accurate differentiation between arterial and venous vessels, and allowed qualitative assessment of the occlusion as smooth muscle cells or fibrous tissue proliferation within the vessel wall. Smooth muscle actin immunohistochemistry with Verhoeff elastin counterstaining may have enabled higher and more accurate detection of PVOD.

We acknowledge the limited clinical data available in the study. We agree that conclusions regarding the usefulness of high-resolution CT scanning in the diagnosis of PVOD are inherently flawed due to the limited data. We are also unable to draw accurate conclusions about the differences in the parameters of noninvasive diagnostic investigations, such as pulmonary function tests, due to the small sample sizes of PVOD and arterial only pulmonary arterial hypertension cases.

Our finding that pulmonary edema did not occur in PVOD patients who received prostanoic therapy also differs from those of previous reports. Although pulmonary edema is a possible and serious adverse effect of prostanoic therapy, these findings suggest that careful use of low-dose prostanoic analogues with slow titration may be appropriate in this pulmonary hypertension subgroup.

We agree that a noninvasive approach to the diagnosis of PVOD should be pursued if possible. However, in some cases the failure to respond to medical therapy may be the best indicator of PVOD, and in these patients early listing for lung transplantation is recommended.

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Financial/nonfinancial disclosures: The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.09-1431

REFERENCE


Longitudinal Assessment of Spirometry in World Trade Center Responders

To the Editor:

Skloot and coworkers are commended for providing follow-up information on the spirometric findings in their large World Trade Center cohort, which they reported recently in CHEST (February 2009). A reader must be impressed by the finding of less than expected loss in FVC and FEV, in this selected symptomatic population who had a high prevalence of spirometric abnormality to begin with. This finding consists of the following:

1. An increase in spirometric values over 3 years in those patients who were initially responsive to therapy with bronchodilators (BDs); and

2. A less than expected decrease in FVC and FEV, in those patients who were not responsive to therapy with BDs, even in the oldest strata of patients.

Examination 1 was performed over a 2-year period beginning 10 months after the inciting event. Both of these considerations created a “baseline” in which pulmonary function would be expected to vary considerably, making comparison with subsequent results difficult to interpret.

A graphically striking finding shown in Figure 1 in the article by Skloot et al is that, given the variability in the change in FVC and FEV, at examination 2, change is not skewed toward excessive loss, as would be seen when progressive impairment had developed in a significant portion of the subjects. Similarly impressive is the resolution of BD responsiveness in fully 72% of those subjects who were initially responsive to BDs. Since 9% of the group responded at examination 1 and 8% responded at examination 2, it is obvious that the two sets of responders were not the same. That the majority of those who were responsive to BDs were not responsive on follow-up is noteworthy. Equally noteworthy, the onset of BD responsiveness 32.4 months after the first test and 4 to 6 years after the initial insult at ground zero bears explanation and suggests that it is not attributable to this distant exposure.

The authors must align their conclusions with their data. In the Abstract of the article by Skloot et al, the authors state that “significant predictors of greater average decline were BD responsiveness at examination 1 . . .” and that “initial BD response [is] . . . associated with greater than normal lung function declines.” However, in the “Results” section they state that “BD responsiveness was associated with an increase in pre-BD spirometry,” which is clearly seen in Table 5 in the article. The authors emphasize the “greater frequency of spirometric abnormalities [in their cohort] . . . compared to a general US population.” There is little justification in comparing a selected symptomatic group with a general population. As well, a more quantitative and clinically relevant definition of dyspnea than “persistent” would be appreciated.

Some of the change in spirometric values may relate to the spirometric technique that was used. The technique used may allow the measurement of a complete exhalation from less than full inspiratory capacity, thereby decreasing the FVC. This artifact is not always easy to detect on review of volume-time or flow-volume curves. Such a quality review is directed more at exhalation.

Nevertheless, the authors seem to confirm their reports of the frequency of low FVC without low FEV/FVC ratio. That this spirometric pattern has been associated with a syndrome of airways dysfunction clinically characterized as irritant-aggravated or irritant-induced asthma, or reactive airways dysfunction syndrome adds to the experience with this pattern of impairment that was first described for patients with asthma.2

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Financial/nonfinancial disclosures: The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Response

To the Editor:

We appreciate the interest that Drs. Miller and Mann have taken in our article. They have made several insightful observations that warrant consideration. The relationship between bronchodilator responsiveness and change in lung function between examinations has already been clarified. Significant predictors of bronchodilator response even in those with significant disease. It does not establish that “outliers” that are located at either extreme of the range of an outcome. The reduction in FVC could be due to a “less than full inspiratory capacity” due to patient errors in technique or alternatively to true restrictive lung disease, loss of the expiratory reserve volume due to body habits or due to airtrapping (increased residual volume). Our technicians were trained to focus on inspiratory maneuvers as well as expiratory maneuvers. This training should have reduced the rate of artificially low FVC. Our results are indeed consistent with the development of reactive airway dysfunction syndrome among some responders with clinical recovery in the majority.

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Predictors of Success in Pulmonary Rehabilitation for Patients With Interstitial Lung Disease

To The Editor:

We read with interest the recent study in CHEST (February 2009) by Ferreira et al, which provides further evidence supporting the beneficial effects of pulmonary rehabilitation (PR) in patients with interstitial lung diseases (ILDs). The aim of this observational study was also to identify patient characteristics that are predictors of benefit for patients receiving PR.

Although nine potential variables were identified a priori, baseline 6-min walk test distance (6MWD) was the only predictor of benefit. Specifically, the results of the study by Ferreira et al indicate that a lower 6MWD at baseline is a predictor of greater improvement in 6MWD following PR. Caution is needed when assessing predictors of success for any intervention. Participants with a very low baseline 6MWD are more likely to have an increase in walking distance even without any actual benefit from the intervention since they are unlikely to do any worse. Similarly, participants with a higher baseline 6MWD will be more apt to experience the opposite effect because they are starting at the “ceiling” of the measured outcome and are not expected to improve any further beyond their baseline values. This phenomenon, often referred to as the regression to the mean, might result in misleading conclusions about the mean change and predictors of success when the values of participants are at the extremes of the range of an outcome.

A careful visual examination of the scatterplot graph in Figure 1 of the article by Ferreira et al supports this concept. It is established that “outliers” that are located at either extreme of the range of values will have an appreciable effect in changing the slope of the best-fitted regression line. In Figure 1, there are outlier values for patients with very low baseline 6MWDs (ie, < 100 m) who were among the participants with the largest change in 6MWD following PR. Similarly, at the other extreme there are participants with very high baseline 6MWDs (ie, approaching 600 m) who had little to no change following PR, likely due to a “ceiling effect.” If these outlier values were omitted from the model, we hypothesize that the best-fitted regression line would most likely be close to a horizontal line, indicating no overall relationship.

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Financial/nonfinancial disclosures: Dr. Skloot has reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article. During the past 3 years, Dr. Enright has received about $20,000 for conducting pulmonary function quality assurance programs for clinical trials of patients with COPD (Pfizer), pulmonary fibrosis (InterMune), and diabetes (MannKind).

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