiac conditions. However, measures of exercise capacity (either maximal or functional) correlate only weakly or moderately with quality-of-life instruments in chronic lung diseases.24,25,34 Therefore, they should not be used to infer quality of life; rather, the latter should be measured directly.

In conclusion, over the last few years, evidence of the effectiveness of respiratory rehabilitation in alleviating symptoms and improving health-related quality of life has evolved from anecdotal reports of success to well-designed, randomized controlled clinical trials. An important development has been the emphasis on measuring health-related quality of life using instruments that are disease-specific, valid, responsive, and interpretable. Such instruments have permitted the demonstration that respiratory rehabilitation is, indeed, an effective treatment for COPD.

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Continued Efforts To Improve the Sensitivity of Transbronchial Needle Aspiration

Since the development of transbronchial needle aspiration (TBNA) in 1978, initial skepticism and slow progression are evidenced by the first editorial comment on this subject by Kvale in 1985 and later a survey conducted by Prakash and colleagues in 1991. Even to date, the TBNA procedure is still underused by bronchoscopists and may still be ignored for staging of lung cancer by surgeons. The skepticism and low acceptance of TBNA are due to its low yield or unpredictable results. Different operators with varying degrees of experience can obtain a wide range of sensitivities using this procedure.

Continued efforts, including improvements to the instrument, preparations of specimens, and education by hands-on courses, have gradually improved the results and acceptance of this procedure.

The article in this issue of CHEST by Rong and Cui (see page 36) typifies the initial difficulty usually experienced when performing TBNA. With initial failure, the authors chose to use the CT-guided method, which immediately increased the success rate from 10 to 60% and made this less-invasive procedure more applicable in their institution for staging of lung cancer. Their idea and technique are quite original. Their message is beneficial and encouraging to CHEST readers who are still skeptical or have difficulties performing this procedure.

I do believe that the low yield of the TBNA procedure is primarily caused by failure to place the needle tip exactly into the lesion. The operator will never have the opportunity to find this out. Instead one may attribute the failure to other factors, such as instruments or cytology laboratory, and so forth.

Although the authors should be congratulated for their perseverance and ultimate success, a follow-up study is needed to analyze whether they have a continuous need for CT guidance or whether the diagnostic yield for TBNA without CT guidance increases after their skills have improved. Even if the authors no longer need CT guidance for TBNA procedures, I do not think that this will diminish the importance of this article. On the contrary, their methodology should be used during the initial executions of TBNA if needed.

To improve TBNA sensitivity, fluoroscopy and occasional CT scan guidance have been used initially. Later, ultrasound was used. In using ultrasound-guided TBNA biopsy, it was concluded that the number of punctures needed on right paratracheal lymph node lesions can be decreased. In 1994, mediastinum and hilar lymph node mapping system was proposed to describe the nomenclature and locations of lymph nodes in the mediastinal and hilar areas from CT scan, and puncture sites for each of those lymph node stations with the airway branching as a landmark were recommended.

Recently, virtual bronchoscopy and a high-tech real-time bronchoscopy tip position technology displayed on previously acquired CT images to guide TBNA has been suggested after a preliminary study on six swine. The authors concluded that the feasibility study showed that real-time bronchoscopy tip position technology coupled to previously acquired CT images can enable TBNA of extrabronchial lesions. Their clinical implication is that, by supporting TBNA with bronchoscopy tip position technology coupled with CT scan images, the need for mediastinoscopy biopsies might be reduced.

The facts are that TBNA has been performed for extrabronchial lesions already and has reduced the need for mediastinoscopy without this new technology. By adding this newer technology, will it increase the sensitivity of TBNA, or will it enhance the learning process of performing TBNA? This does deserve more study.

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