Blood Pressure Management After Mechanical Thrombectomy

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Disclosure

• I have no actual or potential conflict of interest in relation to this program.
The aim of blood pressure management after thrombectomy is to optimize cerebral perfusion to tissues at risk of ischemia and infarction, while mitigating the risk of reperfusion injury and hemorrhage.
Introduction

• Optimal blood pressure after mechanical thrombectomy is not well defined.

• Literature largely limited to observational studies.
### 3.7. Mechanical Thrombectomy (Continued)

<table>
<thead>
<tr>
<th>17. In patients who undergo mechanical thrombectomy, it is reasonable to maintain the BP ≤180/105 mm Hg during and for 24 hours after the procedure.</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>New recommendation.</td>
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</table>

<table>
<thead>
<tr>
<th>18. In patients who undergo mechanical thrombectomy with successful reperfusion, it might be reasonable to maintain BP at a level &lt;180/105 mm Hg.</th>
<th>COR</th>
<th>LOE</th>
<th>New recommendation.</th>
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<tbody>
<tr>
<td>IIb</td>
<td>B-NR</td>
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</table>

There are very limited data to guide BP therapy during and after the procedure in patients who undergo mechanical thrombectomy. RCT data on optimal BP management approaches in this setting are not available. The vast majority of patients enrolled in under 6-hour RCTs received IV alteplase and the trial protocols stipulated management according to local guidelines with BP ≤80/105 during and for 24 hours after the procedure for these participants. Two trial protocols provided additional recommendations. The ESCAPE protocol states that systolic BP ≥150 mm Hg is probably useful in promoting and keeping collateral flow adequate while the artery remains occluded and that controlling BP once reperfusion has been achieved and aiming for a normal BP for that individual is sensible. Labetalol or an IV β-blocker such as metoprolol in low doses is recommended. The DAWN protocol recommends maintaining systolic BP <140 mm Hg in the first 24 hours in subjects who are reperfused after mechanical thrombectomy (defined as achieving more than two thirds MCA territory reperfusion). See Table XXIII in online Data Supplement 1.
Background

• Guideline recommendation derived from:
  • RCTs showing improved patient outcomes after thrombectomy
  • Observational studies showing higher rates of hemorrhage with higher SBP after IV tPA administration.
  • Higher rates of recanalization with endovascular therapy (EVT) than with IV tPA alone.
  • Theorized higher risk of reperfusion injury / hemorrhage after successful thrombectomy
What Defines “Successful” Recanalization?

<table>
<thead>
<tr>
<th>Modified Thrombolysis in Cerebral Infarction (mTICI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0</strong></td>
</tr>
<tr>
<td><strong>1</strong></td>
</tr>
<tr>
<td><strong>2a</strong></td>
</tr>
<tr>
<td><strong>2b</strong></td>
</tr>
<tr>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>
Recanalization (IV tPA)

Recanalization %

- M2 MCA: 44%
- M1 MCA: 30%
- BA: 30%
- Tandem ICA-MCA: 27%
- ICA-T: 6%

70% of clinically meaningful recanalization after IV tPA occurs within 1h of bolus

*Stroke. 2007;38:948-954; Stroke. 2006;37:1000-1004*
SWIFT PRIME Recanalization

N=83 pts
Based on all patients
with final TICI data

TICI 2B/3 rate is 88.0%

Modified TICI scale
TICI 2B: Perfusion of half
or greater of the vascular
distribution of the
occluded artery

TICI 3: Full perfusion
with filling of all distal
branches
• If higher rates of reperfusion are achieved with EVT, it follows that EVT carries a higher risk of reperfusion injury

• Permissive hypertension may not result in reduced ischemia and infarction after successful recanalization

• Hence, lower BP parameters may be preferred after successful EVT compared to IV tPA alone
Blood Pressure and Outcome After Mechanical Thrombectomy With Successful Revascularization

A Multicenter Study

- Retrospective multicenter international study, 1245 patients, largest study to date
- Categorized by mean SBP within 24 hrs after successful reperfusion
- Reference mean SBP 121-140 mm Hg
Higher SBP independently associated with:

- Lower odds of good functional outcome
- Higher odds of sICH
- Higher odds of mortality
- Higher odds of hemicraniectomy

