



# Hypotension and Anesthesia Outcomes

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# Consequence of Anesthesia Delivery

- ◆ **Hypotension is common**
  - Phenylephrine and ephedrine administration routine
- ◆ **Deep anesthetic also common**
  - Physicians and nurses resistant to inhalation agent MAC < 1
    - » Brain function monitoring may be a tool to decrease anesthetic overdose
- ◆ **Recent studies report relationship between intraoperative hypotension (MAP < 65 mmHg) and adverse outcomes:**
  - Acute kidney injury
  - Myocardial injury
  - Cardiac events (e.g. myocardial infarction, cardiac arrest)
  - Mortality



# **Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery**

**Salmasi V, Maheshwari K<sub>1</sub> et al**

**Cleveland Clinic Foundation**

**Anesthesiology 126(1), 47-65: 2017.**



# Methods

- ◆ **Retrospective cohort study of adults who had inpatient noncardiac surgery, 1/2005 – 3/2015 (164,514 patients)**
- ◆ **57,315 patients met inclusion/exclusion requirements**
  - **Inclusion - Preop and postop creatinine, BP recorded preoperatively**
  - **Exclusion - Chronic kidney disease, urologic procedures, anesthesia < 60 min or missing baseline variables, invalid or unavailable data for more than 10 consecutive minutes**
- ◆ **Myocardial injury (MINS) defined as troponin or creatine kinase above upper limit of normal (0.03 ng/ml, 8.8 ng/ml).**
  - **Patients without postop measurements assumed not to have an MI**
- ◆ **Acute kidney injury (AKI) defined by increase in creatinine (1.5 fold increase or more than 0.3 mg/dl)**





