



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

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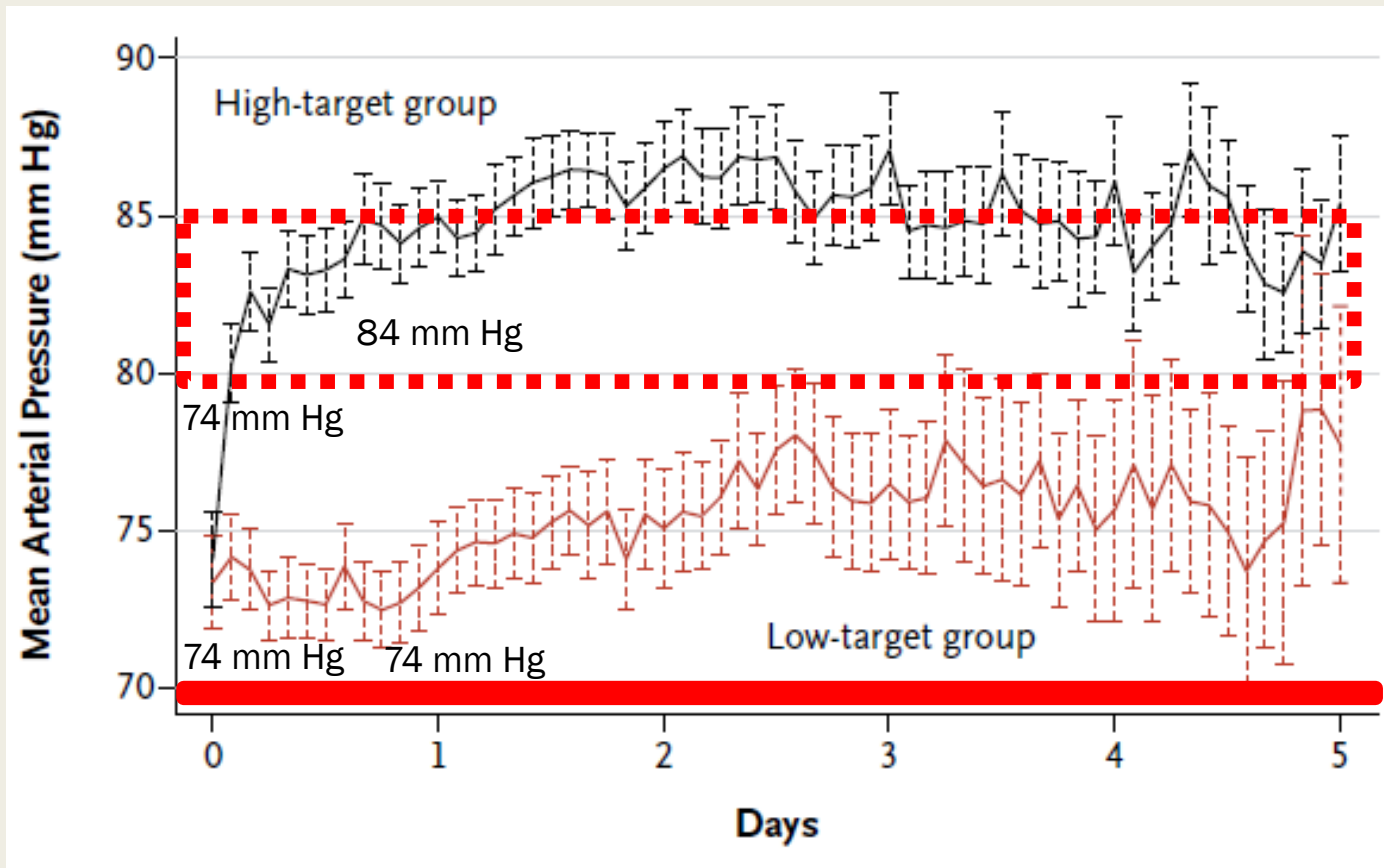
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Sepsis and Mean Arterial Pressure Study - SEPSISPAM

High versus Low Blood-Pressure Target in Patients with Septic Shock

- 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?

