General Anesthesia or sedation for endovascular thrombectomy: Does it matter in 2020?

Stanlies D'Souza
Baystate Health, dsouzastan@yahoo.com
General Anesthesia or sedation for EVT in Acute Ischemic Stroke: Does it matter in 2020?

Stanlies D’Souza MD, FRCA, FCARCSI
Associate Professor,
University of Massachusetts Medical School (UMMS)
Adjunct Associate Professor,
Tufts University School of Medicine
Division Chief, Neuroanesthesiology,
UMMS-Baystate
Member, National Neuroanesthesia Committee,
The American Society of Anesthesiologists (ASA)
Overview

1. Acute ischemic stroke (AIS): current management

2. Sedation vs General Anesthesia (GA) for EVT: Review of data from observational studies and retrospective analysis

3. Sedation Vs GA for EVT: Review of data from randomized controlled trials
4. Sedation vs GA for EVT: Ongoing trials
5. Volatile anesthetic vs total intravenous anesthesia (TIVA) for EVT
6. Sedation Vs GA: current concepts
<table>
<thead>
<tr>
<th>Year</th>
<th>Title</th>
<th>Centers</th>
<th>number</th>
<th>Time</th>
<th>Reference</th>
</tr>
</thead>
</table>
EVT 6-24 hours: DAWN trial

n=206 (107 thrombectomy group, 99 control group) (multicenter)

Outcome measure:
1. Functional independence (mRS 0-2) was better with thrombectomy group compared to standard of care (49% vs 13%)
2. 90 day mortality did not differ between the two groups (19% vs 18%)

Thrombectomy in AIS 6-16 hours: Diffuse 3 trial

Multicenter US trial, 38 center, trial was terminated after recruiting 182 patients (90 EVT group, 90 medical therapy group)

Outcome measures

- Functional outcome better with thrombectomy compared to medical therapy (45% Vs 17%)
- Mortality rate at 90 days was lower with thrombectomy group compared to medical therapy group (14% vs 26%).

IV tPA really necessary?

AIS: EVT vs EVT with tPA (combination therapy)

- Multicenter RCT 41 tertiary academic centers (n=656)

- **Outcome measures**: Reperfusion: before thrombectomy (2.4% vs 7.9%)
- Successful reperfusion after thrombectomy: 79.4% vs 84.5%

- Mortality 17.7% vs 18.8% at 90 days

- **Conclusion**: Endovascular thrombectomy alone is non-inferior to with regard to functional outcome at 90 days.

GA vs Sedation for EVT: Data from observational/retrospective analysis

Multiple observational studies/retrospective analyses and their meta analyses reported:
Better functional neurological outcome with sedation compared to GA.
MR Clean: retrospective data

MR CLEAN retrospective data analysis (n=1378, 60% LA only, 13% conscious sedation, 28% GA)

Results:
1. GA had worse outcome than LA (Odds ratio 0.75)
2. CS worse outcome than LA (Odds ratio 0.45)
3. CS had worse outcome than GA (Odds ratio 0.6)

Ref: NEJM journal watch Jan 7, 2020
Retrospective analysis of DIFFUSE 3 trial

n=92 (GA 26, 28% and sedation 66, 72%)

Results: Sedation compared to GA had

1. Lower NIHSS score at 24 hours
2. Better functional independence @ 90 days with mRS 0-2

Ref: Am J Neurol 2019;40-10011-5
Limitation of observational studies

- Baseline neurological status was better in sedation group
- Patients with posterior circulation stroke were not commonly included in sedation group
- Time to EVT is faster in sedation group
- BP during EVT was slower in GA group.
### GA vs Sedation: Single center RCT’s

<table>
<thead>
<tr>
<th>RCT</th>
<th>Year reported</th>
<th>Country</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIESTA</td>
<td>2016</td>
<td>Germany</td>
<td>150</td>
</tr>
<tr>
<td>AnStroke</td>
<td>2017</td>
<td>Sweden</td>
<td>90</td>
</tr>
<tr>
<td>Goliath</td>
<td>2018</td>
<td>Denmark</td>
<td>128</td>
</tr>
</tbody>
</table>
SIESTA trial (Sedation vs Intubation for Endovascular Stroke treatment)

Trial from Germany; single center RCT
n=150 (GA 73, sedation 77)

Anterior circulation AIS
Sedation: Conscious sedation
GA: Intubation and non standardized anesthesia technique

Ref:
1. JAMA 2016;316:1986-96
SIESTA

BP: 120-180 systolic

PaCO2: 35-45 mm Hg
SIESTA

Primary outcome measure: Early neurological recovery

<table>
<thead>
<tr>
<th></th>
<th>GA</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>At admission</td>
<td>16.8</td>
<td>17.2</td>
</tr>
<tr>
<td>At 24 hours</td>
<td>13.6</td>
<td>13.6</td>
</tr>
<tr>
<td>Difference</td>
<td>-3.2</td>
<td>-3.6</td>
</tr>
</tbody>
</table>
**SIESTA: Secondary outcome measure at 3 months**

<table>
<thead>
<tr>
<th>Outcome measure at 3 months</th>
<th>GA</th>
<th>sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional outcome mRS(0-2)</td>
<td>37%</td>
<td>18.2</td>
</tr>
<tr>
<td>Mortality</td>
<td>24.7%</td>
<td>24.7%</td>
</tr>
</tbody>
</table>
Anesthesia During Stroke (AnStroke) trial

n= 90 (45 sedation, 45 GA group (conducted in Sweden)

GA vs sedation

GA = propofol and remifentanil for induction followed by sevoflurane and remifentanil maintenance

Sedation group: propofol and remifentanil

BP was maintained @ 140-180 mm Hg systolic with vasopressors.