Rate of mRS 0-2 highest in SBP 101-120 group, lowest in >160 mm Hg

Anadani M et al. Stroke. 2019
• Multicenter, nonrandomized retrospective design

• 1019 patients, 8 comprehensive stroke centers

• Compared to SBP <180 mm Hg:
  • SBP <160 mm Hg associated with lower odds of mortality
  • SBP <140 mm Hg associated with higher likelihood good functional outcome, lower odds of hemicraniectomy
## Annals of Neurology 2020

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate of Clinical Outcome</th>
<th>Propensity-Weighted Multivariate Analysis&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IN-BP, MO-BP, GI-BP,</td>
<td>IN-BP vs GI-BP, OR (95% CI) vs GI-BP, OR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>n = 540, n = 142, n = 337</td>
<td></td>
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<tr>
<td><strong>Efficacy outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-day mRS, median (IQR)</td>
<td>2 (3) 2 (3) 3 (4) —</td>
<td>—</td>
</tr>
<tr>
<td>90-day mRS = 0–2, N (%)</td>
<td>283 (52) 74 (52) 148 (44) 1.53 (1.07–2.19)</td>
<td>1.58 (0.06–2.59)</td>
</tr>
<tr>
<td><strong>Safety outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-day mortality, N (%)</td>
<td>84 (16) 20 (14) 71 (21) 0.69 (0.45–1.06)</td>
<td>0.42 (0.22–0.82)</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage, N (%)</td>
<td>16 (3) 11 (8) 18 (5) 0.61 (0.29–1.29)</td>
<td>1.53 (0.36–3.67)</td>
</tr>
<tr>
<td>Hemicranietomy, N (%)</td>
<td>11 (2) 14 (10) 20 (6) 0.18 (0.16–0.21)</td>
<td>0.95 (0.42–2.14)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Results from multivariate analysis adjusted for age, sex, GCS score, and time from symptom onset to randomization.
FIGURE 3: Distribution of efficacy and safety outcomes in hypertensive patients across the 3 blood pressure goal groups. GI-BP = guideline-recommended blood pressure control group; IN-BP = intensive blood pressure control group; MO-BP = moderate blood pressure control group; SICH = symptomatic intracranial hemorrhage.
BEST Study 2019

• Multicenter Prospective Cohort Study

• 485 patients, 12 comprehensive stroke centers

• ICA or MCA M1 or M2 occlusion treated with EVT

• All SBP values recorded for 24 hours post-EVT

• Primary outcome dichotomized 90-day mRS 0-2 vs 3-6
BEST Study 2019

- 186 patients (42%) had good clinical outcomes (mRS 0-2)

- Peak SBP that best discriminated between dichotomized outcomes was 158 mm Hg (95% CI 0.56-0.66; P <0.001)

- 66% of patients with peak SBP >158 mm Hg had bad outcome, compared with 47% with peak SBP <158 mm Hg

- Peak SBP >158 mm Hg unadjusted OR 2.24 (1.52-3.29, P <0.01) for bad outcome

- Peak SBP >158 mm Hg adjusted OR 1.29 (0.81-2.06, P =0.28)
BEST Study 2019

Mistry EA et al. Stroke. 2019
DAWN Trial

- Trial protocol recommended SBP goal of less than 140 mm Hg after successful revascularization.

- 2018 ASA/AHA Guidelines state eligibility criteria for DAWN or DEFUSE 3 “should be strictly adhered to in clinical practice” for patients >6 hrs from last known normal.

- However, the Guidelines do not mandate adherence to post-thrombectomy blood pressure goals delineated in the DAWN protocol.

