Is Supplemental O_2 a Good Supplement?

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Additional DISCLOSURE in this case

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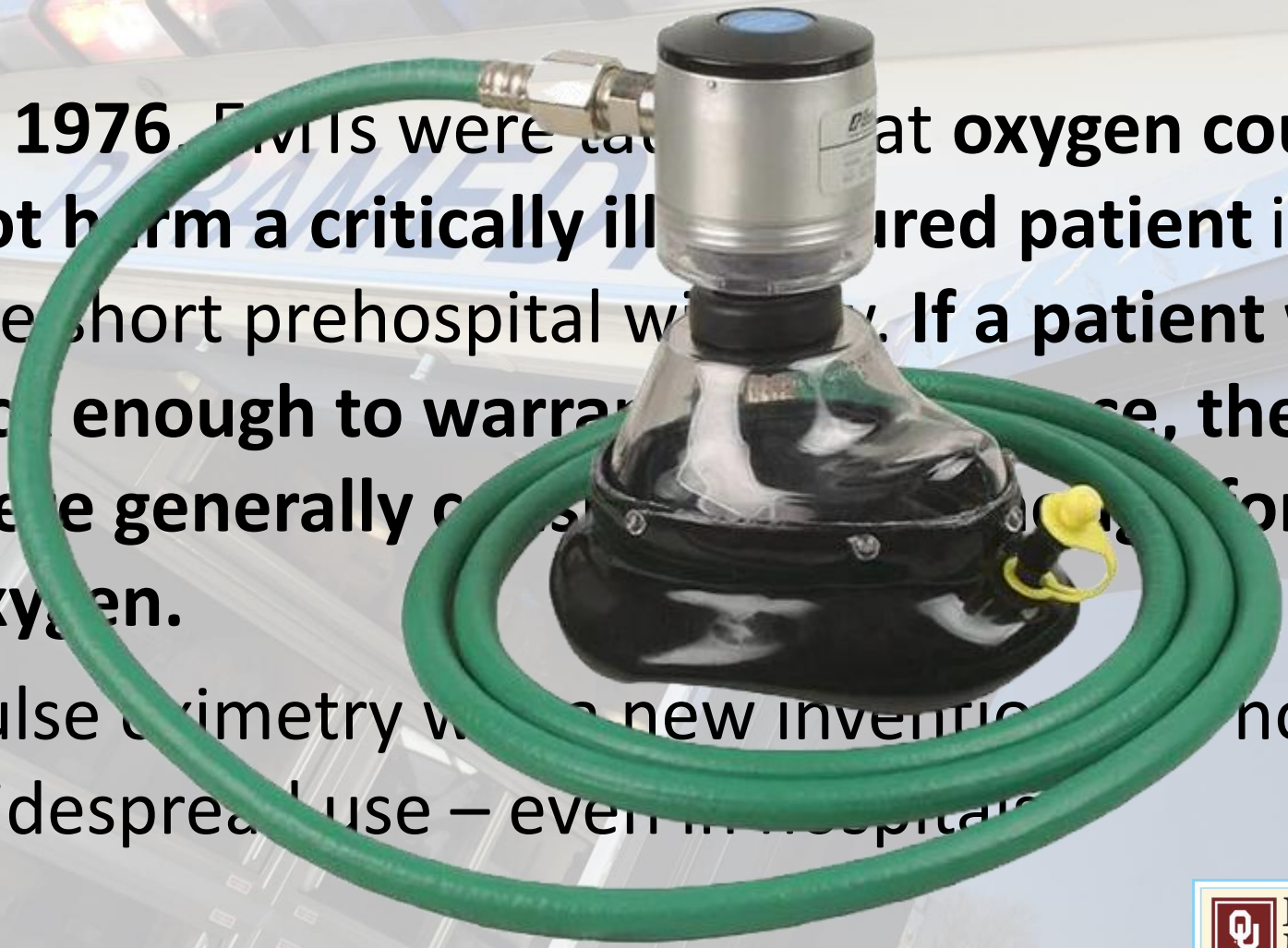
It should be noted that Dr. Goodloe does have a consulting relationship with J&J MedTech, Fisher & Paykel, Medtronic, & Purdue/Knoa Pharma

