Response

To the Editor:

We appreciate the support of Teramoto and colleagues for the concepts outlined in our recent commentary in CHEST (August 2010), which include the importance of a multidisciplinary approach to evaluating interstitial pneumonia (IP) and emphasize the usefulness of specific autoantibodies, such as anticyclic citrullinated peptide (CCP), as part of the assessment for connective tissue disease-associated interstitial lung disease (CTD-ILD). Teramoto and colleagues also briefly describe a patient without synovitis who presented with organizing pneumonia and anti-CCP antibody positivity, who later developed the articular manifestations of rheumatoid arthritis (RA). In our and others’ experience, this is not an uncommon scenario, and it supports the notion that lung disease may be the first manifestation of a CTD and that surveillance for evolving extrathoracic features is needed when caring for patients with “idiopathic” IP. Interestingly, we have recently identified a sizable cohort of patients with anti-CCP positivity and IP without prior history of CTD or the articular features of RA. Although a few of these patients have developed the synovitis of RA within a short interval of follow-up, the vast majority have not. Because these patients with ILD have a highly specific autoantibody in the absence of defining extrathoracic CTD features, and because without inflammatory arthritis they cannot be defined as having RA, we have proposed that it is important to distinguish them from the category of idiopathic IP and consider them to have lung-dominant CTD. With prospective assessments of these types of more precisely characterized and classified phenotypes, we hope that important questions regarding their pathobiology, natural history, and therapeutic responsiveness will be answerable. Finally, we emphasize that a classification of lung-dominant CTD conveys that this entity is distinct from both idiopathic IP and from definite CTD-ILD and that these patients require surveillance for evolution to more defined forms of CTD.

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REFERENCES


Interpreting the P Value

To the Editor:

We read with interest the recently published article in CHEST (September 2010) by Harvey and Lang on hypothesis testing, study power, and sample size. The authors remind us that although the α level is typically arbitrarily set at 0.05, other values may be important to consider, depending on whether a type 1 error would carry better or worse consequences than a type 2 error in a given study. In addition, as rightly pointed out, statistically significant results do not invariably translate into clinically meaningful results. There is another point, often overlooked, that we would like to emphasize with regard to the P value. We illustrate this through analogy with diagnostic test performance characteristics.

The sensitivity of a clinical test is the probability that the test is positive in a patient who has the disease. Specificity is the probability that the test is negative in a patient without the disease. These diagnostic test characteristics require that disease status already be known. However, patients (and physicians) would usually rather know the probability that a patient has the disease, given a specific test result. This probability can be derived by application of Bayes theorem and an estimate of the pretest probability of disease.

As Harvey and Lang note, the P value is the “... probability of observing a result as extreme or more extreme as the one observed,...” if in truth there is no difference between the groups. As for a diagnostic test, this must be contrasted with what we would usually rather know: the probability that the hypothesis tested is in fact true, given the study results. To evaluate this probability, a similar Bayesian approach, incorporating an estimate of the “pre-study” probability that the hypothesis is true, is required.

The interpretation of the P value should therefore take into account not only rates of type 1 and type 2 error and the consequences that would occur by making them but also the pretest probability that a tested hypothesis is true in the first place. For example, a statistically significant P value (often P < 0.05) in a study evaluating an improbable hypothesis should be approached with a healthy dose of skepticism. Similarly, a statistically nonsignificant P value, even with adequate power, may not represent strong evidence in support of the null hypothesis if the pretest probability that the alternative hypothesis is true is high.

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