Bridging therapy in acute ischemic stroke: a systematic review and meta-analysis

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CRD summary
The authors concluded that bridging therapy was associated with acceptable safety and efficacy in stroke patients. The conclusions reflect the presented evidence but potential publication bias, small sample sizes, and unclear quality of included studies make it difficult to confirm their reliability.

Authors' objectives
To assess the efficacy and safety of bridging therapy (combined intravenous and intra-arterial thrombolysis) in patients with acute ischemic stroke.

Searching
PubMed was searched for studies in English published between 1996 and March 2011. Search terms were reported. Reference lists of identified articles were handsearched for additional studies.

Study selection
All observational and interventional studies that reported recanalisation or clinical outcomes in patients (aged at least 18 years) with acute ischaemic stroke, and treated by combined intravenous/intra-arterial thrombolysis were eligible for inclusion. Studies had to enrol at least 10 patients. Clinical outcomes included favourable function (using a modified Rankin score), mortality and symptomatic intracranial haemorrhage.

Included studies were conducted in Spain, Switzerland, USA, Korea, France and Japan. Study durations ranged between 10 months to eight years. The mean age of patients ranged between 60 to 78 years. The proportion of men in the studies ranged between 29% and 69%.

Bridging therapy protocols were varied (direct protocols, rescue therapies). All but one study used intravenous alteplase treatment dose of 0.6 or 0.9mg/kg. Eleven studies used intra-arterial lysis as first-line adjunctive treatment; five of these studies also used additional mechanical revascularization. The mean time to intravenous thrombolysis ranged between 110 to 165 minutes. The mean baseline National Institutes of Health Stroke (NIHSS) scale ranged varied (range 13 to 20).

One author assessed study eligibility for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Data were extracted on intervention (bridging therapy protocol) and outcome (recanalisation, favourable functional outcome, mortality, symptomatic intracranial haemorrhage) using a standardised form.

Two authors independently extracted data; disagreements were resolved by consensus.

Methods of synthesis
Pooled proportions (rates or odds ratios) and 95% confidence intervals (CIs) were calculated using DerSimonian and Laird random-effects model. Heterogeneity was assessed using Cochran Q and I² statistics. Sensitivity and meta-regression analyses were conducted (details reported in paper).

Results of the review
Fifteen studies were included (559 patients); sample sizes ranged between 11 to 59 patients.

The pooled recanalisation rate (partial or complete) was 69.6% (95% CI 63.9 to 75.0; 15 studies; I²=51.3%) favouring the intravenous/intra-arterial group compared to intravenous-treated group. When only complete recanalisation was
evaluated the rate was lower (35.1%, 95% CI 23 to 48.2; 13 studies; \(I^2=87.6\%\)).

Rates favoured the intravenous/intra-arterial group compared to intravenous thrombolysis-treated group for favourable outcome (48.9%, 95% CI 42.9 to 54.9; 15 studies; \(I^2=50.2\%\)); mortality (17.9%, 95% CI 12.7 to 23.7; 15 studies; \(I^2=66.6\%\)); and symptomatic intracranial haemorrhage (8.6%, 95% CI 12.7 to 23.7; 15 studies; \(I^2=66.6\%\)).

The odds of favourable outcome were significantly higher in the intravenous/intra-arterial-treated group compared to intravenous thrombolysis-treated group (OR 2.26, 95% CI 1.16 to 4.40; \(I^2=74\%\)). No difference in mortality or symptomatic intracranial haemorrhage was found between these groups.

In meta-regression the lower the mean time to intravenous thrombolysis treatment, the greater the recanalisation rate, and lower the mortality rate. A positive association was also observed between: recanalisation and rate of patients treated for isolated middle cerebral-artery (MCA) occlusion; mortality and mean study age and NIHSS score; further details were reported in the paper.

**Authors' conclusions**
Bridging therapy was associated with acceptable safety and efficacy in stroke patients. Time to intravenous treatment was critical to improve recanalisation rates and favourable outcomes.

**CRD commentary**
The review addressed a clearly stated question. Only one database was searched for articles published in English and no efforts were made to search grey literature sources, so relevant papers could have been missed. Data extraction was conducted in duplicate which minimised potential error and bias; but a similar process was not used in study selection (so potential for error and bias could not be excluded). Study quality was not assessed; the quality of included studies was therefore unclear. Heterogeneity was explored, and random-effects meta-analysis used to incorporate variations in study results. Included studies were of small sizes.

The authors’ conclusions reflect the presented data but potential publication bias, small study sample sizes and unclear quality of included studies makes it difficult to confirm their reliability.

**Implications of the review for practice and research**
**Practice:** The authors stated that findings emphasize the need to shorten time to bridging therapy and to start additional intra-arterial treatment as soon as possible in patients with documented arterial occlusion.

**Research:** The authors stated that several related randomised controlled trials were ongoing, such as Interventional Management of Stroke III.

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