Ref: Stroke 2017; 48:1601-7
Patient characteristics: Baseline neurological status was similar in both groups.

BP was maintained @ 140-180 mm Hg systolic with vasopressors.

PaCO₂, blood glucose were comparable in both groups.
An stroke trial

Outcome measures: Functional outcome on modified rankin scale (mRS) at 90 days

19 out of 45 patients in GA group (42.2%) and 18 out of 45 (40%) patients in sedation group had mRS less than 2 at 90 days.

Ref: Stroke 2017;48:1601-1607
Successful recanalization was similar in both groups (91.1% GA vs 88.9%)

In hospital mortality was similar in both groups (13.3%)

Ref: Stroke 2017;48:1601-1607
Goliath trial

GOLIATH: General Anesthesia Or Local Anesthesia in Intra-Arterial Therapy

n=128 (65 GA, 63 sedation)

Sedation protocol: fentanyl/propofol

GA protocol: Propofol/alfentanil/succinylcholine for induction

Propofol/remifentanil maintenance

Ref: JAMA Neurol 2018; 75:470-77
GOLIATH

Primary outcome measure: Infarct size measured: mRA 48-72 hours: No difference

Successful perfusion was better with GA group compared to sedation group(76.9% Vs 60.3%)

Better functional outcome in GA group with mRS at 90 days: Odds ratio: 1.91 (95% CI)
BP thresholds in RCTs

BP thresholds in three RCT for adverse functional outcome (mRS @ 90 days)

MAP less than 70 mm Hg for 10 min or MAP greater than 90 mm Hg for more than 45 min had adverse outcome.

Ref: JAMA Neurol 2020;77:622-31
Meta-analysis of 3 RCT’s

n=368 (Siesta, Anstroke, Goliath)

Results:

1. Functional independence on (mRS 0-2)@ 90 days was better in GA group compared to sedation (Odds ratio 1.87, 95% CI, 1.15-3.03)

1. No difference in mortality, anesthesia complications, pneumonia, interventional complications and length of ICU stay.

Ref: J Am Heart Assoc 2019; 8e011754
Meta-analysis of RCT’s

Conclusion: Moderate quality evidence suggests better outcome with GA.
Large RCTs are needed to confirm the benefit.

Ref: J Am Heart Assoc 2019; 8e011754
RCT from China: sedation Vs GA

n= 88

TIVA was used in both groups
ETCO₂ target was: 35-40 mm Hg
Conversion of sedation to GA: 9.52%
(SIESTA 14.3%, Goliath 15.6%)
No difference in functional outcome or mortality rate at 90 days
Ref: Frontiers in Neurology;
doi.org/10.3389/fneuro.2020.00170
Ongoing trials: AMETIS trial

AMETIS trial (Anesthesia Management in Endovascular Therapy for Acute Ischemic Stroke) (France) (n=270) (Anterior circulation AIS) (multicenter)

Protocol:
1. GA and sedation protocols are not standardized
2. Systolic BP should be maintained between 140-180 systolic
3. End Tidal Co2 should be maintained at 30-35 mm Hg

Primary outcome measure: mRS 0-2 At 90 days

Ref: BMJ open 2019;9:e027561  NCT 03229148
Ongoing trials: SEGA trial

SEdation Versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (SEGA)

Country: US

n=270

GA: protocol not standardized

Sedation: not standardized (fentanyl, midazolam, propofol intermittent bolus or low dose infusion, dexmedetomidine infusion with or without bolus at the discretion of the anesthesiologist)

Ref: NCT 03263117
What General Anesthesia technique?

- Total intravenous Anesthesia (TIVA)?
- Volatile anesthesia?
- Or combination of intravenous and volatile anesthetic agents?
Volatile agents Vs TIVA?

- A meta-analysis of 14 RCT’s
- n= 1891
- TIVA: Propofol/fentanyl and Propofol/remifentanil
- Volatile anesthetic agents: Isoflurane/sevoflurane in air/oxygen mixture
- ASA 1-3
- Patients had no or minimal midline shift on CT scan

Ref: Can J Anaesth 2014; 61:347-56
Volatile agents Vs TIVA

1. ICP = \(-5.2\) mm/Hg less (95% confidence interval - 6.81 to -3.6 mm Hg)

2. CPP was +15.3 mm Hg (95% confidence interval 12.2 to 20.46 mm Hg)

3. Limitations: Outcome measures were not studied in these trials of this meta-analysis.

Ref: Can J Anaesth 2014; 61:347-56
Volatile agents vs TIVA

TIVA alone or with lower concentration of volatile anesthetic most commonly used popular technique in neurosurgical patients.

References;
1. Miller's anesthesia 9th edition 2020
2. UpToDate 2020
TIVA Vs Volatile anesthesia?

- Propofol based TIVA maintains cerebral autoregulation curve and decreases the ICP.
- Volatile anesthetic agents suppress the cerebral autoregulation in a dose dependent manner.

Ref:
2. Miller’s Anesthesia 2020; 9th edition
Dose-dependent Depression of Cerebral Autoregulation by Volatile Anesthetics
Conclusion

GA vs sedation: What we should in 2020?

Choice of the technique depends on patients baseline neurological status. Choice of the technique depends on patients baseline neurological status as per 2019 ASA of AHA statement.

Stroke 2019; 50:e344-e418