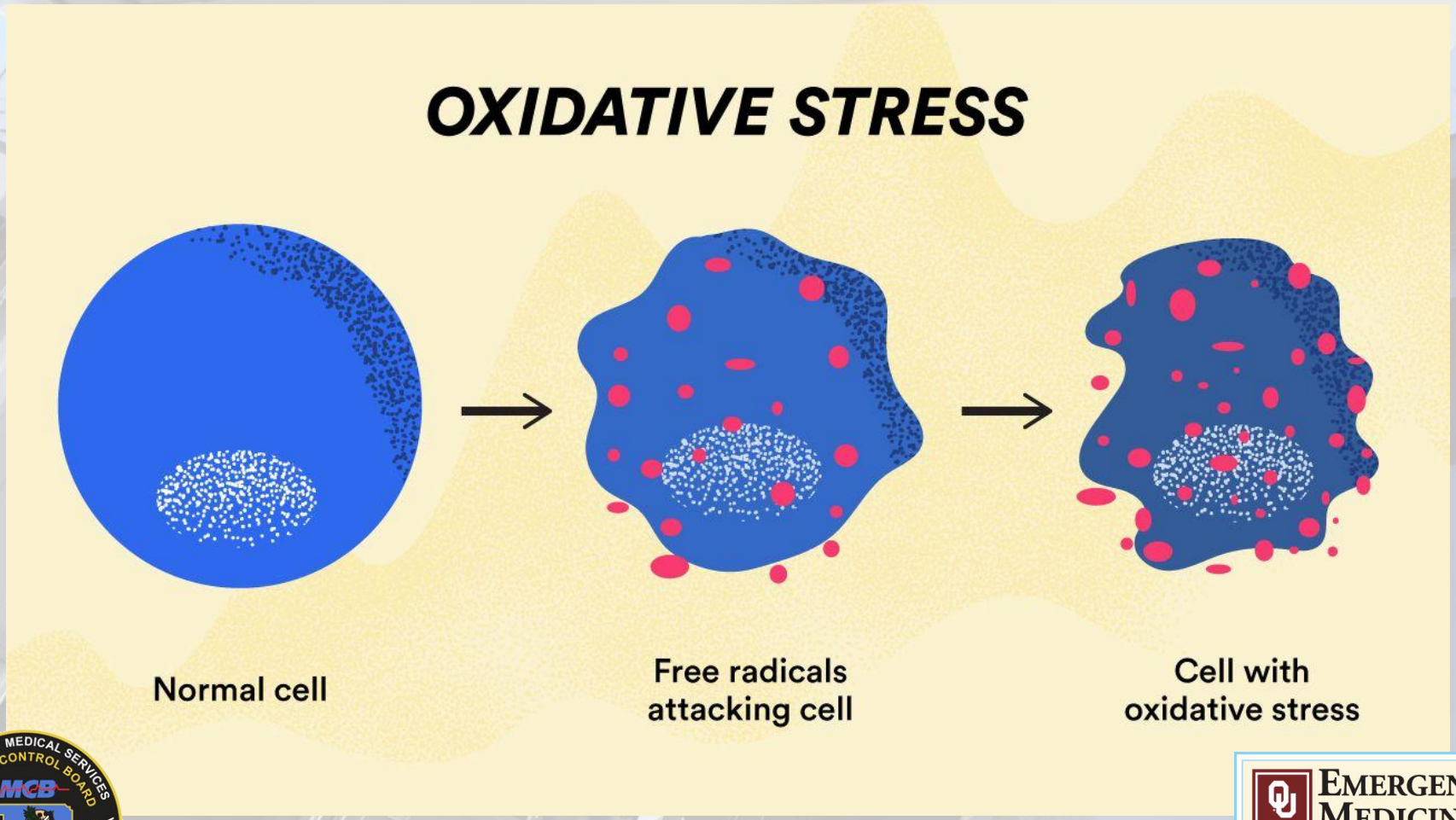
However, this CME activity has been designed and reviewed by an independent committee with no relevant financial ties to ensure that the content is free of commercial bias and evidence-based. Accordingly, all of the relevant financial relationships listed for Dr. Goodloe have been mitigated.

Seems Simple Enough…



- **In 1976, EMTs were taught that oxygen could not harm a critically ill or injured patient** in the short prehospital window. **If a patient was sick enough to warrant EMS service, they were generally considered candidates for oxygen.**
- Pulse oximetry was a new invention, not in widespread use – even in hospitals

Fortunately, We've Learned a Thing or More About More…



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Avoiding Higher Pressures in "High Pressure" Situations

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The Journal of **TRAUMA**® *Injury, Infection, and Critical Care*

Table 1 Mean Values (n = 8) for Cardiopulmonary Variables Using Various Rates of PPV in a Swine Model of Moderate, Controlled Hemorrhage

