

EVMS JC: Critical Appraisal Worksheet: Systematic Review/Meta-analysis

Resident: Nick Huth

Date: 5/11/23

Citation: Huang L, et al, [Efficacy and safety of intra-arterial thrombolysis in patients with central retinal artery occlusion: a systematic review and meta-analysis](#). Graefes Arch Clin Exp Ophthalmol. 2023 Jan;261(1):103-113.

Guide	
1. Did the review explicitly address a sensible question?	Yes. Investigate efficacy and safety of intra-arterial thrombolysis in CRAO
2. Was the search for relevant studies details and exhaustive?	Yes. Authors used relevant search criteria terms and also used bibliographies of included articles to find additional relevant studies.
3. Were the primary studies of high methodological quality?	No. 13/15 studies were retrospective observational studies, only one study was an RCT, making it difficult to directly compare a standardized intervention with IAT to conservative management or other traditional management.
4. Were the criteria for study inclusion pre-determined and clearly stated?	Yes. As were their subgroup analyses: 1. English w/ more than 5 pts w/ CRAO 2. IAT fibrinolysis performed (streptokinase, urokinase, alteplase) 3. Reported VA before and after tx, compared VA w/ conservative tx vs IAT, or rate of improvement 4. Case series, observational (pro and retro), or RCT
5. Did the authors adequately assess the quality of the included studies?	<ul style="list-style-type: none"> - Screened studies with Newcastle-Ottawa Scale (6 or more points = high quality) - 9/16 studies had defined diagnostic criteria for CRAO - 13/15 retrospective observational - 1/15 prospective observational - 1/15 RCT - -Moderate to high quality on NAS scale in the studies that directly compared IAT to non-IAT - 7/15 studies compared VA in IAT and non-IAT groups
CLINICAL IMPORTANCE	
6. What were the overall results of the review? <i>(Are the results of all included studies clearly displayed? Are the results similar from study to study? Is there a clinical</i>	<ul style="list-style-type: none"> - 8 studies (269 pts) reported VA improvement before and after IAT that was statistically significant, low heterogeneity: IAT (MD [LogMAR] 0.55, 95%CI [0.40, 0.69], P < 0.00001; I² = 0% - Two studies reported level of VA improvement

<p>bottom line? If the study results combined, was it appropriate to do so?)</p>	<p>with non-IAT intervention, one with statistically sig improvement and one without</p> <ul style="list-style-type: none"> - 15 studies reported VA change in 507 patients getting IAT, 7/15 reported level of VA improvement in non-IAT group (296 pts), rate of improvement higher in RAO who received IAT (56% vs 32%), however this was not explicitly defined: OR 3.55, 95%CI [1.74, 7.24], P = 0.0005; I² = 65%. - Probability of improvement with IAT was two-fold higher in IAT treatment compared to conservative - IAT benefits are greatest when initiated within 6 hours of symptom onset (OR 4.6 vs 3.36 after) (OR 4.60, 95%CI [1.24, 16.99], P = 0.02; I² = 0%). - Improvement more likely in patient with incomplete vs complete CRAO - Five studies IAT >6hrs. VA improvement favored IAT (OR 3.36, 95%CI [1.43, 7.85], P = 0.005; I² = 75%) - 3 studies compared improvement in 3 stages of CRAO (incomplete, subtotal and total) vs conservative (75 vs 45% in incomplete, 43 vs 19% subtotal phase, and 48% vs 18% in total stage) - Rate of improvement in IAT vs IVT in CRAO 56% vs 47% (difficult to compare results due to lack of consistency in definition of improvement) - <i>Overall results difficult to combine/generalize given lack of consensus on what defines improvement in visual acuity, rate of improvement does not necessarily indicate functional restoration</i>
<p>8. Were the results similar from study to study?</p>	<ul style="list-style-type: none"> - Yes, results overall consistent among studies indicating benefit of IAT vs conservative management, however definition of improvement is difficult to apply across all studies due to lack of consensus on how improvement was defined.
<p>APPLICABILITY</p>	
<p>9. How can I best interpret the results to apply them to the care of my patients?</p>	<ul style="list-style-type: none"> - There does appear to be benefit to IAT, however the results are difficult to interpret given that only one study was RCT, causing potential bias in results. Also, there was a lack of consistency in definition of improvement in

	VA, making it difficult to ascertain the true benefit of IAT. Heterogeneity was pretty high (65%) for studies that were included comparing IAT and non-IAT for improvement in visual acuity
10. Were all patient important outcomes considered?	<ul style="list-style-type: none"> - Regaining sight is of major importance. - Adverse events were considered and documented – 5/507 (0.09%) had ICH in IAT vs 2/127 in IVT, 21 TIA or stroke vs 1 in conservative treatment and may not have been powered for adverse events as individual studies were small - No quality of life assessment between patients who got ITA vs conservative therapy.
11. Are the benefits worth the costs and potential risks?	<ul style="list-style-type: none"> - Risk for ICH, dislodging embolus in carotids during procedure, increasing likelihood of ischemic stroke, all significant. - Under 20% of patients with CRAO regain functional VA, and conservative treatment has been shown to be underwhelming - Lack of RCT data to support the use of IAT along with additional risk of the procedure makes it a viable therapeutic option which needs to have risks carefully weighed before performing and need to be considered with patient on a case-by-case basis. - If available clearly warrants patient-centered decision making.

Limitations:

1. Majority of studies were observational.
2. Only RCT in review did not demonstrate statistically significant improvement in visual acuity and had higher harms.
3. Relatively low sample sizes in included studies and heterogeneity was high
4. No description or standardization of “conservative” non IAT treatments
5. Lack of consensus definition of improved visual acuity among studies
6. Lack of consensus definition of CRAO, classification of CRAO, and standardization of treatment

Clinical Bottom Line: Given the lack of adequate therapy for CRAO and the significant disability it incurs upon patients, IAT should be considered, however, given the technical difficulties of the procedure and risks, more data appears necessary before this becomes standard of care.