CONTROVERSIES IN CRITICAL CARE
HIGHER VS LOWER (STANDARD) MAP IN SEPTIC SHOCK

Elizabeth Bridges PhD RN, CCNS, FCCM, FAAN
Professor, University of Washington School of Nursing
Clinical Nurse Researcher, University of Washington Medical Center
ONE-SIZE FITS ALL
STORE
SALE
776 patients with septic shock undergoing resuscitation – recruited within 6 hours of diagnosis
  - High-target group (goal 80-85 mm Hg) vs Low-target group (65-70 mm Hg)
  - 28 day mortality – no significant difference high-target (36%) vs low-target (34%)
    - HR – high target 1.07 (95% CI 0.84-1.38)
  - 90-day mortality – no significant difference high-target 44% vs low-target 42%
  - Serious adverse events – NS difference
  - Newly diagnosed atrial fibrillation – higher in high target group (7%) vs lower-target (3%)

In patients with chronic HTN – high-target group – less RRT (32%) vs Low-target (42%) (no mortality effect)
Goal MAP

- High target: 80-85 mm Hg
- Low target: 65-70 mm Hg

What is low vs. high?

<table>
<thead>
<tr>
<th></th>
<th>Low-Target Group (n = 388)</th>
<th>High Target Group (N = 388)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative fluid intake (day 1-5)</td>
<td>10 L (5.8-14)</td>
<td>10.5 (5.5-14)</td>
<td>NS</td>
</tr>
<tr>
<td>Cumulative fluid balance (day 1-5)</td>
<td>2.8 (0.0-6.2)</td>
<td>2.4 (0.0-6.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Norepinephrine (IQR) μg/kg/min</td>
<td>0.45 (0.17-0.21)</td>
<td>0.58 (0.26 – 1.8)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>
Recruited up to 24-hours after diagnosis of vasodilatory shock (N = 118)
High target (75-80 mm Hg) vs low-target (60-65 mm Hg)

Results
- Risk of cardiac arrhythmias (low vs high) 20% vs 36% (p = .07)
- Renal SOFA score (day 1 & 2): 1.1 and 1.3 in both groups
- Hospital mortality 30% vs 33% (p = 0.84)
- Age > 75 years – lower MAP target associated with lower hospital mortality (13% vs 60%) – no effect in younger patients
- No significant differences – chronic hypertension, CHF, duration of vasopressor therapy
- Chronic HTN
  - Lower (57%) vs Higher (33%)
  - Median vasopressors for 11 hours (4-17) before enrollment
  - More blood in high-target group

MAP 79 ± 5 mm Hg

MAP 70 ± 5 mm Hg
Penguins are black and white. Some old TV shows are black and white. Therefore, some penguins are old TV shows.
Hypotension Exposure

- Retrospective analysis (N = 8782) – Sepsis with ICU stay ≥ 24 hours (2010-2016)
- Association between MAP and AKI and MI and mortality in patients with septic shock
- Hypotension exposure:
  - *Time-weighted average of MAP (TWA-MAP) below MAP thresholds of 55, 65, 75 or 85 mm Hg (area below threshold/total time exposure monitored)*
  - *Cumulative time (minutes) during which MAP was below absolute threshold (55, 65, 75, or 85 mm Hg)*
Hypotension Exposure

• For every 1 mm Hg increase TWA-MAP < 65 mm Hg, odd of in-hospital mortality increase by 11.4% (95% CI 7.8-15.1%)

• For every 2 hours (cumulative) below MAP threshold 65 mm Hg, increased odds of in-hospital mortality of 3.6%

• For every 1 mm Hg increase in TWA-MAP < 65 mm Hg, odds of developing AKI increase by 7%

• Patients with 6-8 hours of MAP < 65 mm Hg had odds of developing AKI 37% higher that patients without MAP < 65 mm Hg

• NS trend for AKI and MAP thresholds of 75 & 85 mm Hg

Risk for hypotension during vasopressor weaning

• Jeon (2018) – 68% of patients undergoing norepinephrine weaning experienced hypotension within 1 hour of weaning

• Dynamic elastance – prediction of intolerance to weaning (Cecconi 2014)
Varpula (2005)
• Identify optimal threshold values for MAP and SvO2 and 30-day mortality
• Retrospective cohort (N = 111)
• MAP < 65 mm Hg (area of hypotension) – AUC 0.853
• SvO2 < 70% AUC 0.746

Dunser (2009)
• Retrospective cohort – septic patients (N = 274)
• Association between hourly time integral of ABP drops below threshold (MAP < 60 mm Hg)
ARE WE FOLLOWING THE CORRECT PARAMETERS?
Macrocirculation - Microcirculation

Dubin (2009)
Mottling score
- Score 0: No mottling
- Score 1: Modest mottling area (coin size) localized to the center of the knee
- Score 2: Moderate mottling area that does not exceed the superior edge of the kneecap
- Score 3: Mild mottling area that does not exceed the middle thigh
- Score 4: Severe mottling area that does not exceed the fold of the groin
- Score 5: Extremely severe mottling area that exceeds the fold of the groin

Ait Oufella 2013

Correlation: mottling and 14-day mortality in 60 patients with septic shock (requiring vasopressor)

MAP at 6 hours: Survivors 77 (11) vs Non-Survivors 73 (11)

<table>
<thead>
<tr>
<th>Mottling Score</th>
<th>Odds of Death</th>
<th>14-Day Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 (no or modest)</td>
<td>1</td>
<td>13%</td>
</tr>
<tr>
<td>2-3 (mild or moderate)</td>
<td>16 (4-81)</td>
<td>70%</td>
</tr>
<tr>
<td>4-5 (severe)</td>
<td>74 (11-1,568)</td>
<td>92%</td>
</tr>
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Ait Oufella (2011)
Conclusion

- 65-70 mm Hg (sepsis guidelines) is probably appropriate for most patients – However...
  - Control groups (low-blood pressure) in RCTs exceeded this MAP range – so is the target minimum something higher
  - Higher MAP may be beneficial in patients with chronic hypertension to prevent AKI (RCTs – MAP 70-75 mm Hg)
  - Prevention of hypotension (< 65 mm Hg) is critical for all patients

- Are we debating the right question: is it lower (standard) vs higher MAP or is it optimized MAP in conjunction with other parameters

ONE SIZE DOES NOT FIT ALL
References


■ Cecconi M et al. The use of pulse pressure variation and stroke volume variation in spontaneously breathing patients to assess dynamic arterial elastance and to predict arterial pressure response to fluid administration. Anesth Analg, 2014 (epub)


■ Dünser MW, Dubin A. There is more to septic shock than arterial hypotension and elevated lactate levels: another appeal to rethink current resuscitation strategies! Ann Intensive Care, 2018, 8:55

References

- Russell JA. Is there a good MAP for septic shock. NEJM, 2014, 370(17) 1649-1650