

THERAPY UNIT I

tPA for Stroke 4.5 Hours After Symptom Onset

Objectives:

To learn how to apply the results of papers that address issues of therapeutic interventions to clinical practice.

This includes:

1. Determining whether the results of the study are valid.
2. Understanding the magnitude and precision of the effect.
 - Calculating and interpreting RR, RRR, ARR, NNT
 - Interpreting the clinical significance of confidence intervals. Deciding on how to apply the results to your clinical practice

Assignment:

1. Read the attached scenario.
2. Read the attached guidelines for reading articles concerning therapy.
3. Critically appraise the attached article using the accompanying worksheet.
4. Describe how you would address the question regarding the patient's management taking into account your review of the article and the attached Excel spreadsheet calculator.

Clinical Scenario:

July 1. Residency transitions occur every year at the same time, but the bustle of excited apprehensive faces is never repetitious. This year's first case is a 68 year old right-handed female arriving from home with expressive aphasia and right-sided weakness beginning 2.5 hours ago. The communications center astutely initiated the "stroke pager" as the emotional patient and her husband are wheeled back to their room. The Neurologist arrives in the room at the same time as the Emergency Medicine (EM) physician, quickly communicating with patient and husband to complete the NINDS-stroke check list. As labs are sent and the patient transported across the hall for her emergent CT, the nervous new Neurology resident and EM team confirm that no thrombolysis exclusion criteria have yet been identified.

Labs and CT-imaging are available within 25-minutes, pushing your patient to (but not across) the 3-hour no-thrombolysis threshold as Neurology and Emergency Medicine concurrently decide to administer t-PA. Shortly thereafter, your patient leaves the ED for the Neuro-ICU and you decide to explore the evidence supporting stroke thrombolysis.

PICO Question

Population: Emergency Department patients with acute ischemic stroke

Intervention: t-PA administration plus routine care

Comparison: Placebo plus routine care

Outcome: Intracranial hemorrhage, mortality, short- and long-term functional outcomes

Search Strategy:

Since this is a therapy question, you first turn to the Cochrane Database of Systematic Reviews and quickly locate four high-quality randomized controlled trials since 1995. To ensure that more recent trials have not been published since the latest Cochrane Review (2009), you conduct a PUBMED Clinical Query (narrow/specific) for therapy using the search term “acute ischemic stroke thrombolysis” and net 144 citations, but no additional large high quality RCTs.

Enclosed Materials:

1. Guyatt G, Rennie D, Meade MO, Cook DJ Editors, *The Users' Guides to the Medical Literature, A Manual for Evidence-Based Clinical Practice*. 3rd Edition. McGraw-Hill 2015.
2. Tissue Plasminogen Activator for acute ischemic stroke, *N Engl J Med* 1995; 333: 1581-1587.
3. Hacke W, Kaste M, Fieschi C, et al; Randomized double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischemic stroke (ECASS III), *Lancet* 1998; 352: 1245-1251.
4. Clark WM, Wissman S, Albers GW, et al; Recombinant tissue-type plasminogen activator (alteplase) for ischemic stroke 3 to 5 hours after symptom onset: The ATLANTIS study – a randomized controlled trial, *JAMA* 1999; 289: 2019-2026.
5. Hacke W, Kaste M, Bluhmki E, et al; Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke, *N Engl J Med* 2008; 359: 1317-1329.
6. Worksheet for evaluating an article on therapy.