The Role of NT-proBNP as a Prognostic Marker in Pulmonary Hypertension

To the Editor:

In an article recently published in CHEST (May 2006), Fijalkowska et al\(^1\) provided important information on the value of N-terminal pro-type B natriuretic peptide (NT-proBNP) as a prognostic marker in patients with pulmonary hypertension (PH). There is growing interest in the role of natriuretic peptides in understanding the natural history of PH.\(^1,2\) The authors demonstrated that NT-proBNP is correlated with echocardiographic variables of right ventricular function and confirmed previous findings about the correlation of NT-proBNP with invasive hemodynamic variables. Unfortunately, the prognostic utility of NT-proBNP is limited by several factors that were not acknowledged in their article.

First, they did not present 95% confidence intervals around the estimates of sensitivity and specificity for predicting death. Since there were only 16 deaths in this cohort, the confidence intervals were quite wide, making the utility of the proposed NT-proBNP cutoff problematic. Although the sensitivity of this test was reported as 88%, the lower bound of the 95% confidence interval was 63%. The specificity of this test was reported as 53%, but the lower bound of the 95% confidence interval was 38%. Second, the authors used stepwise regression to build their survival model and screened several variables for inclusion. Multivariate models built using stepwise regression techniques are unreliable when there are ≤ 10 outcomes per screened variable.\(^3\) Finally, once the presented model is prognostic rather than explanatory it is important to use appropriate statistical shrinkage techniques to account for the fact that the authors used the same data set to derive and validate this model, and to avoid overfitting.\(^5\)

The study adds further details about the role of natriuretic peptides in the evaluation of PH patients, but its provocative findings about the prognostic value of NT-proBNP remain to be confirmed.

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None of the authors presents any conflict of interest with this letter.

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DOI: 10.1378/chest.130.5.1627

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version of the authors. The stepwise analysis was not performed mechanistically on the whole set of 10 variables. Instead, smaller sets of variables were selected for separate analysis, based on clinical needs and common sense. The models were compared with the χ² test. The best performing model was then selected and presented in the published article.

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DOI: 10.1378/chest.130.5.1627a

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Transbronchial Biopsy and Usual Interstitial Pneumonia
A Step Backward in Disease Management?

To the Editor:

We read with interest the article by Berbescu et al (May 2006).1 who attributed a role for transbronchial lung biopsy (TBLB) in the diagnosis of usual interstitial pneumonia (UIP). Their conclusions raise serious issues, aside from the potential bias in this unblinded retrospective study. Irrespective of operator expertise, TBLB has inherent sampling errors, particularly in patients with established lung fibrosis. Small specimen size makes TBLB a “histopathologist’s nightmare,” with difficulty in distinguishing different patterns within the spectrum of diffuse parenchymal lung diseases; patients may have overlapping histologic features. Berbescu et al2 failed to mention sample size. Adequate biopsy size, ideally a 4-cm maximum diameter when inflated, and a depth of at least 1 to 1.5 cm,3 are critical to identify potential prognostic markers, such as the degree of alveolar space granulation tissue deposition and the extent of early connective tissue formation within the fibroblastic foci, in patients with UIP; such factors may also impact on treatment outcome.3,4 An additional inevitable crush effect, a failure to penetrate beyond the peribronchial sheath, and friable tissue disintegration preclude proper histologic assessment.

In the present study,1 apart from the patient in case 10, sampling is from the same affected lobe. Temporal heterogeneity in patients with idiopathic interstitial pneumonias is a critical histologic hallmark; TBLB samples, especially from the same site, are insufficient to determine the “concordant” and “discordant” patterns between UIP and nonspecific interstitial pneumonia, which has important clinical outcome implications.2 Berbescu et al4 attempted to describe some histologic features that may be helpful in diagnosing UIP. We would argue that the evaluation of these findings in TBLB samples may rest on the expertise of the local service pathologist. Most of the described changes, which involve some secondary in situ fibrogenic process, are nonspecific for UIP and can be found in patients with other lung conditions.

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DOI: 10.1378/chest.130.5.1628

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Transbronchial Biopsy and Usual Interstitial Pneumonia
A Step Forward in Disease Management

To the Editor:

We believe that Drs. Mukherjee and Spiteri misinterpreted the message of our article (May 2006).1 This work was intended to highlight a hypothesis that will require further testing. It was not intended to generate a clinical recommendation to use transbronchial lung biopsies (TBBs) to diagnose usual interstitial pneumonia (UIP). In our article, we clearly stated that TBBs should be tested in a blinded fashion, and in a cohort of patients with diffuse lung diseases, including UIP and non-UIP cases. However, it is undeniable, as we show in several of our figures, and despite the relatively small sizes of the TBB specimens, that in patients with well-