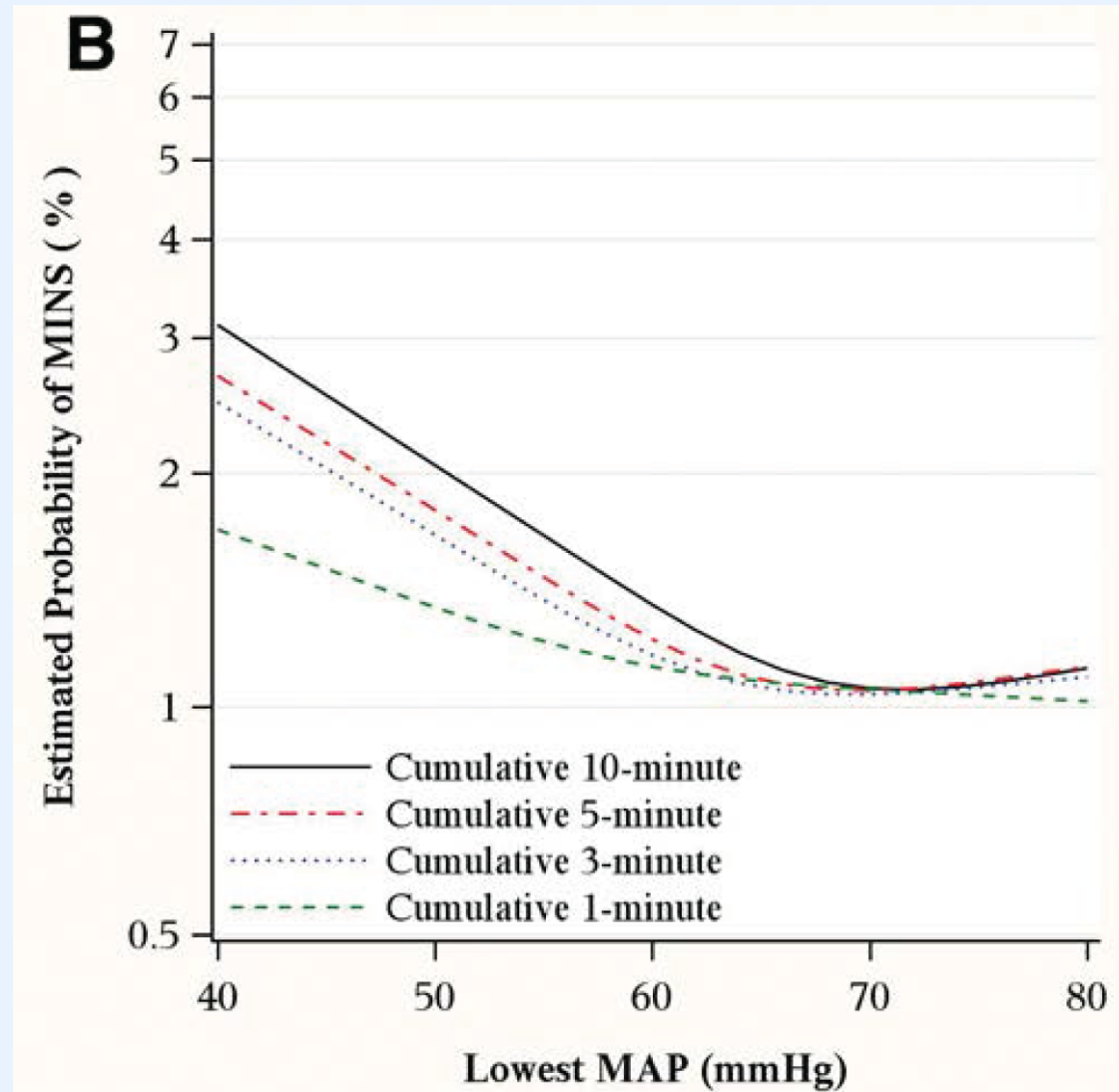
# Hypotension

- ♦ **Determined the absolute and relative (percent below baseline) thresholds below which MINS and AKI began to increase**
  - **Assessed relationships between MINS/AKI and the lowest MAP or the lowest percent decrease from baseline for a total of 1, 3, 5, and 10 min, and time-weighted average under absolute thresholds (e.g,  $< 55$ ,  $< 60$ , ...) or relative thresholds (i.e.,  $< 10\%$ ,  $< 15\%$ , ... of baseline BP)**