Nogueira RG et al. NEJM. 2018
Risk of Intracranial Hemorrhage after Endovascular Treatment for Acute Ischemic Stroke: Systematic Review and Meta-Analysis

Yonggang Hao, Zhizhong Zhang, Hao Zhang, Lili Xu, Zusen Ye, Qiliang Dai, Xinfeng Liu, Gelin Xu

- Meta-analysis comparing rate of intracranial hemorrhage in patients treated with EVT vs medical therapy alone
- 11 studies (9 RCTs), 1499 patients
- IMS I/II/III, Synthesis I/II, MR-RESCUE, MR CLEAN, Escape, EXTEND-IA, SWIFT PRIME, Revascat
Rate of All Intracranial Hemorrhage

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Weight, %</th>
<th>OR M-H, random, 95% CI</th>
<th>OR M-H, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>events</td>
<td>total</td>
<td>events</td>
<td>total</td>
<td></td>
</tr>
<tr>
<td>ESCAPE [4], 2015</td>
<td>66</td>
<td>165</td>
<td>28</td>
<td>150</td>
<td>15.1</td>
</tr>
<tr>
<td>EXTEND-IA [5], 2015</td>
<td>4</td>
<td>35</td>
<td>3</td>
<td>35</td>
<td>5.5</td>
</tr>
<tr>
<td>IMS [18], 2004</td>
<td>39</td>
<td>80</td>
<td>23</td>
<td>182</td>
<td>13.9</td>
</tr>
<tr>
<td>IMS II [19], 2007</td>
<td>34</td>
<td>81</td>
<td>23</td>
<td>182</td>
<td>13.8</td>
</tr>
<tr>
<td>IMS III [15], 2013</td>
<td>146</td>
<td>434</td>
<td>55</td>
<td>222</td>
<td>16.9</td>
</tr>
<tr>
<td>MR-RESCUE [14], 2013</td>
<td>45</td>
<td>64</td>
<td>28</td>
<td>54</td>
<td>12.2</td>
</tr>
<tr>
<td>REVASCAT [3], 2015</td>
<td>27</td>
<td>103</td>
<td>15</td>
<td>103</td>
<td>12.9</td>
</tr>
<tr>
<td>SWIFT PRIME [6], 2015</td>
<td>9</td>
<td>98</td>
<td>8</td>
<td>97</td>
<td>9.7</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1,060</td>
<td>1,025</td>
<td>100.0</td>
<td></td>
<td>2.55 (1.64, 3.97)</td>
</tr>
<tr>
<td>Total events</td>
<td>370</td>
<td>183</td>
<td></td>
<td></td>
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</tbody>
</table>

Heterogeneity: \( \hat{\tau}^2 = 0.26, \chi^2 = 24.68, \text{df} = 7 (\ p = 0.0009), \hat{I}^2 = 72\%

Test for overall effect: \( Z = 4.17 (\ p < 0.0001) \)

35 vs 19%, OR = 2.55, 95% CI: 1.64-3.97, p < 0.00001

Hao et al. Intervent Neurol. 2017
Rate of Asymptomatic Intracranial Hemorrhage

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Weight, %</th>
<th>OR M-H, random, 95% CI</th>
<th>OR M-H, random, 95% CI</th>
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<tr>
<td></td>
<td>events</td>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>events</td>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EXTEND-IA [5], 2015</td>
<td>4</td>
<td>35</td>
<td>6.1</td>
<td>4.39 (0.46, 41.40)</td>
<td></td>
</tr>
<tr>
<td>IMS [18], 2004</td>
<td>34</td>
<td>80</td>
<td>15.8</td>
<td>11.49 (5.41, 24.42)</td>
<td></td>
</tr>
<tr>
<td>IMS II [19], 2007</td>
<td>26</td>
<td>81</td>
<td>15.7</td>
<td>7.35 (3.41, 15.83)</td>
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</tr>
<tr>
<td>IMS III [15], 2013</td>
<td>119</td>
<td>434</td>
<td>18.5</td>
<td>1.62 (1.09, 2.41)</td>
<td></td>
</tr>
<tr>
<td>MR RESCUE [14], 2013</td>
<td>42</td>
<td>64</td>
<td>15.9</td>
<td>2.06 (0.98, 4.32)</td>
<td></td>
</tr>
<tr>
<td>REVASCAT [3], 2015</td>
<td>17</td>
<td>103</td>
<td>15.3</td>
<td>1.65 (0.73, 3.73)</td>
<td></td>
</tr>
<tr>
<td>SWIFT PRIME [6], 2015</td>
<td>9</td>
<td>98</td>
<td>12.6</td>
<td>1.86 (0.60, 5.77)</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>895</td>
<td>107</td>
<td>100.0</td>
<td>3.16 (1.62, 6.16)</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 251 Favor intervention
Total events: 107 Favor control