	Low-Target Group (n = 388)	High Target Group (N = 388)	
Cumulative fluid intake (day 1-5)	10 L (5.8-14)	10.5 (5.5-14)	NS
Cumulative fluid balance (day 1-5)	2.8 (0.0-6.2)	2.4 (0.0-6.0)	NS
Norepinephrine (IQR) $\mu\text{g}/\text{kg}/\text{min}$	0.45 (0.17-0.21)	0.58 (0.26 - 1.8)	< .001

ORIGINAL



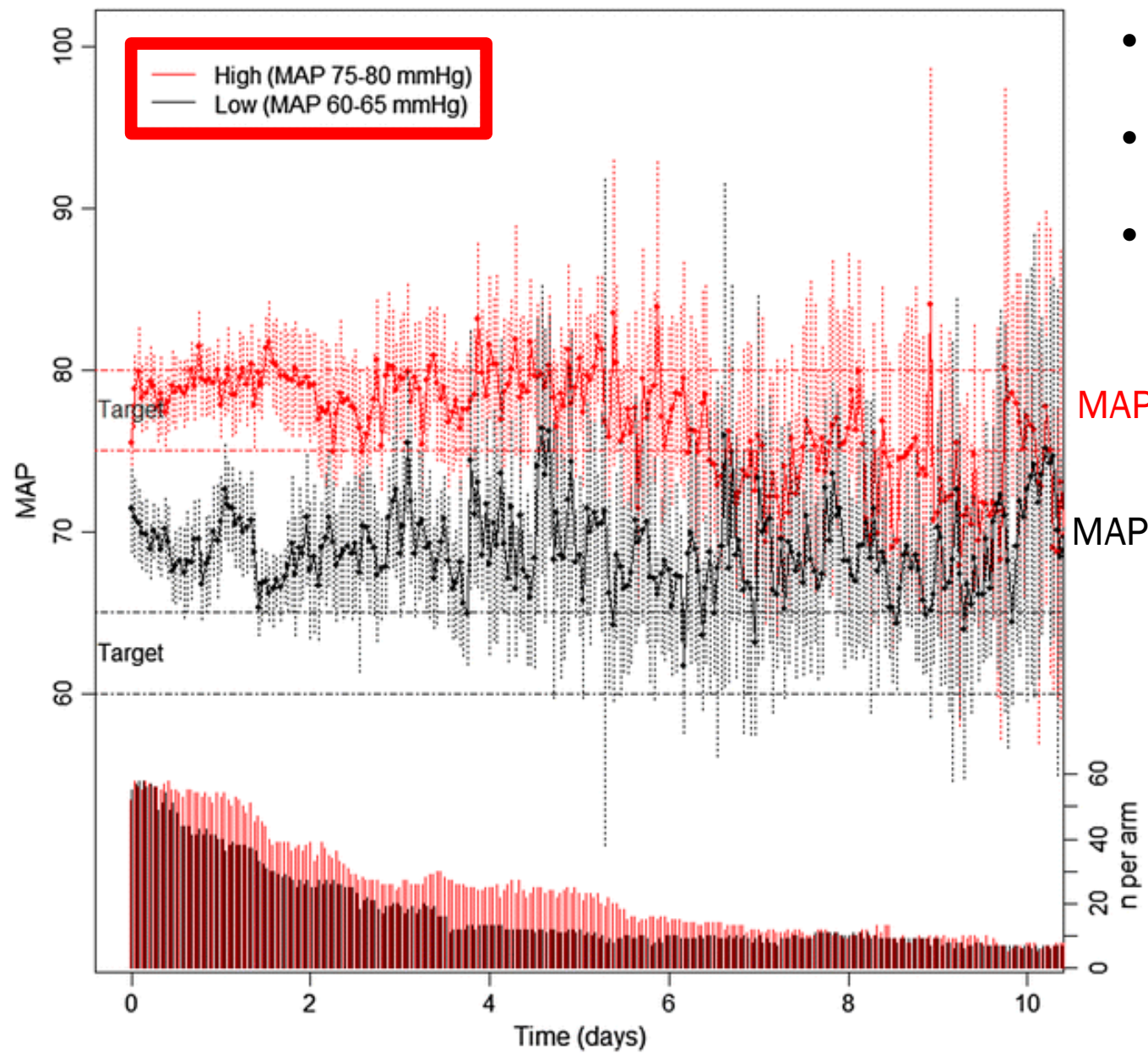
Higher versus lower blood pressure targets for vasopressor therapy in shock: a multicentre pilot randomized controlled trial

