Mean Arterial Pressure
Low could be good

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Permissive hypotension

- 16yr old boy with St. aureus septic shock
- RRT and persistent hypotension with increasing lactate levels
- Goal of MAP: 70 mm Hg
  - Dopamine, Norepinephrine, Epinephrine, Vasopressin
  - current MAP: 45-50 mm Hg
  - Lactate > 10 mmol/L

✓ Do you have an additional option to increase MAP?
In critically ill patients the target MAP should probably be > 60 mmHg and < 75 mmHg for the majority of patients.
Restoring arterial pressure with norepinephrine improves muscle tissue oxygenation assessed by near-infrared spectroscopy in severely hypotensive septic patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before norepinephrine (introduction/increase)</th>
<th>After norepinephrine (introduction/increase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP (mmHg)</td>
<td>86 ± 19</td>
<td>126 ± 18*</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>38 ± 7</td>
<td>52 ± 8*</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>54 ± 8</td>
<td>77 ± 9*</td>
</tr>
<tr>
<td>Heart rate (min⁻¹)</td>
<td>98 ± 25</td>
<td>101 ± 28</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>37.5 ± 1.4</td>
<td>37.5 ± 1.3</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>3.1 ± 1.0</td>
<td>3.6 ± 1.3*</td>
</tr>
<tr>
<td>GEDVI (mL/m²)</td>
<td>687 ± 117</td>
<td>730 ± 156*</td>
</tr>
<tr>
<td>EVLWI (mL/kg)</td>
<td>13 ± 9</td>
<td>13 ± 7</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>94 ± 5</td>
<td>93 ± 4</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>122 ± 73</td>
<td>115 ± 63</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>40 ± 16</td>
<td>40 ± 15</td>
</tr>
<tr>
<td>pH</td>
<td>7.34 ± 0.10</td>
<td>7.33 ± 0.10</td>
</tr>
<tr>
<td>ScvO₂ (%)</td>
<td>68 ± 9</td>
<td>72 ± 7*</td>
</tr>
</tbody>
</table>
Effects of changes in arterial pressure on organ perfusion during septic shock
Thooft et al. Crit Care 2011;15:R222

Key messages
• Increasing mean arterial pressure by norepinephrine during septic shock can increase cardiac output and improve microvascular flow and reactivity in stable resuscitated patients without modification of global oxygen consumption.
• There is considerable inter-individual variability in microvascular response, suggesting that the level of mean arterial pressure should be adapted to each patient.
Increasing arterial blood pressure with NE does not improve microcirculatory blood flow

\[ y = -0.9432x + 13.038 \]
\[ R^2 = 0.9472 \]
\[ p < 0.0001 \]
Weil: However, the primary defect of shock is not so much a failure to maintain pressure as it is a failure to maintain flow of blood.
California Medicine 1962

Huckabee on treatment of lactic acidosis:
… it seems likely that the circulatory defect is of the nature of a distributional change, since actual rates of blood flow are not low. It might prove very interesting if someone will try vasodilating drugs in such a patient….
Am J Cardiol 1963
There is a growing interest in the treatment of endotoxin shock with vasodilating agents.

- Lethal injection of purified Escherichia coli endotoxin (7.5 mg per kg)
- Non-fluid resuscitated model
arterial microcirculation

arteriolar constriction

arteriolar vasodilation

microcirculation

venous
arterial microcirculation

venous constriction
increased venous pressures

A

arteriolar vasodilation

hypotension
arterial microcirculation

venous
decreased venous pressures

arteriolar vasodilation

venous constriction
increased venous pressures

A

B
decreased venous pressures
The effects of intravenous nitroglycerine and norepinephrine on gastric microvascular perfusion in an experimental model of gastric tube reconstruction
van Bommel et al. Surgery 2010;148:71-77

Nitroglycerine is a nitric oxide (NO)-donating compound; in the vascular endothelium NO functions as a regulator of vascular tone, and thereby of microvascular perfusion. NO plays an important role in the autoregulation of gastric mucosal blood flow, and it is likely that NO plays a role in protecting...
The effect of perfusion pressure on gastric tissue blood flow in an experimental gastric tube model

Dynamics of StO$_2$ mortality

- March-September 2011 § 221 consecutive patients enrolled expected LOS: 2 days
- Complete initial resuscitation and stabilization § follow up to Day 28