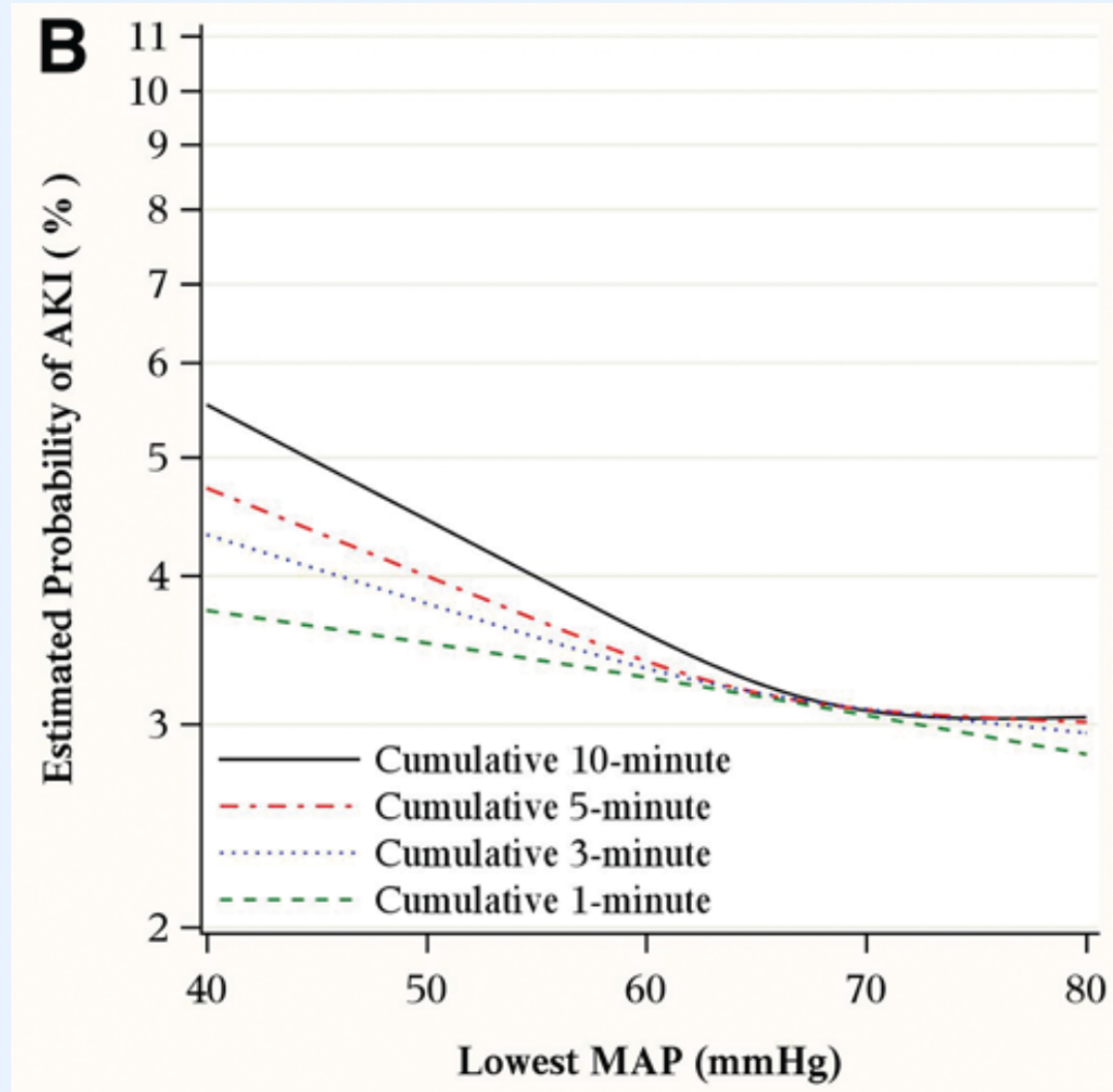


# Results

- ◆ **Absolute threshold of 65 mm Hg and relative thresholds of 20% decrease from baseline MAP associated with increased risk of both MINS and AKI.**
  - Overall incidence of MINS 3.1% and AKI 5.6%
  - **Only 14.9% of patients had postoperative troponin**
- ◆ **Increasing time-weighted average MAP under various threshold was associated with increased odds of MINS and AKI**
  - Relationship strengthened at lower thresholds (e.g. observed slope for < 60 mmHg steeper than for < 65 mmHg)
  - Using different absolute or relative thresholds did not increase discriminative ability
- ◆ **Absolute BP was as good as percent decrease from baseline**



**Lowest mean arterial pressure (MAP) thresholds for myocardial injury (MINS) after noncardiac surgery.**



**Lowest mean arterial pressure (MAP) thresholds for acute kidney injury (AKI) after noncardiac surgery**



# Discussion

- ♦ **MAP < 65 mmHg for > 13 minutes associated with significantly higher odds of myocardial and kidney injury**
  - **Injury more common at lower MAP and exposure was prolonged**
    - » **MAP of 50 mmHg for just 1 min significantly increased risk for MINS and AKI**
- ♦ **There was no advantage to using relative over absolute threshold for AKI or MINS**
  - **Anesthetic management can thus be based on intraoperative pressures without regard to preoperative pressure.**
- ♦ **Maintaining intraoperative MAP > 65 mmHg reduces the relative risk of myocardial and renal injury – the leading causes of 30-day postoperative mortality**



# **Relationship between Intraoperative MAP and Clinical Outcomes**

**Walsh M, Devereaux PJ, et al**

**Cleveland Clinic Foundation**

**Anesthesiology Vol.119(9), 507-515:2013**



# Methods

- ♦ **33,330 noncardiac surgical patients**
- ♦ **Evaluated the association between intraoperative MAP from less than 55 to 75 mmHg and postoperative acute kidney injury (AKI), myocardial injury, and cardiac complications**
- ♦ **Determined the threshold of MAP where risk is increased**
  - **< 55, < 60, < 65, < 70, < 75 mmHg; 0, 1-5, 6-10, 11-20, > 20 mins**