OVATION Optimal Vasopressor Titration

- 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

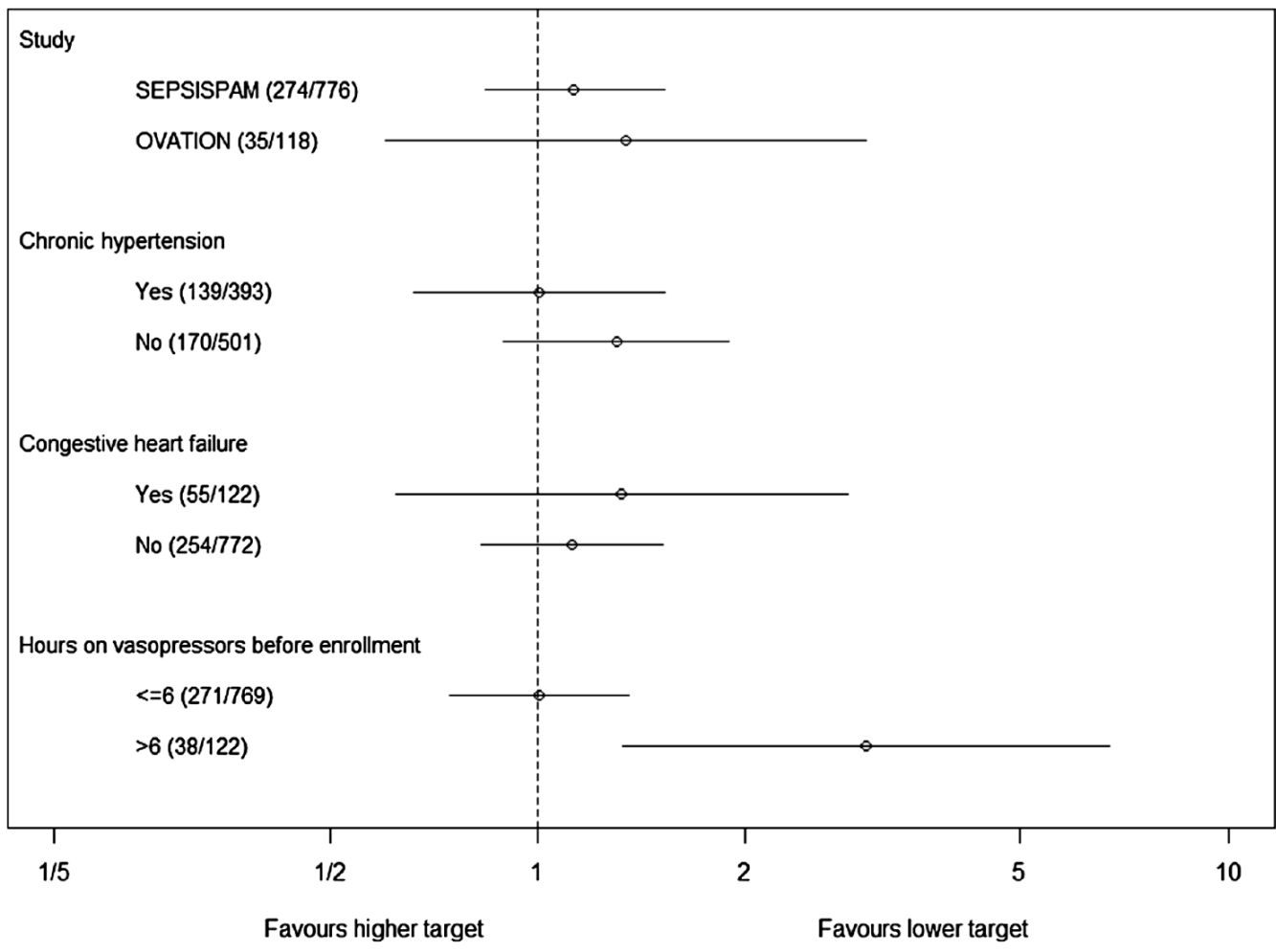
- Risk of cardiac arrhythmias (low vs high) 20% vs 36% (p = .07)
- Renal SOFA score (day 1 & 2): 1.1 and 1.3 in both groups
- Hospital mortality 30% vs 33% (p = 0.84)
- Age \geq 75 years – lower MAP target associated with lower hospital mortality (13% vs 60%) – no effect in younger patients
- No significant 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



Hypotension Exposure

The relationship between ICU hypotension and in-hospital mortality and morbidity in septic patients

