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General Anesthesia or sedation for EVT in Acute Ischemic Stroke: Does it matter in 2020?

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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

Year	Title	Centers	number	Time	Reference
2015	MR CLEAN	16, Dutch	500	6	Ref28: N Engl J Med 2015; 372:11-20
2015	EXTEND IA	14, Australia, New Zealand	70	4.5	Ref 29: N Engl J Med 2015; 372: 1009-18
2015	ESCAPE	21, International	316	12	Ref 30:N Engl J Med 2015; 372:1019-30
2015	REVASCAT	4 Spanish centers	206	8	Ref 31: N Engl J Med 2015; 372:2296-2306
2015	SWIFT PRIME	39, international	196	6	Ref 32: N Engl J Med 2015; 372:2285-2295



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%)

Ref: N Engl J Med 2018; 378:11-21



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.

Ref:N Engl J Med 2020; 382:1981-1993



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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.



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GA vs Sedation: Single center RCT's

RCT	Year reported	Country	n
SIESTA	2016	Germany	150
AnStroke	2017	Sweden	90
Goliath	2018	Denmark	128



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
2. Am J Neuroradiol 2017; 38:1580-85



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SIESTA

BP: 120-180 systolic

PaCO₂: 35-45 mm Hg



SIESTA

Primary outcome measure: Early neurological recovery

Mean NIHSS Score	GA	Sedation
At admission	16.8	17.2
At 24 hours	13.6	13.6
Difference	-3.2	-3.6



SIESTA: Secondary outcome measure at 3 months

Outcome measure at 3 months	GA	sedation
Functional outcome mRS(0-2)	37%	18.2
Mortality	24.7%	24.7%



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



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Anstroke

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



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Anstroke trial

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

19 out 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



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AnStroke trial

Other measures

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



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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 *M*anagement in Endovascular Therapy for Acute *I*schemic 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



Ongoing trials: SEGA trial

*SE*dation Versus *GA*neral 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



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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/remifentanyl
- 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.



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
3. Pasternak JJ: Neuroanesthesiology Update. J Neurosurg Anesthesia 2019; 2; 178-98



TIVA Vs Volatile anesthesia?

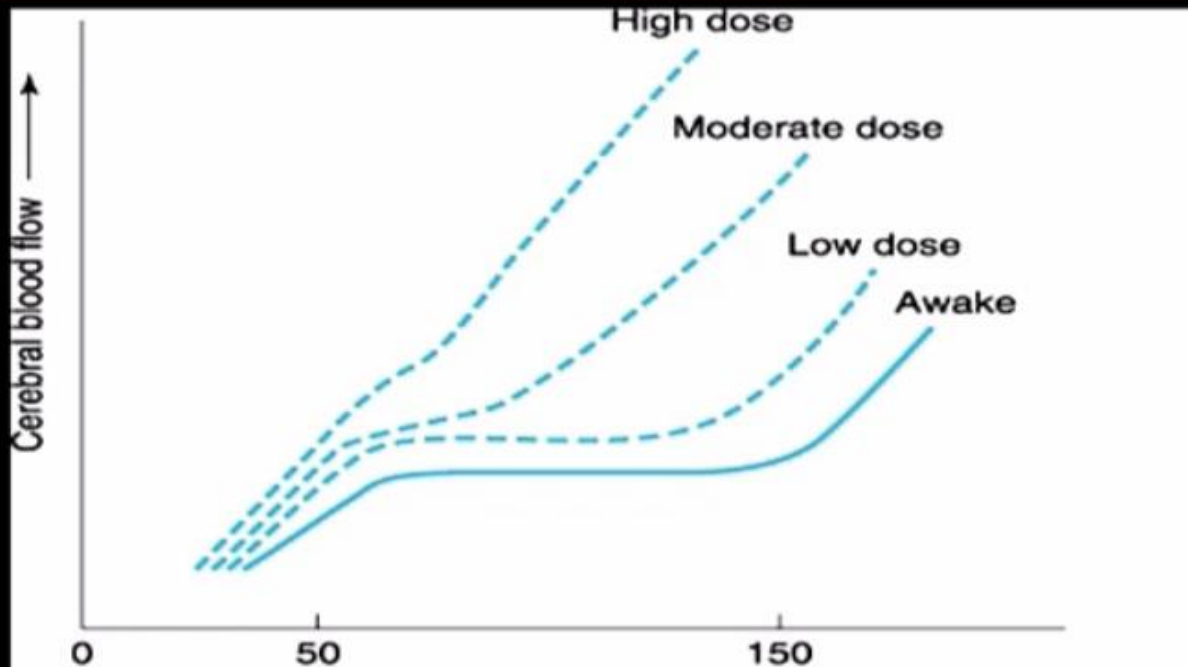
- Propofol based TIVA maintains cerebral autoregulation curve and decreases the ICP.
- Volatile anesthetic agents suppress the cerebral autoregulation in a dose dependent manner.

Ref:

1. **Armstead WM: Cerebral autoregulation and dysregulation. Anesthesiol Clin. 2016 34: 465–477**
2. **Miller's Anesthesia 2020; 9th edition**

Sharma: ASA 2019 meeting

Dose-dependent Depression of Cerebral Autoregulation by Volatile Anesthetics





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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