**Carbon Dioxide, Blood Pressure, and Perioperative Stroke: a Retrospective Case-Control Study**

**Supplemental Digital Content 3:** Total Area Under the Curve Calculations

For calculating total area under the curve, the use of invasive vs. non-invasive MAP was operationalized as follows: in the event of missing MAP data, invasive and non-invasive MAP were estimated using the formula 1/3 systolic + 2/3 diastolic; invasive systolic and diastolic pressures were used to compute invasive MAP, and non-invasive systolic and diastolic pressures were used to compute non-invasive MAP. For any case with ≥ 80% valid non-artifact minute-to-minute invasive MAP measurements, the invasive MAP values were used to compute total area under the curve for this variable. For any case with <80% valid non-artifact minute-to-minute invasive MAP measurements, non-invasive MAP values were used for this computation.

To provide an example of these calculations (based on study results), for a MAP of 50 mmHg for 10 minutes, the area under the curve would be 50 mmHg-min (5 mmHg below the threshold x 10 minutes). For an EtCO2 of 28 mmHg for 10 minutes, the area under the curve would be 30 mmHg-min (3 mmHg within/below the threshold for 10 minutes). In this scenario, the increased stroke risk would be the following:

 -Increased risk based on MAP<55 mmHg threshold (primary analysis): 1.01050 = 1.64

 -Increased risk based on EtCO2 30 mmHg threshold (primary analysis): 1.00730 = 1.23

There is an additive risk between these exposure variables; as such, we multiply the new, adjusted odds ratios (1.64 x 1.23) to reveal a **2.02 (202%)** increased risk.

Intraoperative Blood Pressure Monitoring, Signal Processing, and Arterial Blood Pressure Artifact Reduction

For arterial line waveform data or non-invasive blood pressure monitoring data, when simultaneous values are recorded, the higher of the two MAP values were used. When blood pressure monitoring is non-continuous during a case (i.e., non-invasive blood pressure measurements, or arterial line disconnected), blood pressure will be assumed constant and equal to the previous measurement if within five minutes from the most recent measurement. If five minutes or greater from any blood pressure measurement value, blood pressure will be presumed unknown and treated as missing data.

Additional blood pressure monitoring artifact reduction will be performed as follows:

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| **Artifact Elimination Strategy** | **Rules/Logic** |
| Provider Marked Artifacts | Marked as artifact in real-time by the provider |
| Artifact from arterial line clamping, damping, or flushing; or cuff under external pressure | SBP > 200 AND PP < 50 |
|  | SBP > 150 and SBP ≤200 AND  PP < 30 |
|  | SBP ≥ 100 AND SBP ≤ 150 AND PP < 15 |
|  | SBP < 100 AND PP < 10 |
| Artifact from arterial line or cuff transducing signal but disconnected from patient | SBP ≤ 10 OR DBP ≤ 10 |
|  | SBP = DBP = MAP |
|  | MAP < 0 |
|  | MAP ≥ 140 |
|  | If any BP is marked as artifact, then all BP measurements for that time will be marked as artifact |

SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; MAP = Mean Arterial Pressure; PP = Pulse Pressure (SBP-DBP). If artifact other than provider-marked, is detected for SBP, DBP, or MAP for a specific reading, then all three blood pressure values are marked as an artifact.