is, the two groups are not statistically different, even though the authors do not state that fact in that sentence.

Under "Discussion," the authors say that "a 28 percent reduction in hospital mortality was observed when CI [cardiac index] was titrated to 6 L/min/m²"—the latter being the definition of the OT group. This statement is misleading; since the two groups are not different, there is no demonstrable reduction in mortality.

In the next paragraph, they continue: "The lack of statistical significance in the overall mortality rates probably reflects the spontaneously higher CIs . . . ." We would like to offer a much simpler explanation for the lack of statistical significance: lack of statistical power, which we estimated at 60 percent.7 The usually accepted level of statistical power is 80 percent; in order to achieve it, we calculate that the authors would have needed a sample size of 95 total patients, provided that all other factors, including the mortality rates in the two groups, remain equal.

Since there was no statistically significant difference between the mortality rates in the two groups, and since this comparison did not achieve sufficient statistical power, the authors cannot make any statement with regard to survival and mortality in the two groups.

Marcy F. Petrine, Ph.D., and Joe R. Norman, M.D., F.C.C.P., Division of Pulmonary Diseases/Critical Care Medicine, University of Mississippi Medical Center, Jackson

REFERENCES

To the Editor:

In the July 1992 issue of Chest, Dr. Tuchschmidt and colleagues present a provocative article showing a therapeutic benefit of augmenting cardiac output and oxygen delivery in patients with septic shock.

In the "Results" section, the authors contrast the difference in outcome between the NT and OT groups. Twice as many patients in the OT group received dobutamine at 2.6 times larger dosages to achieve the predetermined therapeutic endpoint of 6 L/min/m².

Mortality rate correlated strongly with postresuscitation oxygen delivery (r = 0.94, p = 0.016) in all patients. However, when analyzed by "intention to treat," there was no statistically significant difference in survival between the two groups (p = 0.14). Most likely the lack of statistical significance is related to a small sample size (ie, type II error), rather than the inability to achieve the desired endpoint in a portion of the patients in the OT group, as the authors postulate. Furthermore, their subset analysis is misleading by comparing patients in the OT group with a CI greater than 4.5 L/min/m² (ie, responders) to the patients in the NT group with a CI less than 4.5 L/min/m². Although a significant difference in mortality was observed, this subgroup analysis does not represent a look at the data according to treatment received. A comparison of all patients who achieved a CI greater than 4.5 L/min/m² (n = 25) with those with a CI less than 4.5 L/min/m² (n = 27) would have been more helpful to address the question of therapeutic impact on survival. However, even using this approach, there appears to be no statistically significant difference in survival—again, likely due to a small sample size.

I regret that the investigators discontinued the study prematurely based on a trend favoring the OT group and the "wrong" subgroup analysis. Further randomized, prospective, and preferably multicenter studies are needed before we routinely flog the hearts of our patients and call this "optimal treatment."

Dan Schuller, M.D., F.C.C.P., Respiratory and Critical Care Division, Washington University School of Medicine, St. Louis

REFERENCES

To the Editor:

We appreciate the letters in response to our article.

The letter by Dr. Bredle is quite correct. The abstract erroneously transposed mortality data for the NT and OT groups. Clearly, this was our oversight. The letters by Drs. Petrine and Norman and by Dr. Schuller refer to the same issue. They correctly point out that the difference in mortality between the NT and OT groups fails to reach statistical significance primarily because of the small sample size. A power analysis of our data by intention to treat suggests that the difference in mortality, were it to remain unchanged, would become significant if twice as many patients were in each group. Our study was prospective, randomized, and controlled but could not have been blinded, for obvious reasons. As we discussed, the study was stopped to avoid the potential for bias and because subset analysis of our data suggested a benefit to optimizing CI.

From the inception of this study, we realized that some hyperdynamic patients with high cardiac outputs would be randomized to the NT group and that a few patients in the OT group would not raise their CI in response to therapy. These outliers thus end up having achieved CI values much closer to those of the treatment group opposite to the one to which they were randomized. Thus, we performed our subset analysis in order to compare two groups of patients who met our treatment goals. We believe moving the NT group outliers to the OT group and the OT group outliers to the NT group would have been statistically inappropriate. Interestingly, patients randomized to the NT group who achieved a CI greater than 4.5 m/min/m² on their own had a mortality rate (50 percent) very similar to that in those patients in the OT group whose cardiac output was improved through therapeutic intervention (40 percent).

Finally, we agree with Dr. Schuller's comment that a multicenter, randomized, prospective, and controlled trial is warranted. A number of studies15 suggest that there is a benefit to raising CI in patients with septic shock to greater than normal values, but all these studies have limitations, and we suspect that a multicenter study would too.

James A. Tuchschmidt, M.D., F.C.C.P., Section of Pulmonary Disease and Critical Care Medicine, University of Southern California School of Medicine, Los Angeles

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