Sex-Based Differences in the Effect of Intra-Arterial Treatment of Stroke
A Plea to Stop Torturing the Old Data and Do Large Trials!

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This analysis sought to explore whether gender influences response to intra-arterial thrombolysis. This was stimulated by an earlier meta-analysis of the trials of intravenous recombinant tissue plasminogen activator which showed, after adjustment for baseline factors, that there was some evidence female gender modified the response to thrombolysis. We feel these analyses were both inappropriate and potentially misleading.

This study does not confirm the results of the earlier meta-analysis. In this study, a different treatment effect estimate has been used (using a cut-off of Rankin ≤1, rather than Rankin ≥2), and results are presented adjusted for baseline factors where the previous study presented unadjusted results. Presumably, if identical methods to the earlier meta-analysis had been used, it would not have been possible to confirm the results.

The hazards of inappropriate subgroup analyses in small trials and small meta-analyses have been highlighted by Schulz and by Collins; a surprising amount of statistical power is needed for the reliable detection of subgroup interaction with the effects of particular treatments. An example of the hazards of underpowered subgroup analyses is the Canadian Aspirin Trial, which was—mistakenly—interpreted as showing that aspirin was not of net benefit to women with transient ischemic attacks, and led to the FDA delaying the licensing of aspirin for stroke prevention in women. Untold numbers of women were therefore denied effective treatment with aspirin and experienced strokes that might have been avoided. It required a meta-analysis of all the available randomized trials (including data on some 70 000 patients) to demonstrate that the benefits of antiplatelet therapy (chiefly with aspirin) were similar in men and women. The PROACT trial had just sufficient power to demonstrate an effect of treatment, but was wholly under-powered reliably to explore subgroup effects. New, much larger-scale trials (such as IST-3, which seeks to recruit 6000 patients between thrombolysis and control), are needed and not reanalyses of old data to get sufficient power reliably to confirm or refute the hypothesis that gender really does influence response to thrombolysis.

Disclosures

None.

References


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