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

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Rogério Souza, MD, PhD, Pulmonary Department, University of São Paulo Medical School, R. Afonso de Freitas 451, No. 112, São Paulo, Brazil 04006-052; e-mail: rogerio.souza@incor.usp.br

DOI: 10.1378/chest.130.5.1627

REFERENCES


4 Diamond GA. Stepwise transgression. Am J Cardiol 1990; 65:1047


To the Editor:

We thank very much Dr. Souza et al. for their interest in our article (May 2006) on the potential clinical role of N-terminal-pro-brain natriuretic peptide (NT-proBNP) estimation in patients with pulmonary arterial hypertension (PAH). We also agree with their concerns regarding the universal validity of the prognostic cutoff values that were reported in our article. Clearly, with a study group of slightly > 50 patients we would not impose or recommend such values for universal prognostic use. Furthermore, we do not believe that even the most sophisticated statistical analysis could extract more objective truth from such a database. On the other hand, by looking at the receiving operating characteristic analysis and trying to identify prognostic thresholds we wanted to avoid the common practice of reporting the prognostic significance of median values. While highly dependent on the initial characteristics of the study group of the index trial, such median values later often become surprisingly “magic numbers” and are extrapolated to other populations with even less evidence. This was the case both for a 6-min walk test distance of 332 m or an NT-proBNP concentration of 150 pg/L as a result of the reports of Nagaya et al. and Miyamoto et al. Therefore, rather than defending our 1,400 and 3,400 pg/L thresholds, even though they were derived from a receiving operating characteristic analysis, we would reply by issuing a call for pulling together data on PAH patients whose baseline clinical characteristics and NT-proBNP concentrations were tested with a method similar to the one used in our study. This may be true, for instance, for the study population of a trial recently published by Souza et al. We have recently witnessed a great step forward in the understanding of the efficacy of the new drugs developed for the treatment of PAH thanks to global collaboration between expert centers. It is time to try to start building networks of collaboration to learn more about prognostic indexes and clinical end points. We would be available for this type of collaboration.

Regarding other, technical remarks, the 95% confidence intervals were not given for prognostic thresholds in order to make the presentation of the results clearer. However, all data needed for the calculation of those intervals were available in the published article.

Correspondence to: Christopher Brightling, PhD, FCCP, Institute for Lung Health, University of Leicester, Glenfield Hospital, Groby Rd, Leicester LE3 9QP, UK; e-mail: ceb17@le.ac.uk

DOI: 10.1378/chest.130.5.1626a

REFERENCES

1 Brightling CE. Chronic applications of induced sputum. Chest 2006; 129:1344–1345


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. 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. 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 model, and to avoid overfitting. The study adds further details about the role of natriuretic peptides in the understanding of the efficacy of the new drugs developed by Souza et al. We have recently witnessed a great step forward in the understanding of the efficacy of the new drugs developed for the treatment of PAH thanks to global collaboration between expert centers. It is time to try to start building networks of collaboration to learn more about prognostic indexes and clinical end points. We would be available for this type of collaboration.

Regarding other, technical remarks, the 95% confidence intervals were not given for prognostic thresholds in order to make the presentation of the results clearer. However, all data needed for the calculation of those intervals were available in the published article.
version of the article. The stepwise analysis was not performed mechanically 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.

Anna Fijalkowska, MD
Adam Torbicki, MD
Marcin Kurzyna, MD
National Research Institute of TB and Lung Diseases
Warsaw, Poland

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.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Anna Fijalkowska, MD, National Research Institute of TB and Lung Diseases, Plocka 26, Warsaw 01-138, Poland; e-mail: a.fijalkowska@igichp.edu.pl

DOI: 10.1378/chest.130.5.1627a

REFERENCES

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), who attributed a role for transbronchial lung biopsy (TBLB) in the diagnosis of usual interstitial pulmonary fibrosis (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 al.² 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.³⁴ 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 al³ 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.

Saranjan Mukherjee, MD
Monica Spiteri, PhD
University Hospital of North Staffordshire
Stoke-on-Trent, UK

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.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Saranjan Mukherjee, MD, Department of Respiratory Medicine, University Hospital of North Staffordshire, Newcastle Road, Stoke-on-Trent ST4 6QG, UK; e-mail: smukherjee66@yahoo.com

DOI: 10.1378/chest.130.5.1628

REFERENCES

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-

Downloaded From: http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22050/ on 06/28/2017