or revascularization, information that is absolutely essential in light of the findings of the Should WeEmergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. An institutional protocol that uses intra-aortic balloon pumps (IABPs) only in those patients with refractory CS, despite the use of therapy with vasopressors, is not dispensing state-of-the-art care to patients with CS. While the benefit of therapy with vasopressors on outcome in patients with CS is doubtful, a survival benefit is evident in patients who are supported with an IABP, and this is included in the current American College of Cardiology/American Heart Association guidelines. Data from the SHOCK trial and Registry demonstrated that the reversal of systemic hypoperfusion following IABP therapy is associated with improved 30-day survival, independent of early revascularization.

Hochman also has proposed alterations to the current model and has suggested expanding the paradigm in a recent review. Large myocardial infarctions that are complicated by CS may be accompanied by a substantial inflammatory response with the release of various mediators, including cytokines, leading to high levels of nitric oxide and peroxynitrite with deleterious effects. A nitric oxide synthase inhibitor will be utilized in the SHOCK-2 trial to test this hypothesis.

A recent concept introduced into the lexicon of shock terminology is the cardiac power output. This parameter is calculated by multiplying the mean arterial pressure by the cardiac output. This parameter was found on multivariate analysis to be the single hemodynamic factor associated with in-hospital mortality among patients in the SHOCK Registry. It would be interesting to know whether Lim and colleagues will confirm this finding in their cohort of patients as they have data on the mean arterial pressure and CO for each patient.

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P Wave in Pulmonary Impairment

To the Editor:

We read with great interest the article by Asad et al in CHEST (August 2003) on acute right atrial strain, and P-wave amplitude and axis in the treatment of obstructive airways disease in patients experiencing exacerbation. Their key message was the rapid reversal of characteristic ECG changes with treatment from the emergency department presentation to hospital ward admission. Similarly, in 1973, Carril et al demonstrated in a retrospective study the predictive value of P-wave amplitude and axis in estimating the severity of nonasthmatic airway obstructive disease in the quiescent state. A good correlation of P-wave amplitude and axis with FEV1/FVC and residual volume/total lung capacity was seen, also demonstrating a continuum in regression equations. We agree with Yue et al in their accompanying editorial, that the study was well-designed but lacking in clinical and functional data. Patients with clinical phenotypes of diffuse obstructive airways disease (ie, chronic bronchitis/bronchiolitis, emphysema and bronchial asthma) are a clinically and pathophysio logically heterogeneous population. These various phenotypes most often coexist, and the proportion of each is difficult to quantitate clinically by pulmonary function testing and chest-imaging techniques.

The variability of airways obstruction is a defining criteria for the asthmatic type. Although these data are lacking in the

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To the Editor:

We thank Drs. Munoz and Thomas for their comments on our article. Indeed, the 18 patients with acute myocardial infarction whose conditions evolved into cardiogenic shock were treated according to the guidelines that were in effect at the time of the study. The patients were admitted to the hospital in one of the following three ways: (1) most were revascularized using percutaneous angioplasty unless coronary angiography disclosed diffuse and/or distal lesions; (2) several patients developed shock a few days after apparently successful thrombolysis; and (3) a small group of patients did not receive any revascularization intervention due to the long delay between the onset of symptoms and hospital admission. All patients were treated with antiplatelet agents and heparin. Intra-aortic balloon counterpulsation was used when possible, but this procedure was contraindicated in some patients (in more nonsurvivors than survivors). These factors do not invalidate our findings, as the aim of the study was to describe the hemodynamic evolution of nonsurvivors, regardless of the results of any revascularization procedure they may have received. Nine of the 23 nonsurviving patients developed hyperdynamic shock, suggesting that pump failure was not the primary cause of death. As both BP and cardiac output were relatively preserved, cardiac power was not significantly decreased in these patients.

Finally, we agree, and indeed discussed briefly in our article, that nitric oxide and peroxynitrite may be involved in this process. It will be interesting to see the results of the SHOCK-2 trial.