# Definition of Injury

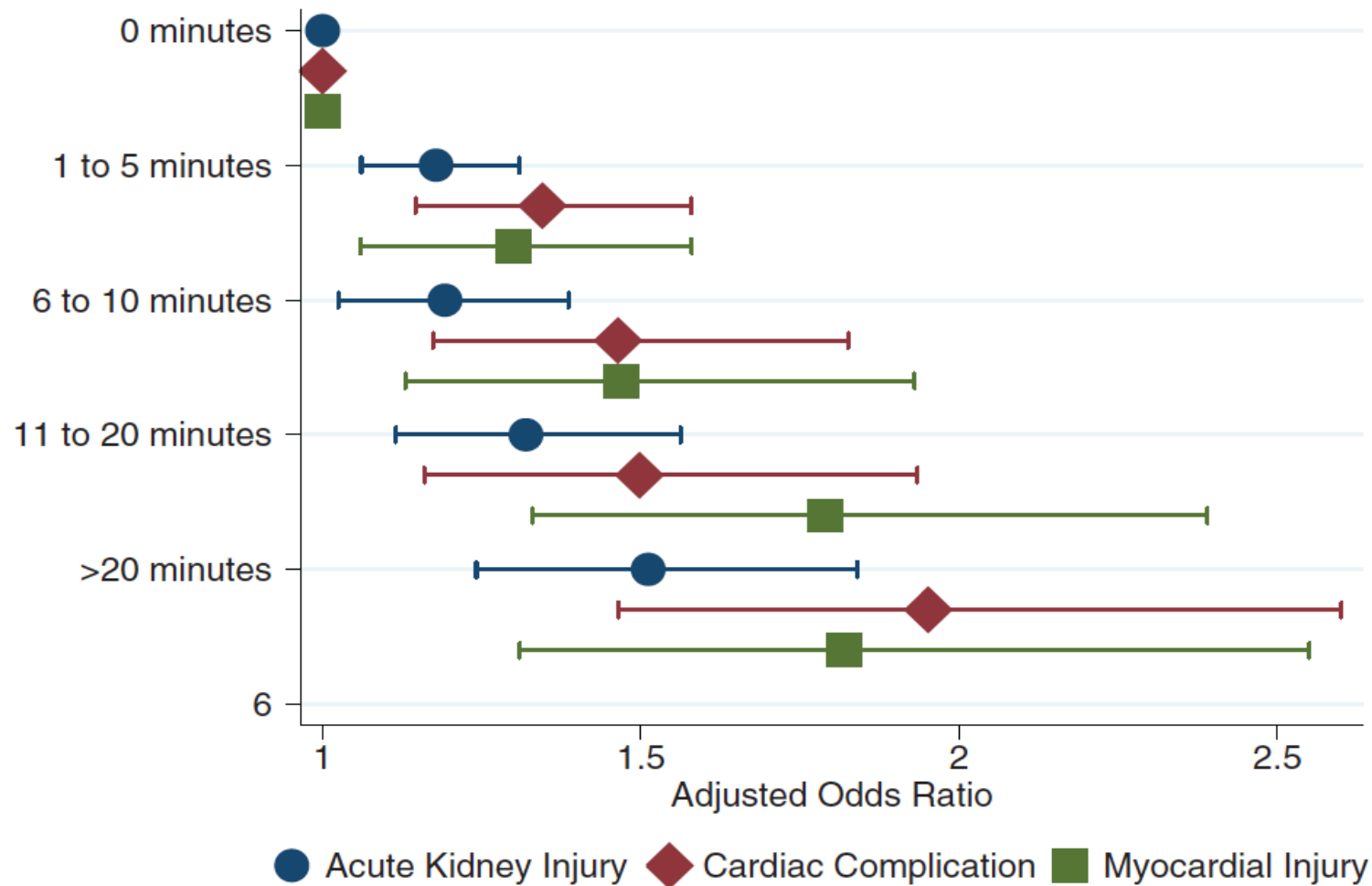
- ◆ **Acute kidney injury (AKI) (rise of serum creatinine 1.5 fold or more than 0.3 mg/dl)**
  - 7.5% of noncardiac surgery patients.
  - **Associated with increased mortality**
- ◆ **Myocardial injury (rise in cardiac biomarkers, troponin T greater than necrosis limit and creatinine kinase-MB greater than upper limit of normal)**
  - 11.6% of surgical patients
- ◆ **Cardiac complications – myocardial infarction, heart failure, cardiac arrest**





