and in our study hypothermia clearly delayed increased intracranial pressure and thereby prolonged a higher cerebral perfusion pressure \((P=0.01)\).

We propose that even in a well-controlled experimental study, and despite prolonged postinsult control of extracerebral variables, 2 with an adequately severe cerebral focal ischemic insult small animal-to-animal variations will lead to the inevitable death of a certain percentage of the animals. Present treatment modalities are inadequate in preventing this mortality from diffuse brain swelling and herniation. Prolonged moderate hypothermia \((31^\circ C)\) but not mild hypothermia \((35^\circ C)\) postpones intracranial hypertension while the hypothermia lasts, but it does not prevent the delayed intracranial hypertension that leads to herniation and brain death during rewarming in some of the animals. 23 The modalities that are effective decrease the cerebral ischemic damage of surviving animals, as expressed by the brain infarct size and cerebral perfusion.

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References

Statistical Significance Versus Clinical Importance

The article by Walzl et al describes the results of heparin-induced extracorporeal low-density lipoprotein precipitation (HELP) treatment in patients with acute embolic stroke and multi-infarct dementia. The authors conclude that "the apheresis causes an immediate and significant improvement of the hematologic pattern, obviously followed by an improvement of clinical symptoms, which has so far not been achieved by any hematologically active substance to a comparable degree and time." I seriously doubt the validity of the conclusion on several grounds.

1. It is not clear how bias was controlled in selecting the control group of 30 patients from the 96 who were assigned to the non-HELP group by the computer. More importantly, no attempt was made to blind the outcome evaluators. This is particularly important in assessing disability (as opposed to death), where measurement is more prone to bias. Thus, a possibility exists that the results are influenced by bias in the selection and/or the measurement processes of the study.

2. Statistical significance does not equal clinical importance. It only tells us that the observed differences in the outcome are unlikely to be due to "chance alone." This may be a useful first step in evaluating the importance of the observed differences, but it is important to examine the clinical importance of the observed differences. We should keep in mind that there may be differences between groups that are "statistically significant" but "clinically meaningless." 2

The treatment resulted in a 3.6- to 6.3-point difference in the Mini-Mental State Examination (MMSE). There is no evidence to suggest that these represent clinically important differences. According to the Barthel Index scale, the minimum change that can be recorded is 5 points, and this represents just one level of change in only one of the items. In view of this, most clinicians would not consider a 6-point difference as clinically important. Similarly, in the MMSE, a 2- to 3-point difference may not mean improvement in even one item for several of the items. Therefore, it is doubtful that this will be considered clinically important.

To summarize, the study demonstrates a statistically significant but clinically insignificant difference. This is not to say that the scales are meaningless but to emphasize that their use requires careful consideration of their properties. One good example of its proper use is the multicenter United Kingdom trial of nimodipine in acute stroke, 3 in which the Barthel Index score of 60 or more was used to define "independence," which was their primary outcome. This cutoff score was obviously irrelevant in the study by Walzl et al, 4 because they included only cases with a score of 84 or more. One wonders what the authors expected to achieve in patients with a score of 84 or more, but a cutoff to meet their expectation could have been chosen. In the jargon of measurement theory, the scale has well-established "discriminative" but less validated "evaluative" properties. 4 Some authors consider simple methods of assessing outcome as equally valid 5 and rebrand the use of stroke scales. Even though this position seems extreme, it serves as a useful reminder to select outcome measures that are (1) clinically relevant and meaningful; and (2) reliable, valid, and sensitive for the purpose of the study.

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References

Association of Abdominal Aortic Aneurysm and Carotid Artery Stenosis

We read with interest the article by Karanjia et al 7 that identified the association of aortic aneurysms with carotid artery disease. We have also identified this association in a previously published article that to our knowledge is the only other article to do so. 8 The authors identified aortic aneurysms in 20% of patients with carotid stenosis greater than 30% as measured by duplex ultrasonad. The criteria that the authors used, however, defines an aortic aneurysm as any focal dilation of the vessel greater than 2.5 cm. Although a measurement of this diameter may be considered aortic aneurysm if a saccular dilatation is identified, it does not appear evident from the article. The subcommittee on reporting standards for arterial aneurysms has defined an aneurysm as a permanent
Statistical significance versus clinical importance.
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