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study by Asad et al, the point is well-made that P-wave changes reflect the natural history of pulmonary arterial hypertension (PAH) in patients with diffuse obstructive airways disease. Transient elevations in pulmonary artery pressures occur with slowly progressing chronic PAH resulting from alveolar hypoxia during exacerbations with vascular reactivity and remodeling of the pulmonary artery vasculature. Although the common denominator for diffuse obstructive airways disease is PAH, only 10 to 15% will have P pulmonale. With coexistent heart disease, the P-wave changes are obscured. Other factors, such as the type of inflammation or the predominance of a specific phenotype associated with parenchymal destructive changes and fibrosis, have a major role in morbidity and mortality. Asthmatic obstructive airways disease differs significantly in the type of airways inflammation and the response to therapy. It is believed that both types may coexist in an individual. We make a plea to define the term COPD with greater specificity on presentation or in clinical studies. Distinguishing phenotypes will result in optimizing the diagnosis and prognosis, and in targeted management choices.

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To the Editor:

Drs. Carilli and Seiden present work that amplifies our findings. The results were based on pulmonary considerations (e.g., severity of noninvasive airway obstruction), whereas ours were from a cardiac perspective, that is, P waves under consideration from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

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LINEZOLID AND VANCOMYCIN FOR METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS NOSOCOMIAL PNEUMONIA

The Subtleties of Subgroup Analyses

To the Editor:

Wunderink et al (November 2003) claim that initial therapy with linezolid was associated with significantly better survival and clinical cure rates compared to that with vancomycin in patients with nosocomial pneumonia (NP) due to methicillin-resistant *Staphylococcus aureus* (MRSA). However, the authors based their conclusions on subgroup analyses. The use of subgroup analyses to draw conclusions is associated with several difficulties. Post hoc subgroups are not randomized. Nonrandomized data are more likely to reach false-positive conclusions than are randomized data. Randomization controls for unmeasured and unknown factors, as well as for measured factors. While the patient characteristics of the entire population and the MRSA subset appear to be similar in Table 1 of the article, this does not account for other potential unmeasured or unknown factors. The imbalance in treatment groups favoring linezolid therapy in the MRSA subgroup, most notably cardiac disease and diabetes, may influence outcome and survival. Logistic regression may actually increase bias when adjusting for baseline variables in analyzing nonrandomized data.

When the primary end point in a trial shows similar efficacy for two drugs but a subgroup analysis shows superiority for one of the drugs, it follows that there also is a subgroup in which the other drug must show an advantage. In this article, there is no difference in the mortality or clinical cure rates for all patients with NP or *S aureus* (SA) NP despite the claimed advantage for linezolid therapy in patients with MRSA NP. This translates into higher survival rates (88.1% [67 of 76 patients] vs 76.3% [71 of 93 patients], respectively) and clinical success rates (50% [37 of 74 patients] vs 45% [34 of 75 patients], respectively) for therapy with vancomycin compared to that with linezolid in patients with methicillin-susceptible *S aureus* (SA) NP. One could question the biological plausibility of this discrepancy, as the *in vitro* activity of both drugs is similar between MRSA and methicillin-susceptible SA.

It is unclear whether any of these subgroup analyses merely represents chance findings. The authors’ subgroup analyses are based on a p value of 0.05 as being statistically significant. A p value of 0.05 means that there is a probability that 1 of 20 comparisons in a clinical trial may represent a false-positive conclusion (ie, a type 1 error). However, when multiple comparisons from subgroup analyses, the likelihood of accepting a false-positive conclusion increases. For 10 comparisons, the risk of accepting a false-positive conclusion increases from 5 to 40%. For this reason, it is appropriate to adjust for multiple comparisons using a p value of < 0.05 to indicate statistical significance. This correction is based on the number of comparisons made, not the number of comparisons presented. It is unclear how many comparisons the authors made when evaluating subsets for this article. Regardless, the authors do not present any correction for multiple comparisons.

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