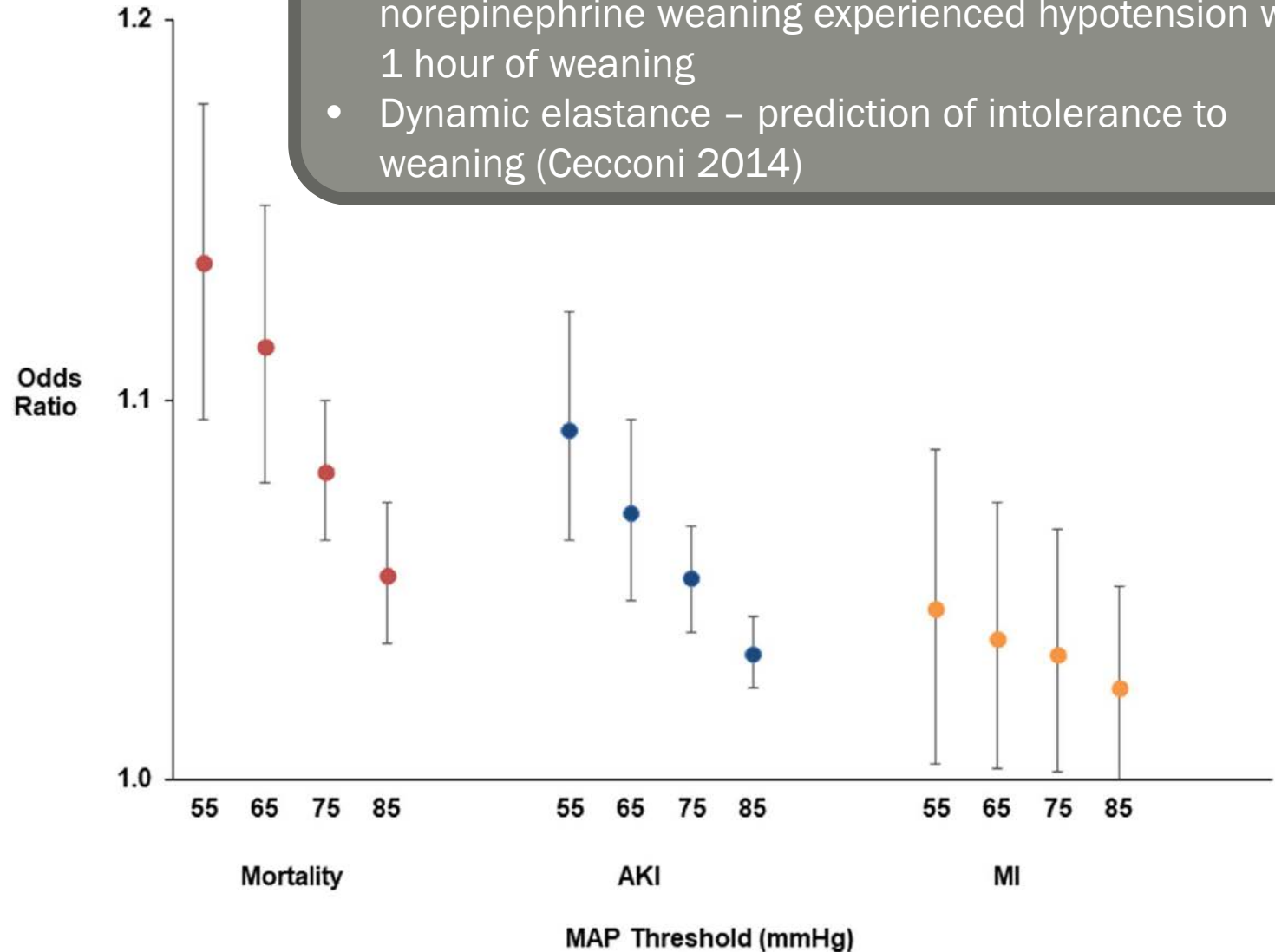
Kamal Maheshwari^{1,7*}, Brian H. Nathanson², Sibyl H. Munson³, Victor Khangulov³, Mitali Stevens⁴, Hussain Badani³, Ashish K. Khanna⁵ and Daniel I. Sessler⁶

Intensive Care Med, 2018

- Retrospective analysis (N = 8782) – Sepsis with ICU stay \geq 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

