Impact of General Anesthesia on Treatment Effect in the MR CLEAN trial

a post-hoc analysis

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for the MR CLEAN investigators
Disclosures

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- Top Medical/Concentric
Rationale

- Type of anesthetic management in IAT remains controversial
  - Practice variation
  - Recent systematic review suggested IAT without general anesthesia was associated with better neurological and radiological outcomes\(^1\)

- Subdivided in:
  - General anesthetic approach (GA)
  - Non-general anesthetic approach (Non-GA)

\(^1\) Brinjikji et al., AJNR 2015
Advantage / Disadvantage

GA:  - shorter procedural duration and safer
     - delayed treatment intitation
     - higher risk of (aspiration) pneumonia\(^1\)

Non-GA:  - faster treatment initiation
         - neurological assessment during IAT
         - patient movement with risk of vessel perforation/dissection
         - conversion to GA with emergency intubation with higher
           likelihood of (aspiration) pneumonia\(^2\)

\(^1\) Hassan et al., 2012
\(^2\) Rosenberg et al., 1991
Aim

To assess the difference under anesthetic management types (GA vs Non-GA) in functional outcome & safety in patients undergoing intra-arterial therapy.
Design of MR CLEAN trial

- Multicenter, prospective, randomized trial with open label treatment and
  - Blinded assessment of functional outcome at 90 days
- Primary outcome was modified Rankin Scale (mRS) at 90 days
MR CLEAN inclusion criteria

• Acute ischemic stroke

• Intracranial anterior circulation occlusion (confirmed by CTA)

• IA treatment within 6 hours from onset was possible

• Age ≥18

• NIHSS ≥ 2
Study specific characteristics

• General anesthetic management (GA):
  • intubation combined with IV and/or inhaled anesthetic agents

• Non-general anesthetic management (Non-GA):
  • IAT with or without consious sedation

• All centers adhered to local protocols with a fixed choice for either GA or Non-GA.

• First anesthetic management was used for analysis, crossovers were collected
Statistical analysis

**Primary outcome:**
Score on the mRS

**Secondary outcomes:**
Timing
Safety parameters
Procedural related adverse events

**Primary effect parameter**
- adjusted common odds ratio (acOR)
- estimated with ordinal regression
- also called shift analysis

All effect estimates were **adjusted** for
- age
- NIHSS
- time since onset to randomization
- previous stroke
- atrial fibrillation
- diabetes mellitus
- carotid terminus occlusion
500 patients were included in the MR CLEAN trial

233 allocated to IAT
267 allocated to control

17 did not reach angiosuite

216 entered angiosuite
266 standard tx
1 received IAT under GA

Conversion rate:
6 / 137 = 4.4 %
Clinical characteristics at baseline

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>GA (N=79)</th>
<th>Non-GA (N=137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years - median (IQR)</td>
<td>63 (52-75)</td>
<td>67 (57-76)</td>
</tr>
<tr>
<td>Male sex – n (%)</td>
<td>47 (59%)</td>
<td>79 (58%)</td>
</tr>
<tr>
<td>NIHSS score - median (IQR; range)</td>
<td>18 (15-21;4-30)</td>
<td>17 (14-21;4-30)</td>
</tr>
<tr>
<td>Time intervals in minutes – mean (SD)</td>
<td>GA (N=79)</td>
<td>Non-GA (N=137)</td>
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<tr>
<td>Door to start IAT</td>
<td>162 (69)</td>
<td>134 (60)</td>
</tr>
<tr>
<td>Randomization to start IAT</td>
<td>64 (29)</td>
<td>50 (32)</td>
</tr>
<tr>
<td>Procedural duration</td>
<td>76 (35)</td>
<td>79 (41)</td>
</tr>
<tr>
<td>Onset to revascularization/last angiogram</td>
<td>348 (80)</td>
<td>334 (86)</td>
</tr>
<tr>
<td>Safety parameters</td>
<td>GA (N=79)</td>
<td>Non-GA (N=137)</td>
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<tr>
<td>---------------------------------------</td>
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</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
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<tr>
<td>Within 7 days – n (%)</td>
<td>12 (15%)</td>
<td>18 (13%)</td>
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<tr>
<td>Within 30 days – n (%)</td>
<td>14 (18%)</td>
<td>26 (19%)</td>
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<tr>
<td>Vessel perforations – n (%)</td>
<td>0 (0%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Procedure related dissections – n (%)</td>
<td>2 (2.6%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>ENT – n (%)</td>
<td>8 (10%)</td>
<td>12 (10%)</td>
</tr>
<tr>
<td>Conversion to GA – n (%)</td>
<td>- (-)</td>
<td>6 (4.4%)</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>GA (N=79)</td>
<td>Non-GA (N=137)</td>
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<td>---------------------------------------------------------------</td>
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<tr>
<td>Patients with at least one SAE – n (%)</td>
<td>43 (54%)</td>
<td>57 (42%)</td>
</tr>
<tr>
<td>Symptomatic ICH – n (%)</td>
<td>6 (8%)</td>
<td>11 (8%)</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2 (PH2) – n (%)</td>
<td>5 (6%)</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Recurrent acute ischemic stroke – n (%)</td>
<td>4 (5%)</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Progressive ischemic stroke – n (%)*</td>
<td>24 (30%)</td>
<td>17 (12%)</td>
</tr>
<tr>
<td>Pneumonia – n (%)</td>
<td>11 (14%)</td>
<td>13 (9%)</td>
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<tr>
<td>Other complications – n (%)</td>
<td>10 (13%)</td>
<td>11 (8%)</td>
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</tbody>
</table>
Primary outcome in the MR CLEAN trial

Common adjusted odds ratio: 1.67 (95% CI: 1.21 to 2.30)
Effect on GA/Non-GA on the Primary outcome

Common adjusted odds ratio Non-GA vs Control = 2.13 (95%CI 1.46 – 3.11)

Common adjusted odds ratio GA vs Control = 1.09 (95%CI 0.69 – 1.71)

\( P = 0.013 \)
Effect on GA/Non-GA on good functional outcome (mRS 0-2)

Adjusted odds ratio Non-GA vs Control – 2.79 (95%CI 1.70 – 4.59)

Adjusted odds ratio GA vs Control – 1.09 (95%CI 0.56 – 2.12)
Conclusion

- **General anesthesia** is associated with delayed treatment initiation in the MR CLEAN trial
  - Procedural durations were equivalent in both groups
  - There was no significant difference in time to revascularization

- There were no procedural safety concerns in both groups

- There was a significant interaction with treatment. The effect on outcome that we found in the MR CLEAN trial, was not observed in the subgroup of patients treated with **general anesthesia**
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Data monitoring committee: Martin Brown, Thomas Liebig, Theo Stijnen.
Additional slides

• Results needs to be confirmed in randomized controlled trials:
  
  • “ANSTROKE” - Sedation Versus General Anesthesia for Endovascular Therapy in Acute Stroke - Impact on Neurological Outcome (Sahlgrenska University Hospital, Sweden) [NCT01872884]
  
  • “GOLIATH” - General Or Local Anaesthesia in Intra Arterial TTherapy (Aarhus, Denmark) [NCT02317237]
Additional slides

- On-treatment analyses
- acOR GA 1.13 (0.73 – 1.78)
- acOR Non-GA 2.12 (1.45 – 3.11)