<table>
<thead>
<tr>
<th>StO$_2$</th>
<th>Admission</th>
<th>Evolution during first 24h</th>
<th>ICU mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (&gt;75%) n=166</td>
<td>Normal n=160</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>Abnormal (&lt;75%) n=39</td>
<td>Abnormal n=21</td>
<td>57%</td>
</tr>
</tbody>
</table>

Odds for mortality: persistent low StO2 during first 24h **7.9** (CI: 3-21, P<0.001)
Odds for mortality: when StO2 decreased to <75% during first 24h **7.1** (CI: 2-21, P<0.001)
Odds for mortality: persistent low StO2 and low peripheral perfusion **9.9** (CI: 3-41, P<0.001)
Abnormal peripheral perfusion
effect of a stepwise increasing dose of NTG

- Evaluation of the effects of nitroglycerine in the peripheral circulation

- Study population: critically ill patients who had undergone initial resuscitation and stabilization within 24h of ICU admission with abnormalities in peripheral perfusion, defined as:
  - cold extremities/delayed CRT (>5s),
  - forearm – finger T°C >2 (or PFI<1,4),
Abnormal peripheral perfusion
effect of a stepwise increasing dose of NTG

cold extremities/delayed CRT (>5s) § forearm – finger T°C >2 § PFI<1.4
Abnormal peripheral perfusion
effect of a stepwise increasing dose of NTG

Global hemodynamic variables during execution of the study protocol (n = 13). Time points are defined as before nitroglycerine infusion ($T_{baseline}$), at the maximum dose of nitroglycerine ($T_{Max}$) and 30 min after cessation of nitroglycerine ($T_{end}$).

<table>
<thead>
<tr>
<th></th>
<th>$T_{baseline}$</th>
<th>$T_{Max}$</th>
<th>$T_{end}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart rate, bpm</strong></td>
<td>95 [90-103]</td>
<td>97 [91-100]</td>
<td>98 [89-106]</td>
</tr>
<tr>
<td><strong>Mean arterial pressure, mmHg</strong></td>
<td>71 [70-80]</td>
<td>62* [57-69]</td>
<td>71 [70-76]</td>
</tr>
</tbody>
</table>

Values are expressed as median [25th-75th] § P<0.05 vs. TBL1 and TBL2
Effect of NTG on \( \text{StO}_2 \)

\[
y = -0.6667x + 119.06 \\
R^2 = 0.71029
\]

4 patients
Abnormal peripheral perfusion
effect of a stepwise increasing dose of NTG

<table>
<thead>
<tr>
<th></th>
<th>$T_{\text{baseline}}$</th>
<th>$T_{\text{max}}$</th>
<th>$T_{\text{end}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capillary refill time, sec</strong></td>
<td>9</td>
<td>4 *</td>
<td>7*</td>
</tr>
<tr>
<td></td>
<td>[8-12]</td>
<td>[4-6]</td>
<td>[4-10]</td>
</tr>
<tr>
<td><strong>Perfusion index, %</strong></td>
<td>0.7</td>
<td>2.7 *</td>
<td>1.6 *</td>
</tr>
<tr>
<td></td>
<td>[0.4-1.8]</td>
<td>[2.1-3.0]</td>
<td>[1.1-2.0]</td>
</tr>
<tr>
<td><strong>Tskin-difference, °C</strong></td>
<td>3</td>
<td>0.8 *</td>
<td>1.4 *</td>
</tr>
<tr>
<td></td>
<td>[2.1-3.4]</td>
<td>[-1.1-1.4]</td>
<td>[0.8-2.0]</td>
</tr>
<tr>
<td><strong>StO2 (%)</strong></td>
<td>77</td>
<td>85 *</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>[64-82]</td>
<td>[74-92]</td>
<td>[73-88]</td>
</tr>
</tbody>
</table>

Values are expressed as median [25th-75th] § * P<0.05 vs. TBL1 and TBL2
Abnormal peripheral perfusion
effect of a stepwise increasing dose of NTG

Percent changes of StO2 during NTG infusion plotted against StO2 values at baseline before NTG infusion. The magnitude of changes in StO2 is more accentuated for lower StO2 values.
Conclusions

- The target blood pressure for the majority of patients should probably be higher than 60 mmHg and lower than 75 mmHg.

- Improving tissue perfusion is the ultimate goal of manipulating perfusion pressure.
  - Large inter-individual differences
  - The worst microcirculations seem to benefit most
    - Increasing MAP may improve tissue perfusion
    - Decreasing MAP may improve tissue perfusion

- Setting the ultimate optimal MAP should be individualized by means of tissue perfusion and the target probably changes over time.