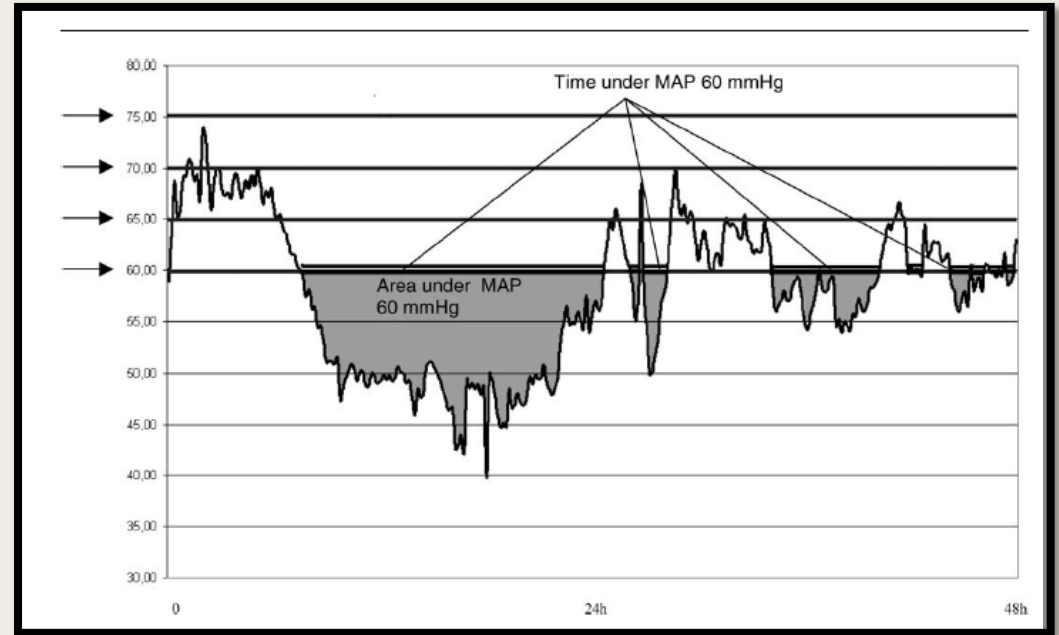


Risk for hypotension during vasopressor weaning

- Jeon (2018) – 68% of patients undergoing norepinephrine weaning experienced hypotension within 1 hour of weaning
- Dynamic elastance – prediction of intolerance to weaning (Cecconi 2014)

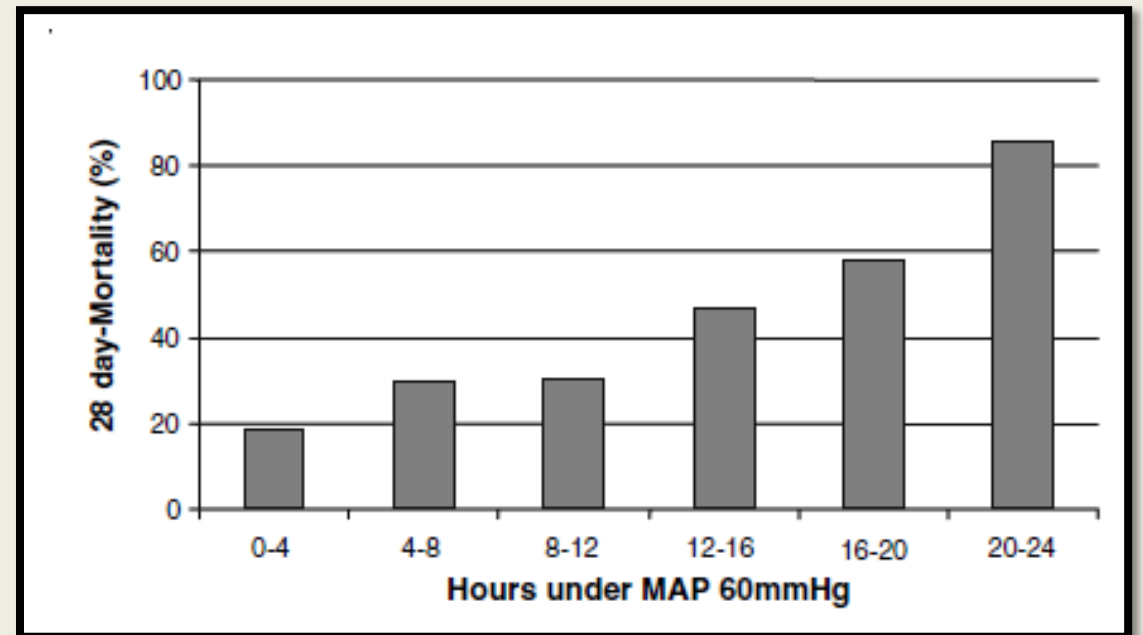
Varpula (2005)

- 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)