Heterogeneity: Tau^2 = 0.59, \chi^2 = 29.56, df = 6 (p < 0.0001), I^2 = 80%
Test for overall effect: Z = 3.36 (p = 0.0008)

28 vs 12%, OR = 3.16, 95% CI: 1.62-6.16, p <0.001
Rate of Subarachnoid Hemorrhage

6.9 vs 2.2%, OR = 2.37, 95% CI: 1.33-4.22, p < 0.01

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Weight, OR</th>
<th>OR M-H, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>events</td>
<td>total</td>
<td>M-H, fixed</td>
<td>M-H, fixed</td>
</tr>
<tr>
<td>IMS III [15], 2013</td>
<td>48</td>
<td>417</td>
<td>81.0</td>
<td>2.11 (1.10, 4.07)</td>
</tr>
<tr>
<td>MR CLEAN [2], 2015</td>
<td>2</td>
<td>233</td>
<td>2.6</td>
<td>5.78 (0.28, 120.96)</td>
</tr>
<tr>
<td>REVASCAT [3], 2015</td>
<td>5</td>
<td>103</td>
<td>10.9</td>
<td>2.58 (0.49, 13.59)</td>
</tr>
<tr>
<td>SWIFT PRIME [6], 2015</td>
<td>4</td>
<td>98</td>
<td>5.5</td>
<td>4.09 (0.45, 37.23)</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>851</strong></td>
<td><strong>674</strong></td>
<td><strong>100.0</strong></td>
<td><strong>2.37 (1.33, 4.22)</strong></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>59</strong></td>
<td><strong>15</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.69, df = 3 (p = 0.88), I^2 = 0$

Test for overall effect: $Z = 2.93 (p = 0.003)$
Rate of Symptomatic Intracranial Hemorrhage

5.6 vs 5.2%, OR 1.09, 95% CI: 0.79-1.50, p =0.61

Hao et al. Intervent Neurol. 2017
• Multicenter, open-label, randomized controlled trial

• 324 patients, 4 French academic hospital centers

• Patients randomly assigned to SBP 100-129 mm Hg or 130-185 mm Hg

• Primary outcome: intraparenchymal hemorrhage at 24-36 hrs

• Secondary outcome: Favorable outcome (mRS 0-2), excellent outcome (mRS 0-1), change in NIHSS at 24-36h
BP-TARGET

• Mean SBP was 128 mm Hg in intensive target group, 138 mm Hg in the standard target group

• No difference (42 vs 43%) in rate of radiographic intraparenchymal hemorrhage (p=0.84)

• No significant difference in secondary outcome measures

Mazighi M et al. Lancet Neurol. 2021
• Survey of blood pressure goals at stroke centers across US

• 16 of 58 centers (28%) accepted AHA/ASA Guideline on systolic blood pressure goal of <180 mm Hg

• Most stroke centers adhered to lower blood pressure goals
Blood Pressure Goals After Successful Reperfusion

• 21 (36%) target SBP 120-139 mm Hg
• 12 (21%) target SBP 140-159 mm Hg
• 16 (28%) accept any value equal to or less than 180 mm Hg

Blood Pressure Goals After Unsuccessful Reperfusion

• 25 (43%) target SBP less than or equal to 180 mm Hg

• 6 (10%) target SBP less than or equal to 220 mm Hg
Trials in Progress

- BEST-II
  - Randomized clinical trial
  - Treatment arms (target SBP <180, <160, and <140 mm Hg)
  - Primary outcomes: infarct volume and 90-day functional status
  - Est. Completion 3/30/2023
Trials in Progress

• OPTIMAL-BP
  • Randomized clinical trial
  • Randomized to SBP goal <140 mm Hg vs <180 mm Hg
  • Primary outcomes: 90-day mRS 0-2, sICH, 90-day mortality
  • Est. Completion December 2024
Key Points

• Definitive data on optimal blood pressure after mechanical thrombectomy is lacking

• Accruing data suggests that lower blood pressure goals may improve patient outcomes, however this was not confirmed by BP-TARGET

• Reasonable to tailor BP goals according to reperfusion grade (dichotomized, mTICI 2b-3 vs 0-2a)
Thank you