

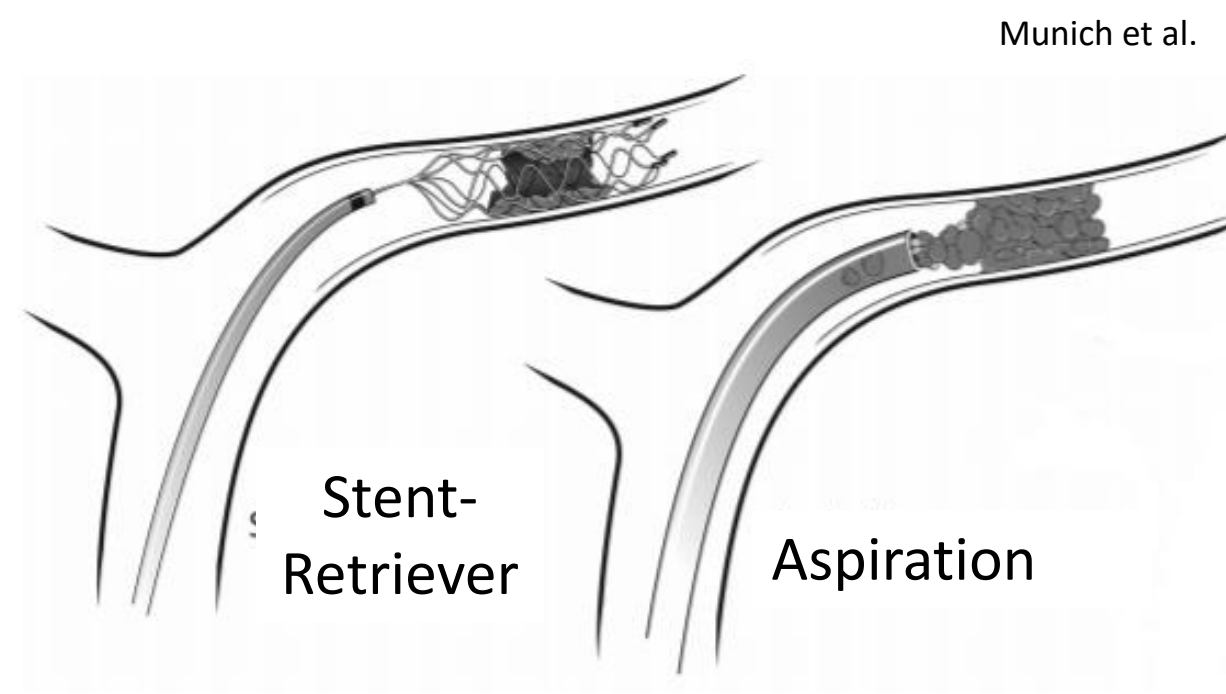
A Comparison of Acute Ischemic Stroke Functional Independence Rates between Mechanical Thrombectomy after IV Thrombolysis v. IV Thrombolysis Alone

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Introduction

- Strokes affect more than 17 million people annually
- 2nd most common cause of death globally
- Thrombotic and embolic ischemia account for 85% of all strokes
- Standard of treatment for ischemic strokes was IV thrombolysis (IVT), tissue plasminogen activators (tPA) (ie. alteplase)
 - tPA has many exclusionary criteria and was still only moderately efficacious for small portion of patients
 - Less effective for larger clot burdens
- MR CLEAN studied use of tPA with other adjuncts, ie. mechanical thrombectomy (MT)
- **Hypothesis:** IVT + MT would lead to increased rate of 90-day functional independence vs. just IVT alone.



Methods

- PubMed, EBSCO, Google Scholar were used for a literature search
- Randomize control trial > Retrospective Cohort Study > Case-control Studies > Cross-sectional > case reports
- **Inclusion Criteria:**
 - Compared IVT vs IVT + MT (Stent-retriever, Aspiration)
 - Treatment time <6 hours of onset of symptoms
 - Outcome Measure of 90-day functional independence rate
- **Exclusion Criteria:**
 - systematic reviews or meta-analysis
 - did not compare dual therapy with individual therapy
 - Studies that observed the effects of one therapy (IV or MT)
 - Treatment time >6 hours of symptom onset
- MR CLEAN was not used as its treatments were too varied (used IA tPA, IV tPA, and/or both IVT/IAT + MT vs supportive treatment)
- This review compared seven trials that fit criteria.