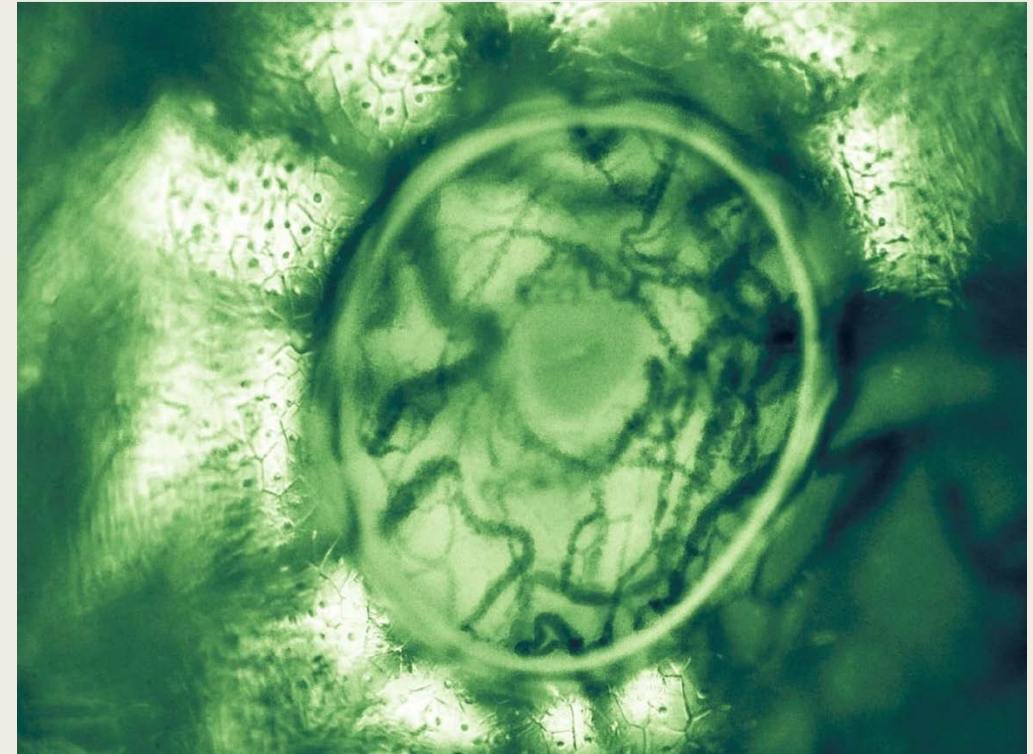
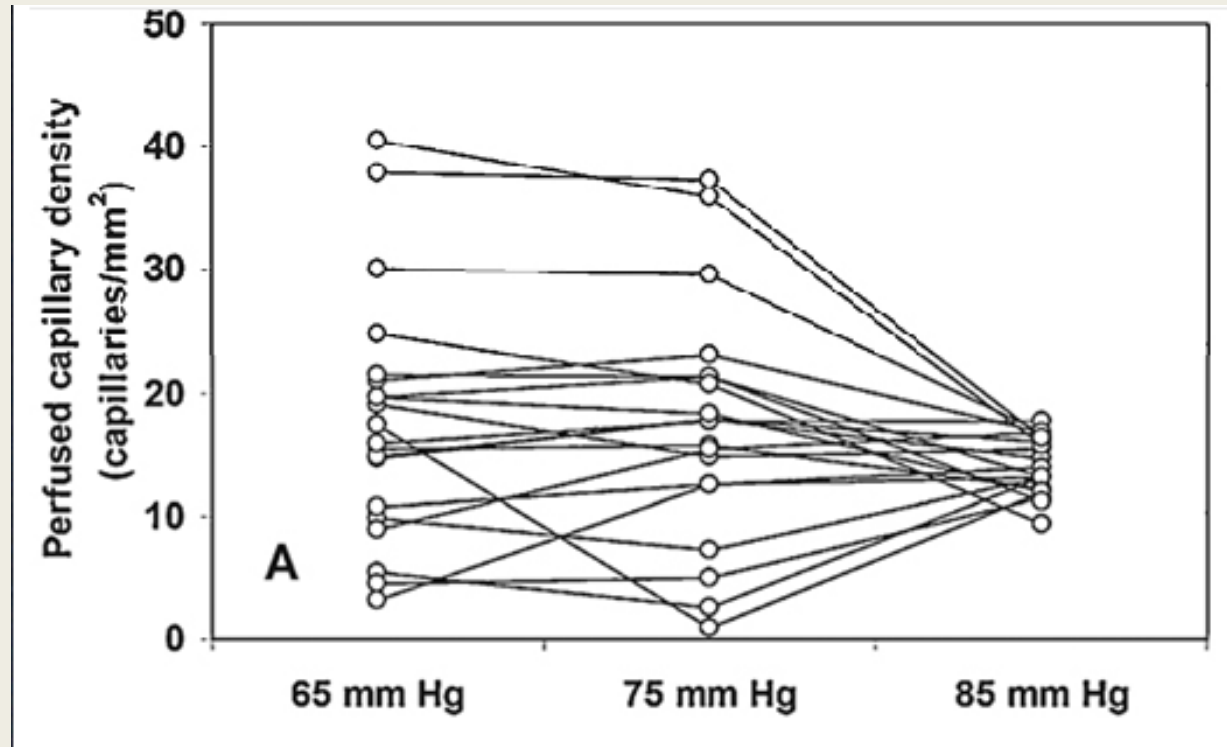
- Retrospective cohort – septic patients (N = 274)
- Association between hourly time integral of ABP drops below threshold (MAP < 60 mm Hg)