	RR (breaths/min)				
	12	6	20	30	6
RA (mm Hg)*	1 ± 1	0 ± 1	4 ± 1	5 ± 1	0 ± 1
ITP (mm Hg)	15 ± 2	12 ± 2	16 ± 2	19 ± 2	11 ± 2
Ao Syst (mm Hg)*	65 ± 2	84 ± 4	73 ± 4	66 ± 5	95 ± 6
Ao Diast (mm Hg)	51 ± 2	71 ± 5	59 ± 4	52 ± 5	81 ± 6
Pao_2 (mm Hg)	68 ± 4	138 ± 13	113 ± 7	115 ± 3	174 ± 20
$Paco_2$ (mm Hg)	35 ± 1	62 ± 2	28 ± 1	19 ± 1	58 ± 2
pH (arterial)	7.46 ± 0.02	7.28 ± 0.02	7.51 ± 0.01	[illegible] 0.02	7.28 ± 0.01
CPP (mm Hg)	50 ± 2	60 ± 4	47 ± 3	42 ± 4	71 ± 6
Qr (L/min)	2.4	2.8	2.5	2.4	3.0

RA, right atrial diastolic pressure; ITP, *mean intrathoracic airway pressure;* Ao Syst, *aortic systolic pressure;* Ao Diast, *aortic diastolic pressure;* Pao_2, *arterial oxygen tension;* $Paco_2$, *arterial carbon dioxide tension;* CPP, *coronary perfusion pressure (averaged over 10 min);* Qr, *Cardiac output.*

* Measured at end-expiration.

Pepe PE et al. Emergency Ventilatory Management in Hemorrhagic States: Elemental or Detrimental?. The Journal of Trauma: Injury, Infection, and Critical Care 54(6):p 1048-1057, June 2003. | DOI: 10.1097/01.TA.0000064280.05372.7C

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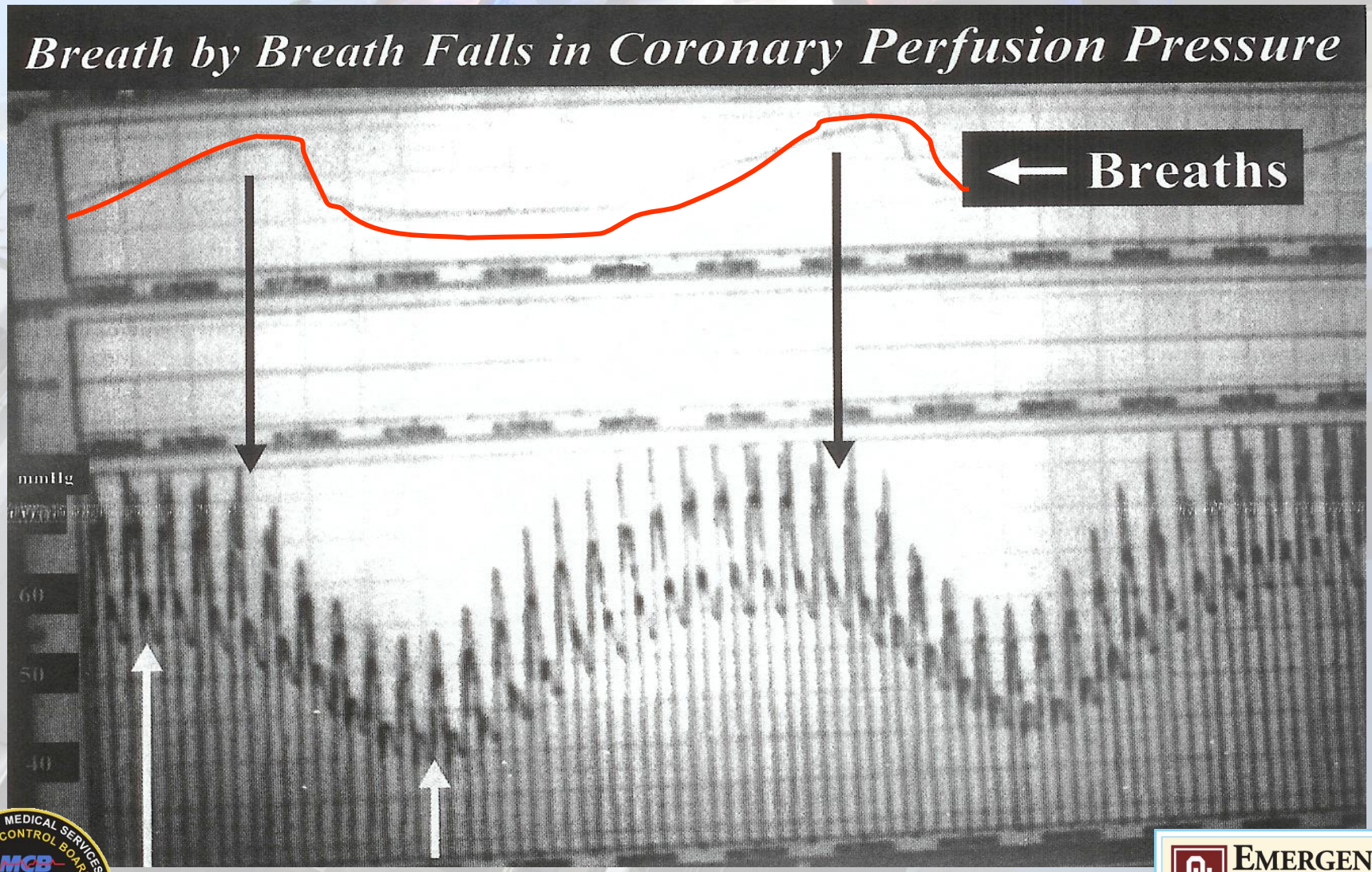
Breath by Breath Falls in Coronary Perfusion Pressure



