

Critical Review Form

Meta-analysis

Risk of stroke early after transient ischaemic attack:
a systematic review and meta-analysis, *Lancet* 2007; 6: 1063-1072

Objectives: “To systemically review studies of the risk of stroke within 7 days after a TIA, to estimate stroke risk overall and to determine the influence of study method, setting, population, treatment, and case mix”. (p.1063)

Methods: Following guidelines for meta-analyses of observational studies (MOOSE guidelines <http://pmid.us/10789670>) the authors searched MEDLINE and EMBASE using logical MESH terms (though not stroke or cerebral ischemia). Additionally, they hand-searched the references of all included studies, relevant review articles, and stroke conference scientific abstracts. Full text review was performed on any abstract reporting post-TIA 6-month stroke risk, excluding studies reporting only risk beyond 7-days or confined to patients with specific underlying pathologies (carotid stenosis or atrial fibrillation). Cohorts including both stroke and TIA were excluded if stroke risk after TIA was not described separately. To explore heterogeneity of reported stroke risk the authors conducted further analysis including

- 1) Comparing intra-study stroke risk at 0-7 days with 8-90 days by correlation with regression weighted by sample size.
- 2) Categorizing studies by method, setting, population, case mix, and urgency of treatment of analysis of heterogeneity was reported within categories.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes -- what is the one-week stroke risk after a TIA and how does the study design impact detected risk.
2.	Was the search for relevant studies details and exhaustive?	Yes, although the authors could have searched additional electronic data bases (LILACS, Cochrane) and contacted industry/researchers for unpublished data.
3.	Were the primary studies of high methodological quality?	Unlike RCT's (Jadad scale) or diagnostic studies (QUADAS), prognostic studies currently have no methodological grading scales, so objective evidence of quality cannot be presented.
4.	Were the assessments of the included studies reproducible?	No report provided on who conducted the search, reviewed the abstracts, or extracted the data. If one individual performed all of these measures the results would be subject to bias and random error.
II.	<i>What are the results?</i>	

1.	What are the overall results of the study?	<ul style="list-style-type: none"> • Of 11,365 publications identified by electronic and hand-search, 84 were reviewed in full text and 18 independent studies were identified studying 10,126 patients (Table 1, p.1065) including eight involving ED population. • Lumping all studies together, the 2-day stroke risk was 3.1% (95% CI 2 - 4.1) while the 7-day stroke risk was 5.2% (3.9 – 6.5%). The ED-based 2-day stroke risk ranged from 1.4% - 5.3% while the 7-day stroke risk ranged 4.1% - 8.0% (Fig 1 p.1066) • Significant heterogeneity was noted between studies so the further planned analysis was conducted. • The correlation coefficient between 0-7 day and 8-90 day stroke risk was 0.89 (p<0.0001) and the weighted regression r² was 0.66 suggesting that 66% of variability could be explained by study differences. • Studies were grouped into the following categories: <ul style="list-style-type: none"> ○ Population based with active follow-up ○ Population based with administrative follow-up without exclusions ○ Population based with administrative follow-up with exclusions ○ Single-center ED-based ○ ED-based ○ Routine clinic based ○ Specialist stroke service based <p>This classification alone accounted for 78.6% and 85.6%, respectively, of the 2-day and 7-day pooled estimate heterogeneity.</p> <ul style="list-style-type: none"> • <u>ED-based stroke risk was 3.1% (0-6.5%) and 5.8% (3.7-8.0%) at 2- and 7-days without significant heterogeneity (p=0.27). In comparison the specialist stroke services, 2-day risk was 0.6% and the 7-day risk 0.9%.</u> • Only one study was not predominantly white, although few reported their racial makeup. • Neurology consult rates varied from 4-100% and hospital admission varied from 0-100%. • Wide variation in the use of aspirin and anticoagulation was also reported. (Table 3 p.1069) • All studies in the meta-analysis were published after 2000. • Stroke-risk in four studies in which patients were treated emergently by specialist stroke services were consistently low in contrast to the three studies with the longest delay (median 4-days) despite both groups using similar method of face-to-face follow-up (minimizing ascertainment bias). <u>This alone supports the argument for TIA to be managed on an emergency basis in specialist units.</u> •
2.	How precise are the results?	Reasonably narrow CI's as noted above, although the ED-based lower CI of zero is interesting.

3.	Were the results similar from study to study?	No – significant heterogeneity was quantitatively identified and corrected by the authors with stratification of studies followed by re-analysis.
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	Among TIA presenting to the ED, 2-day and 7-day stroke risk is significantly greater than zero. Either all of these patients require admission or a low-risk subject safe for discharge needs to be identified (aka the ABCD ² rule).
2.	Were all patient important outcomes considered?	No, patient important outcomes were identified. Post-stroke outcomes of interest to patients might include short-term mortality, functional independence, and re-admission rates.
3.	Are the benefits worth the costs and potential risks?	No cost-benefit analysis was performed or discussed, but the implications of admitting all TIA patients for observation/diagnostic testing is profound given our aging population and hospital overcrowding. Pessimists will need to see a benefit to admitting TIA patients in terms of reduced stroke rates (http://pmid.us/17928270) or reduced costs (http://pmid.us/17490788).

Limitations

- 1) Impressive search strategy, though still incomplete.
- 2) No attempt to assess study-to-study quality, although the tool to do so doesn't yet exist.

Bottom Line

Impressive meta-analysis quantitatively identifying multiple sources of differences in post-TIA short-term stroke risk. ED populations presenting with TIA have a higher 2- and 7-day stroke risk (3.1% and 5.8%, respectively) and observational evidence suggests lower stroke rates when TIA patients are cared for by stroke specialists. These figures provide the best prognostic estimate EM physicians can provide to patients, families, and consultants and argues for admission of TIA patients. Until a low-risk subject of TIA patients can be identified (see the PGY-II ABCD² rule) suitable for outpatient management, all TIA patients presenting to the ED need consideration of stroke specialist management.