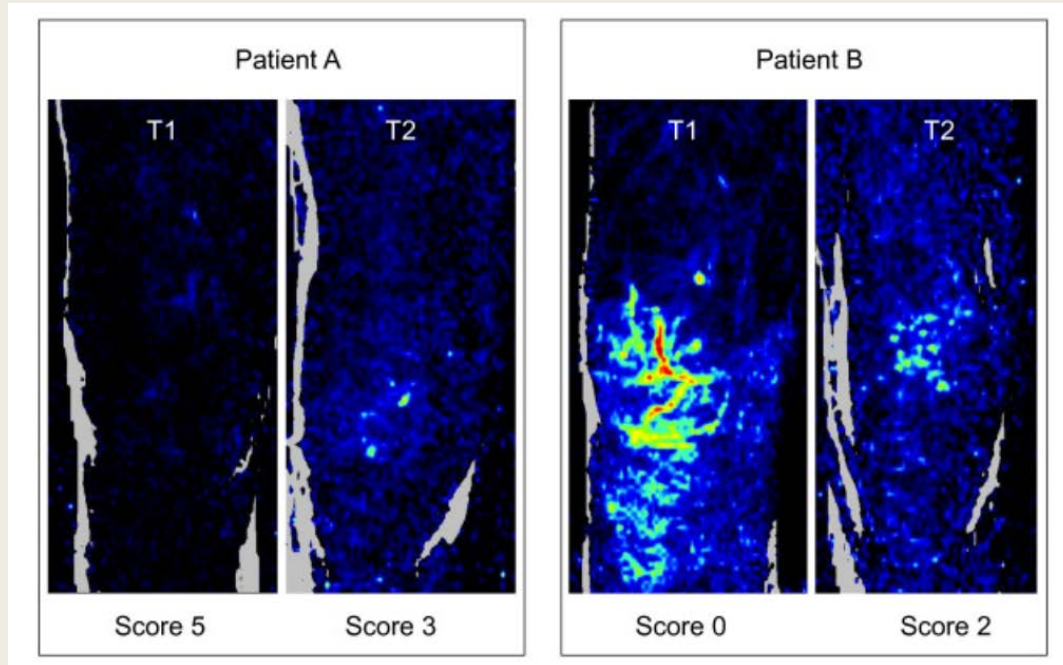
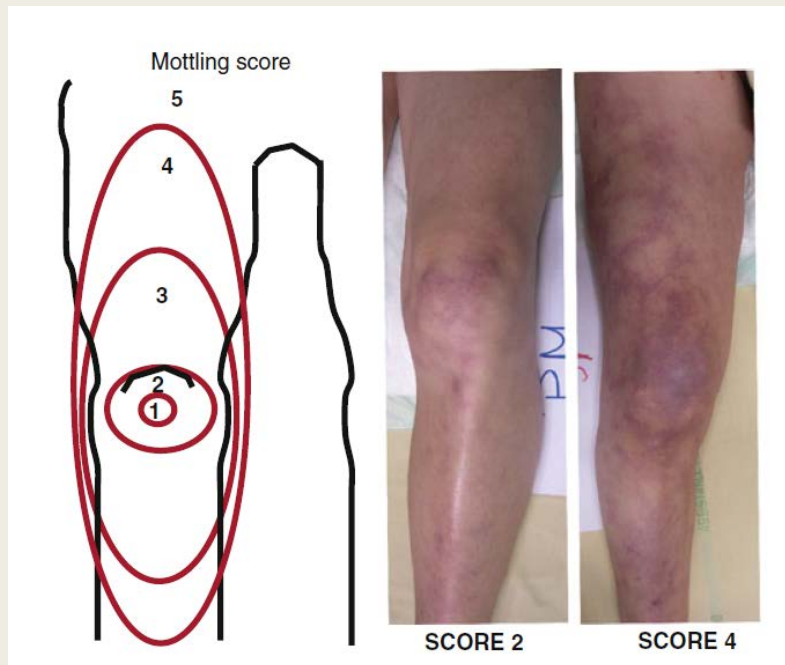
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ARE WE FOLLOWING THE
CORRECT PARAMETERS?

Macrocirculation - Microcirculation



Dubin (2009)



