

# Should all patients with septic shock have a mean arterial pressure threshold of 65 mmHg?

Sepsis requiring cardiovascular support is a common reason for critical care admission. The threshold for mean arterial pressure in septic shock has been set at a population-wide threshold of 65 mmHg by a European consensus statement, but should the threshold be higher?

## The threshold mean arterial pressure should be 65 mmHg

The currently recommended mean arterial pressure threshold of 65 mmHg, set by the by the European Society of Intensive Care Medicine Task Force Consensus Statement (Cecconi et al, 2014), originated from studies that considered the correlation between mean arterial pressure thresholds, survival and end-organ damage in the context of septic shock. Dünser et al (2009) reported that increased time with a mean arterial pressure below 65 mmHg increased mortality. Following this, in 2014, Asfar et al randomised patients with septic shock to either a low mean arterial pressure threshold (65–70 mmHg) or a high mean arterial pressure threshold (80–85 mmHg). The authors found no difference in 28-day or 90-day mortality between the two groups. The average values in the low mean arterial pressure threshold group were actually above 70 mmHg and in the high mean arterial pressure threshold group were around 85 mmHg.

In 2018 Jean-Louis Vincent's group looked at the current standards of care for patients with distributive shock by performing a retrospective analysis of the MIMIC-III dataset (which included variables for 50 000 intensive care unit admissions) (Vincent et al, 2018). The authors found that there was increasing mortality in patients on the intensive care unit with increasing duration of exposure to mean arterial pressures of less than 65, 60 and 55 mmHg. Interestingly, the analysis also revealed that patients' mean arterial pressure is often not being maintained above the threshold: more than 60% of patients with distributive shock had a continuous mean arterial pressure of less than 65 mmHg for at least 2 hours.

## The threshold mean arterial pressure should be 80–85 mmHg

Proponents of higher thresholds argue that a mean arterial pressure threshold of 65 mmHg risks acute kidney injury in poorly controlled hypertensive patients whose renal blood flow auto-regulation curve is shifted to the right. Asfar et al's (2014) study supports this theory. The authors found that in the subgroup of patients with poorly controlled hypertension and septic shock, a higher threshold mean arterial pressure (80–85 mmHg) reduced both acute kidney injury and the need for renal replacement therapy (number needed to treat 9.5). However, this did not translate into a mortality benefit (Asfar et al, 2014).

Higher mean arterial pressure thresholds require higher doses of vasopressors with an increased risk of associated side effects. Vasopressors, in particular adrenaline, have been associated with reduced splanchnic perfusion and increased rates of ischaemia in patients with septic shock (De Backer et al, 2003). The use of high-dose vasopressors has been associated with 50–80% 30-day and 90-day mortality (Brown et al, 2013). Asfar et al (2014) also reported an increased incidence of dysrhythmias (7.6% new onset atrial fibrillation) in the group with the higher mean arterial pressure threshold. It is therefore important to balance the adequacy of the mean arterial pressure against the risks of giving increasing doses of vasopressors.

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## Conclusions

National and international guidelines advocate a mean arterial pressure threshold of 65 mmHg in patients who are in septic shock. It remains unclear if this 'one size fits all' threshold is appropriate for all patients. When purely considering mortality, the evidence does broadly support a low threshold mean arterial pressure. However, it is worth noting that the threshold in the low mean arterial pressure group in the landmark paper from Asfar et al (2014) was actually above 70 mmHg. Perhaps this (70 mmHg) should be the threshold mean arterial pressure for patients in septic shock?

In addition, other outcomes such as acute kidney injury need to be considered: patients with poorly controlled chronic hypertension benefit from a threshold mean arterial pressure of 80–85 mmHg. The adequacy of the mean arterial pressure needs to be carefully considered on a patient by patient basis. Finally, the currently accepted threshold mean arterial pressure of 65 mmHg is not consistently being maintained and this needs to be improved. If the threshold mean arterial pressure should be higher for an individual, then not achieving the 65 mmHg threshold becomes even more significant.

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