

ischemia by 41% (!), the number of patients with >60 min of transient myocardial ischemia decreased by 10% and silent episodes by 5%.

These data all suggest a reduction in transient myocardial ischemia when heparin is added to aspirin. However, the differences did not reach statistical significance, probably because of the small sample size. The authors speculate "that 260 patients would be needed to give sufficient power (85%) to show a 70% reduction in transient myocardial ischemia." According to our calculations, to achieve a similar power to show a more realistic 25% reduction, a sample size of 910 patients would have been needed. The authors' own data actually do suggest a reduction of this magnitude. In our opinion, to expect a 70% reduction in ischemia incidence from the addition of heparin to aspirin, a treatment modality in itself of proved efficacy, was quite unrealistic.

Too small a sample size in randomized controlled trials having negative results seems to be a common error according to data published recently in *JAMA* (3). Of 102 such studies, only 16% and 36% had sufficient statistical power to detect a 25% or 50% relative difference, respectively.

We believe that the authors' data do not support their conclusion that heparin plus aspirin is no more effective than aspirin alone in unstable angina pectoris. In fact, their data suggest but do not prove that heparin plus aspirin is more effective. To draw definitive conclusions, a substantially bigger study involving ~1,000 patients would be required.

IMRE BODÓ, MD
CSILLA NÉMETH, MD
LASZLO LITTMANN, MD, FACC
*Department of Internal Medicine
Carolinas Medical Center
P. O. Box 3286
Charlotte, North Carolina 28232*

References

1. Holdright D, Patel D, Cunningham D, et al. Comparison of the effect of heparin and aspirin versus aspirin alone on transient myocardial ischemia and in-hospital prognosis in patients with unstable angina. *J Am Coll Cardiol* 1994;24:39-45.
2. Rutherford JD, Braunwald E. Chronic ischemic heart disease. In: Braunwald E, editor. *Heart Disease*. 4th ed. Philadelphia: Saunders, 1992:1292-364.
3. Moher D, Dulberg CS, Wells GA. Statistical power, sample size, and their reporting in randomized controlled trials. *JAMA* 1994;272:122-4.

Reply

Bodo et al. raise a point that should be asked when any comparison of different treatment strategies indicates the treatment modalities in question to be the same with respect to predefined end points. They suggest that an inadequate sample size may be responsible for our finding that combination therapy with heparin and aspirin was no different than aspirin alone in reducing the incidence of transient myocardial ischaemia in patients with unstable angina. We welcome the opportunity to defend our sample size calculation.

The sample size was based on the expected incidence of transient myocardial ischemia and the effects of heparin and aspirin on transient myocardial ischemia. We indicated in the report that the calculations were made on the basis of data from the study by Serneri et al. (1) in which the effects of heparin, aspirin and alteplase on myocardial ischemia were compared in patients with unstable angina. Using continuous ST segment Holter monitoring they compared the effects of these treatments on the frequency of angina, number of silent

ischemic episodes, total number of ischemic episodes and total duration of ischemia. Their results indicated that treatment with heparin reduced anginal episodes by 94%, silent ischemic episodes by 71%, total ischemic episodes by 78% and total duration of ischemia by 81%. In contrast, aspirin had no significant effect. The typical odds reduction for recurrence of angina with heparin versus other treatments was 66% (SD 6.4%) for days 0 to 3 ($p < 0.0013$). On the basis of these results we believe that our original power calculation was reasonable. We estimated that 260 patients would be required to show a 70% reduction in transient myocardial ischemia with heparin and aspirin compared with aspirin alone, assuming a 20% incidence of transient ischemia in patients treated with aspirin, giving a power of 85%. Because some patients will be included who, in retrospect, will be diagnosed as having myocardial infarction, we increased the sample size by a further 10%. We believe that it is reasonable to expect a 70% reduction in ischemia with the addition of heparin because that is supported by the data from Serneri et al. (1).

As Bodo et al. indicate, the sample size of any trial should be carefully inspected, but they should not be drawn into making statements about treatment guidelines by interpreting data "trends" when statistical significance is not reached. For example, they make several comments about the data in Table 2 from which they suggest that combination therapy is superior to aspirin. To state that the number of patients with transient myocardial ischemia was 25% less in the combination group is misleading when the absolute numbers of patients were 31 in the aspirin group versus 27 in the heparin and aspirin group—a difference of 4 patients. Similarly, the other variables mentioned by Bodo et al. are particularly influenced by one patient in the aspirin group who contributed 1,360 min of transient ischemia, which constituted >25% of the total ischemia in that group. We highlighted the point in the text of our article. Consequently, we believe that Bodo et al. have no basis for suggesting that our data indicate that heparin and aspirin therapy is superior to aspirin alone.

DIANA R. HOLDRIGHT, MRCP
KIM M. FOX, FRCP
*The Middlesex Hospital
Mortimer Street
London W1N 8AA, England, United Kingdom*

Reference

1. Serneri GGN, Gensini GF, Paggi L, et al. Effect of heparin, aspirin or alteplase in reduction of myocardial ischaemia in refractory unstable angina. *Lancet* 1990;335:615-8.

Early Repair of Tetralogy of Fallot and Ventricular Arrhythmia

It has been suggested that in patients with tetralogy of Fallot, occurrence of late ventricular arrhythmias and possibly sudden death would decrease if surgical correction is performed early in life. The work of Joffe et al. (1) has attempted to address this important issue. This study describes the long-term follow-up results in 29 patients after repair of tetralogy of Fallot.

"Early" versus "late" repair of tetralogy of Fallot is not clearly defined in published reports. Nevertheless, "early" commonly implies complete repair at the time of, or even before, development of the need for palliative surgery, which usually occurs during the first year of