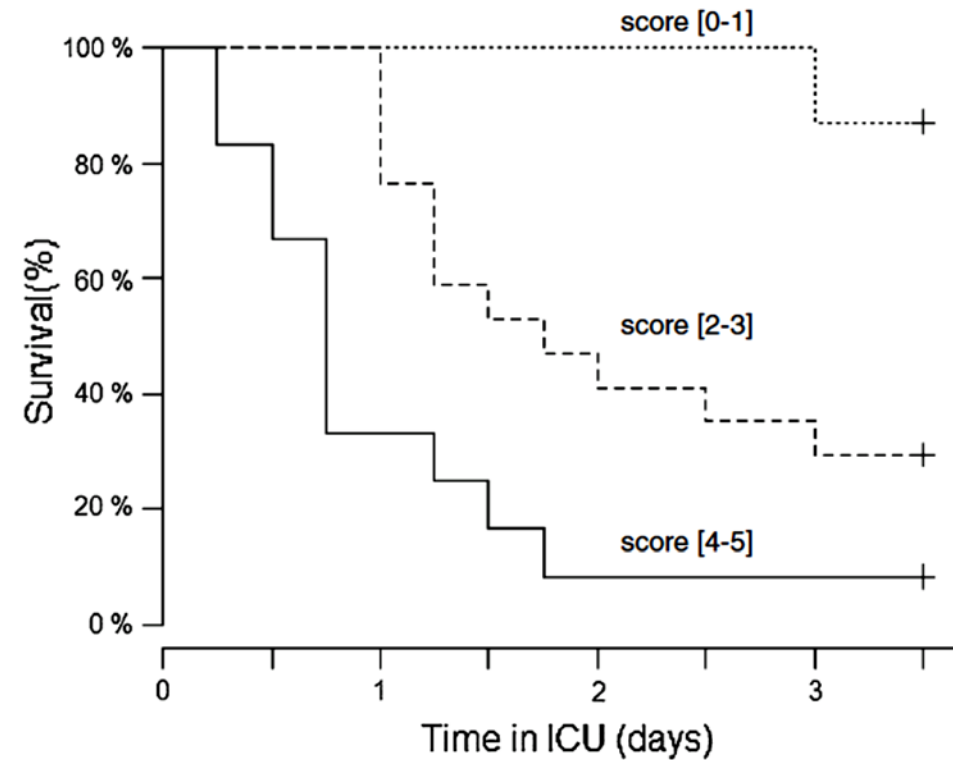
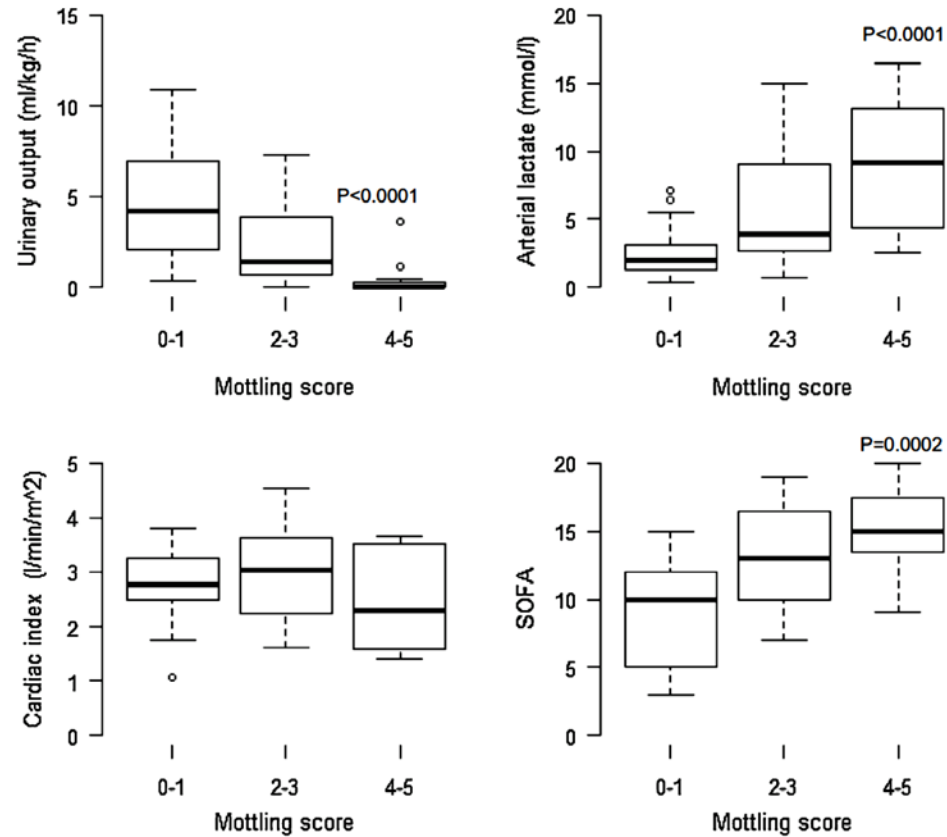
Ait Oufella 2013

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

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)



Mottling Score	Odds of Death	14-Day Mortality
0-1 (no or modest)	1	13%
2-3 (mild or moderate)	16 (4-81)	70%
4-5 (severe)	74 (11-1,568)	92%

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

W

BE BOUNDLESS

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