Google Scholar

PubMed

EBSCO

Table 1: Comparison of study design. Combination treatment vs. IV thrombolytic

Study	Design	Total N (IVT/CT)	Occlusion site	Time window for intervention	Mechanical Thrombectomy Device Type	Primary Outcome Measure	Primary Safety Outcome
Bracard (THRACE)	RCT	412 (208/204)	ICA, MCA, Basilar A.	<5 hours from onset	Stent-retriever, Aspiration	mRS = 0-2 at 90 days	Mortality at 90 days
Saver (SWIFT PRIME)	RCT	196 (98/98)	ICA, MCA	<6 hours from onset	Stent-retriever	mRS = 0-2 at 90 days	Mortality at 90 days
Mocco (THERAPY)	RCT	108 (54/54)	ICA, MCA,	<4.5 hours from onset	Aspiration	mRS = 0-2 at 90 days	Mortality at 90 days
Khoury (EASI)	RCT	77 (37/40)	ICA, MCA, Basilar A.	<5 hours from onset	Stent-retriever, Aspiration	mRS = 0-2 at 90 days	Mortality at 90 days
Campbell (EXTEND-IA)	RCT	70 (35/35)	ICA, MCA	<6 hours from onset	Stent-retriever	mRS = 0-2 at 90 days	Mortality at 90 days
Muir (PISTE)	RCT	65 (32/33)	ICA, MCA	<4.5 hours from onset	Stent-retriever, Aspiration	mRS = 0-2 at 90 days	Mortality at 90 days
Cabral et al	RCS	113 (82/31)	ICA, MCA, Basilar A.	<6 hours from onset	Stent-retriever	mRS = 0-2 at 90 days	Mortality at 90 days

Key: THRACE: THrombectomy des Artères Cerebrales, SWIFT PRIME: Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment, THERAPY: The Randomized, Concurrent Controlled Trial to Assess the Penumbra System's Safety and Effectiveness in the Treatment of Acute Stroke, EASI: Endovascular acute stroke intervention, EXTEND-IA: Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial, PISTE: Pragmatic Ischaemic Thrombectomy Evaluation, RCT: Randomized Control Trial, RCS: Retrospective Cohort Study, CT: Combination treatment) IVT: Intravenous therapy, ICA: Internal Carotid Artery, MCA: Middle Cerebral Artery, rtPA: recombinant tissue plasminogen activator, NIHSS: National Institutes of Health Stroke Scale, mRS = 0-2 at 90 days: modified Rankin Scale score of 0-2 at 90 days

Results

- Analyzed to critique common factors of each articles:
 - Control for bias
 - Blinding of researchers
 - Inclusion and exclusion criteria
 - Adherence to treatment time window
 - Primary Outcome: 90-day functional independence rate
 - Primary Safety Outcome: 90-day mortality rate
 - Shortcomings and advantages

Table 2: Validity Assessment. Combination treatment vs. IV thrombolytic

Study	Selection Bias	Performance Bias	Blinding	Time window for intervention (<6 hrs)	Intention to treat analysis
Bracard (THRACE)	A	A	I	A	A
Saver (SWIFT PRIME)	A	A	A	A	I
Mocco (THERAPY)	A	A	A	A	A
Khoury (EASI)	A	A	A	A	A
Campbell (EXTEND-IA)	A	A	A	A	A
Muir (PISTE)	A	A	A	A	A
Cabral et al	I	A	A	A	I

Key: A: Adequate, assessment/measure (ie. blinding, intention to treat analysis) was completed and used appropriately through the study, I: Inadequate evidence, assessment/measure was not completed or discussed in the study. **Selection Bias** is considered adequate if the study randomized patients as they were placed into their treatment groups. **Performance Bias** is adequate if patient factors (ie. comorbidities, age, sex) were adjusted for in the study's statistical analysis. **Blinding** is considered adequate if the study blinded the analysis process and/or data collection after treatment (ie. staff member was blinded to the treatment group when collecting the mRS score of the patients at 90 days). **Time window for intervention** is adequate if patients began treatment within 6 hours of symptoms onset. **Intention-to-treat analysis** is adequate if it was performed in each respective study.

Discussion

- Compared trials to assess approaches to each factor
- MR CLEAN's publication interrupted many of the trials, some were unable to reach targeted sample size, thus two of the seven had inconclusive results (THERAPY, EASI)
- However, most of the trials still had significant results
- Those that were inconclusive still trended in support of the hypothesis

Table 3: Comparison of Results. Combination treatment vs. IV thrombolytic

Study	IVT mRS = 0-2 at 90 days	Combination Treatment mRS = 0-2 at 90 days	IVT Mortality at 90 days (%)	Combination Mortality at 90 days (%)
Bracard (THRACE)	S	S	NS	NS
Saver (SWIFT PRIME)	S	S	NS	NS
Mocco (THERAPY)	I	I	I	I
Khoury (EASI)	I	I	I	I
Campbell (EXTEND-IA)	S	S	NS	NS
Muir (PISTE)	S	S	NS	NS
Cabral et al	S	S	NS	NS

Key: IVT: Intravenous therapy, S: Significant (p<0.05), NS: Not Significant (p>0.05), I: inconclusive due to interruption of trial

Conclusion

- **Significant increase in 90-day functional independence rate in IVT + MT groups vs IVT groups**
- **No significant difference in 90-day mortality rate between the two groups**
- Combinative therapy does have a place in treatment of acute large vessel occlusion
- Areas of further research:
 - how health and economic inequities may hinder implication of MT
 - Efficacy in posterior circulation strokes
 - Role of MT in later presenting strokes (>6 hours)
 - MT stent-retrievers vs MT aspiration

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