# Results

- ◆ **Independent graded relationship between the length of time spent with a **MAP < 55 mmHg** and acute kidney injury and cardiac complications**
  - **Longest periods of MAP < 55 mmHg had a 1.5-fold increased risk of AKI or MINS and a 2-fold increase in cardiac complications ( $p < 0.001$ ).**
  - **As time increased with MAP < 55 mmHg, there was a trend to a higher 30-day mortality**
    - » **Exposure to more than 20 mins was statistically significance**
  - **There was no evidence of interaction between preoperative HTN and time with a MAP < 55 mmHg**



**Fig. 4.** Adjusted odds ratios for acute kidney injury, cardiac complications, and myocardial injury by time spent with a mean arterial pressure <55 mmHg.



# Discussion

- ◆ **MAP < 55 mmHg associated with acute kidney injury, myocardial injury, and cardiac complications**
- ◆ **Risk escalates rapidly and there was no safe duration for a MAP < 55 mmHg**
- ◆ **Acute kidney injury and myocardial injury are common, strongly associated with morbidity and mortality, and are costly**
- ◆ **Suggests that hypotension is independent of other risk factors in a diverse cohort of non-cardiac surgery patients**
- ◆ **Results were consistent across numerous sensitivity analyses**



# **Association between Intraoperative Hypotension and Hypertension and 30-day Postoperative Mortality in Noncardiac Surgery**

**Monk TG, Bronsert MR, et al  
Duke University, Durham, NC  
Anesthesiology 123(2), 307-19; 2015**



# Methods

- ◆ **Retrospective cohort study of 18,756 noncardiac surgery patients in 6 VA hospitals**
  - Determine risk-adjusted associations between intraoperative BP (hypotension and hypertension) and 30-day mortality
- ◆ **Deviation in BP were assessed using 3 methods:**
  - Population thresholds (individual patient summary of area under or over threshold (2 standard deviations from mean population intraoperative BP))
  - **Absolute threshold (e.g. MAP < 55 mmHg)**
  - Percent change from baseline BP



# Results

- ♦ **30-day mortality was associated with:**
  - **Population threshold systolic hypotension**
    - » **SBP < 67 mmHg for > 8 mins) [OR 3.3 (2.2 - 4.8)]**
    - » **MAP < 49 mmHg for > 4 mins) [OR 2.8 (1.9 - 4.3)]**
    - » **DBP < 33 mmHg for > 4.5 mins) [OR 2.4 (1.6 - 3.8)]**
  - **Absolute threshold**
    - » **SBP < 70 mmHg for > 5 mins [OR 2.9 (1.7 - 4.9)]**
    - » **MAP < 49 mmHg for > 5 mins [OR 2.4 (1.3 - 4.6)]**
    - » **DBP < 30 mmHg for > 5 mins [OR 3.2 (1.8 - 5.5)]**
  - **Percent change: MAP decreased to more than 50% from baseline for > 5 mins – [OR 2.7 (1.5-5.0)]**
- ♦ **Intraoperative hypertension was not associated with an increase in 30-day mortality**



# Discussion

- ♦ **Results are consistent with Salmasi and Walsh**
  - **Significant intraoperative hypotension (both magnitude and duration) is associated with adverse outcomes – AKI, cardiac injury/complications and 30-day mortality**
- ♦ **These are large studies of about 57, 30 and 20 thousand patients, respectively.**
- ♦ **Monk's study is multi-institutional adding strength to their findings**
- ♦ **These are observational studies and can only address association and not causality.**
  - **Are patients suffering from AKI or dying within 30 days in the more severely hypotensive groups were at a greater risk to begin with because of unmeasured variable?**



# **Perioperative Quality Initiative Consensus Statement on Intraoperative Blood Pressure, Risk and Outcomes for Elective Surgery**