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It's All a Balanced Equation

- Get the patient back to "normal"
- Promote perfusion
- Avoid excessive partial pressures of O_2
- Avoid excessive pressures in PPV

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Oxygen and Outcomes in Acute Ischemic Stroke

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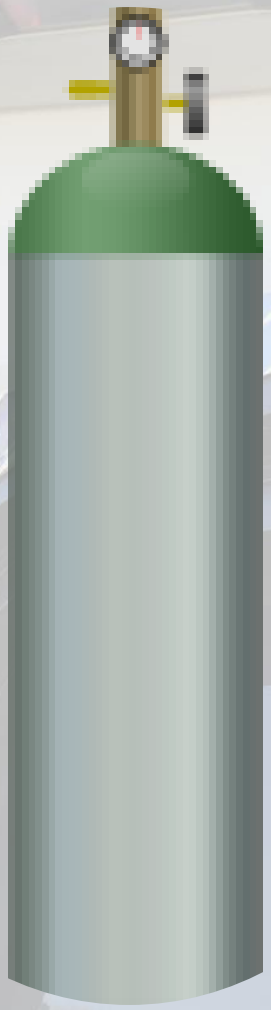
Oxygen



IS HYPEROXYGENATION OXYGEN HARMFUL IN ACUTE ISCHEMIC STROKE PATIENTS?

IS HYPEROXYGENATION BENEFICIAL IN ACUTE ISCHEMIC STROKE PATIENTS?

Oxygen

In-hospital Management of AIS: General Supportive Care
4.3 Supplemental Oxygen

Recommendations	COR	LOE
1. Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction that causes compromise of the airway.	I	C-EO
2. Supplemental oxygen should be provided to maintain oxygen saturation >94%.	I	C-LD
3. Supplemental oxygen is not recommended in nonhypoxic patients hospitalized with AIS.	III: No Benefit	B-R

American Heart Association.

Oxygen Use in Acute Stroke
Current AHA Guidelines

Does oxygen help or is it harmful?

Recommend O2 Saturations between 94–98%.

Hyperoxia may cause oxidative damage?

Supplemental O_2 only if SpO_2 <94%

Recommendation: Avoid routine O_2 unless hypoxic?

Randomized – Normoxemic Stroke (Non-EVT)

Stroke Oxygen Study (SO_2S) (JAMA 2017)

Design & timing: Multicenter, single-blind RCT; **8,003 adults with acute stroke**, randomized **within 24 h of hospital admission** across 136 UK centers. Arms: (1) **continuous O_2 for 72 h**, (2) **nocturnal O_2 only** (**21:00–07:00 for 3 nights**), (3) **control** (O_2 only if clinically indicated).

- **Dose & delivery:** Nasal cannula **3 L/min if SpO_2 ≤93%** or **2 L/min if >93%**.

- **Population:** Median NIHSS 5; **mean baseline SpO_2 ≈96.6%** (i.e., largely normoxic).

- **Primary outcome (mRS shift at 90 d): No difference** for pooled oxygen vs control (OR **0.97**, 95% CI 0.89–1.05) and **no difference** continuous vs nocturnal (OR **1.03**, 95% CI 0.93–1.13).

- **Safety/secondary: No significant harms**; serious AEs similar across groups. No subgroup with clear benefit identified.

- **Adherence/physiology notes:** The trial added midnight/6am spot checks in later enrollees; prior pilot signals didn't replicate, and **severe desaturations were not significantly different** between treatment and control.

