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SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

ARTICLE OF THE MONTH

Blood Pressure Thresholds and Neurologic Outcomes After Endovascular Therapy for Acute Ischemic Stroke: An Analysis of Individual Patient Data From 3 Randomized Clinical Trials

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Anesthesiology 2020 Aug;133(2):304-317

Welcome to the October 2020 SNACC Article of the Month, where we will be furthering the discussion on best practice for patients undergoing thrombectomy for acute stroke. Our commentary this month comes from Tariq Esmail, MB BCh BAO, BMSc; and Tumul Chowdhury MD, DM, FRCPC, from the Department of Anesthesiology and Pain Medicine, Toronto Western Hospital – University Health Network, Toronto, ON, Canada.

Dr. Chowdhury is an Assistant Professor of anesthesiology. He also serves as the Vice Chair for the Neuroanesthesia section at the Canadian Anesthesiologists' Society. He has been an active member of SNACC since 2011, and has been actively involved with several of the subcommittees. His primary research interests are on awake craniotomy and brain/heart interactions. He is internationally known for his work on the trigeminocardiac reflex. Dr. Tariq Esmail is currently a fellow in Neuroanesthesiology at Toronto Wester Hospital.

As always, readers are welcome to join us for further discussion and feedback on the SNACC **Twitter** feed, or on **Facebook**.

- Oana Maties, MD, Amie Hoefnagel, MD, Shilpa Rao, MD, and Nina Schloemerkemper, MD

Commentary

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A disruption to blood pressure (BP) autoregulation in acute ischemic stroke (AIS) indicates that the lowering of mean arterial blood pressure (MABP) can accelerate the loss of penumbral tissue and increase the infarct size.1 MABP targets are a topic of great clinical interest. We have seen in the literature comparisons between General Anesthesia (GA) and Procedural Sedation (PS) to facilitate intervention and their relative benefits or deficits. Clinically, is has been assumed that PS is better because it maintains patient comfort and cooperation while minimizing the number of medications administered6, though PS is not universally accepted, or proven to be better. It comes to light in this month's article that perhaps our previous focus is not what is most important when managing these cases. Rasmussen et al. provide evidence that clinical outcomes may be influenced more by the manipulation of hemodynamic parameters under the anesthesiologists control and thus MABP may play a greater role regardless of type of anesthetic.

In February 2020, Dr. Rasmussen wrote an excellent commentary for the Article of the Month on their work-- Association of General Anesthesia vs Procedural Sedation with Functional Outcome among Patients with Acute Ischemic Stroke Undergoing Thrombectomy: A Systematic Review and Meta-analysis--with the association of GA vs PS and functional outcomes in AIS undergoing thrombectomy (EVT). This meta-analysis used three, single center, randomized controlled trials (SIESTA, ANSTROKE and GOLIATH) with almost similar inclusion criteria and hemodynamic protocols to investigate the effects of hemodynamics on outcomes. These were all single-centre randomized trials. To further assess the impact of anesthetic strategy on functional outcome, the SAGA (SIESTA-ANSTROKE-GOLIATH Association) collaboration was established.

ANSTROKE – Investigated the impact of anesthesia technique on neurological outcomes in acute ischemic stroke patients. They concluded in EVT for AIS that no difference was found between GA and conscious sedation in neurological outcome at 3 months post stroke.2

SIESTA – Intended to compare intubated to non-intubated patients receiving EVT of acute ischemic anterior circulation stroke. Primary endpoint was early neurological improvement by Health Stroke Scale (NIHSS) after 24hr. Secondary endpoints included functional outcome at 3 months. Conscious sedation did not result in any better neurological outcome compared to General Anesthesia.3

GOLIATH – Designed to examine the effect of the type of anesthesia during EVT and its effect ton infarct growth and clinical outcome. It was concluded that GA was not worse than conscious sedation on clinical outcomes. This was specifically for patients who underwent EVT for AIS causes by a large vessel occlusion in anterior circulation.4

Through prospectively gathered data in the SAGA collaboration, this study was able to retrospectively investigate if there is an optimal blood pressure targets during EVT for AIS, as none are currently defined.

Rasmussen et al included patients with anterior circulation strokes presenting for EVT. The primary outcome was the modified Rankin Scale (mRS) score at 90 days. It was hypothesized that hypotensive episodes less than a critical threshold (and potentially the duration of the hypotension) may have an effect on the collateral circulation, the final infarct size, and ultimately the functional outcome of patients. All three studies had comparable anesthetic and hemodynamic protocols Blood pressure (BP) measurements were taken every five minutes, from either non-invasive or invasive blood pressure monitoring. Baseline measurements were the last BP prior to induction. MABP thresholds for the definition of hypotension (<70, <80 and <90mmHg) and hypertension (>90, >100, >110mmHg) were set. Part of the statistical analysis included the number needed to harm (NNH), which looked at the continuous and cumulative time at a blood pressure threshold for one patient to have a poor clinical outcome.

365 patients with BP measurements were analyzed. There were an equal number of patients undergoing GA and PS, and the demographic and clinical characteristics of the patients were balanced. The lower thresholds showed a trend towards having higher 90-day mRS scores. This was seen first for a MABP <80 [adjusted OR, 1.52; 95% CI, 1.01-2.28; P = .04] and <70mmHg (adjusted OR, 1.81; 95% CI, 1.12-2.90; P = .02).

For each 10min <70mmHg the odds of shifting towards worse outcomes increased by 30% [adjusted OR, 1.30; 95% CI, 1.03-1.65; P = .03]. As little as 5 min with a MABP less than 70mmHg showed statistically significant shifts towards a higher 90-day mRS score. For every continuous 10min with less than 70mmHg there was a 62% increase in odds of shifting towards worse outcomes (adjusted OR, 1.62; 95% CI, 1.15-2.27; P = .005). NNH was 10.

The upper thresholds demonstrated a smaller increase (8%) of odds for each 10min greater than MABP 90mmHg (adjusted OR, 1.08; 95% CI, 1.04-1.11; P <.001), which became statistically significant if MABP was greater than 90mmHG for more than 45min. NNH also 10.

The MABP was lower in GA patients, it was postulated that this could explain the association between GA and worse outcomes in EVT, and further provide evidence for the reason why, as Dr. Rasmussen mentioned, that the effects of anesthetic medications do precipitate hypotension but it doesn't happen in isolation to GA only. One-third of patients with PS required hemodynamic intervention.

We think it was appropriate in this study, that Systolic Blood Pressure (SPB) was not identified as a maximum or minimum but rather the MABP was used, which represents a more sensitive assessment. MABP is essentially the "driving force" for cerebral perfusion pressure (MAP-ICP=CPP). This is despite guidelines and expert recommendations to "target SBPs" which seem to be based on weaker evidence5.

As anesthesiologists we consistently focus our efforts on preventing hypotension, appropriately. This article also highlights the other sides of the coin albeit to a smaller degree but the effects of hypertension are detrimental in excess.

We may now start to see the importance of further defining MABP targets for our clinical practice. Certainly, in the stroke management guidelines it would be important to identify this subtle but important value. This would result in a more precise calculation of cerebral perfusion pressure.

In addition, as this study required three separate studies to achieve a number of patients where statistical differences could be observed, it indicates the need for larger controlled trials in this area to further define targets and guide clinical practice.

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