Practical takeaway

For **non-hypoxic** acute stroke patients, **routine low-dose oxygen (2–3 L/min) for 72h—continuous or nocturnal—does not improve 90-day death/disability and appears safe but unnecessary**.
Use oxygen **selectively**, e.g., when **SpO_2 <94–95%** or clinically indicated.

Evolution of Normobaric Hyperoxia (NBO) in Acute Ischemic Stroke

OPEN I: 2019

Can Oxygen save brain tissue?

- Single center EVT, Randomized controlled
- 86 Randomized; 43 EVT alone & 43 NBO + EVT
- NRB 10L, 4 Hours
- 47% reduction in infarct Volume (20.1ml vs 37.7ml)
- mRS 90 Days: (NBO + EVT=2) vs (EVT Alone = 3)
- **Proof of Concept: Decrease Infarct Volume**

Phase II: OPENS-2 Dose Finding (2024 – Stroke).

How Much Oxygen exposure is needed?

- Multicenter EVT-era dose-finding trial.
- 10 L/min O_2 vs 1 L/min sham for 4 h post-EVT.
- 2H, **4H,** 6H duration of Oxygen, 72 H infarct volume
- 4H = Best outcomes, **50% reduction in infarct volume** vs control (19.7 ml vs 39.4ml) and no adverse effects
- Established safe, optimal dose for confirmatory trial.

Phase III: OPENS-2 (2025 – Lancet) (Confirmatory Evidence)

Does this translate into better patient outcomes?

- Multicenter RCT, 282 EVT-treated patients
- Randomized 10 L/min O_2 vs 1 L/min (sham) for 4 h post-EVT
- 4 Hour period, Peri-Thrombectomy
- **Improved 90-day mRS (median 2 vs 3) , 40% reduction in Infarct volume,**
- Mortality 10% vs 12%
- **No increase in ICH or oxidative injury**

OPENS-2 trial (Li et al, *Lancet* 2025), Normobaric Hyperoxia combined with endovascular treatment for acute ischemic stroke in China— multicenter, randomized, single-blind, sham-controlled trial.

Objective: To test whether augmenting endovascular therapy (EVT) with normobaric hyperoxia (NBO) improves 90-day functional outcomes, without compromising safety, in patients with acute ischemic stroke from large-vessel occlusion in the anterior circulation.

Design & Methods

- Multicenter (26 comprehensive stroke centers in China)
- Randomized 1:1, single-blind (patients + outcome assessors blinded) to:

- **Intervention:**
  - NBO arm: inhalation of 100% O_2 at 10 L/min via non-rebreather mask for 4 h (or FiO_2 = 1.0 if intubated)
  - Sham arm: 100% O_2 at 1 L/min (i.e., low flow) → approx FiO_2 ~0.3

- **Inclusion**: age 18–80, within 6 h of onset, anterior-circulation large-vessel occlusion, eligible for EVT
- Primary outcome: distribution of modified Rankin Scale (mRS) scores at 90 days (ordinal shift) in intention-to-treat population
- Safety: mortality, serious adverse events, oxygen-related AEs

Enrollment & Baseline Characteristics

- Screened: **473 patients** → **Randomized: 282 (140 NBO + EVT, 142 sham + EVT)**
- Median age: 65 years (IQR 57–71)
- Sex: 75 (27%) female, 207 (73%) male
- All participants were Han Chinese ethnicity

Functional outcomes (90 days)

- Median mRS: 2 (IQR 1–4) in NBO group vs 3 (1–4) in sham group.
- **Overall a 1 point improvement in mRS for the Oxygen arm of the trial, 40% reduction in infarct volume**
- Adjusted common odds ratio (cOR) for better shift on mRS: 1.65 (95% CI 1.09 – 2.50), p = 0.018
- In other words, patients in the NBO + EVT arm had higher odds of a better outcome distribution.

Mortality & Safety

- Deaths by 90 days: 14/140 (10%) in NBO vs 17/142 (12%) in sham; adjusted risk difference (95% CI –0.09 to 0.06)
- Serious adverse events: 28 (20%) in NBO vs 33 (23%) in sham; adjusted risk difference (95% CI –0.12 to 0.07)
- No significant increase in oxygen-related complications was reported.

Authors' Interpretation

NBO-augmented EVT yielded superior functional outcomes at 90 days (ordinal mRS shift) compared to sham, without a safety penalty. The authors suggest NBO may serve as a neuroprotective adjunct to EVT.

Key Takeaways

Oxygen in AIS:

Oxygen NRB 10L 4-hour duration peri EVT, **MAY** improve outcome

- mRS 90 days
- Decrease Infarct Volume

* No RCT demonstrates harm from short-term O_2.