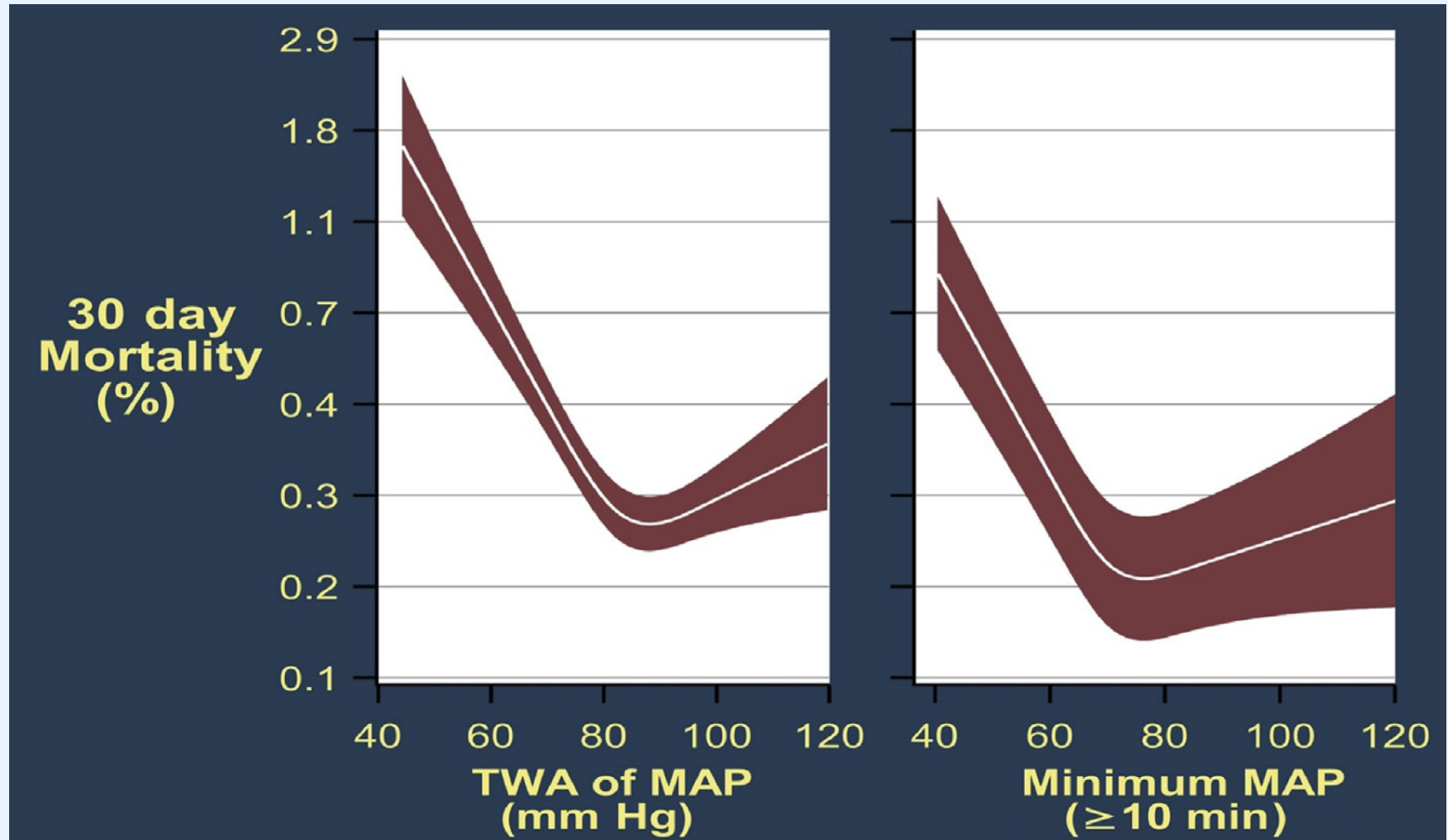
**Sessler DI, Bloomstone JA, et al  
British Journal of Anaesthesia  
Accepted January, 2019**





# Background

- ◆ **Death within 40 days of surgery remains common**
- ◆ **Perioperative MI is associated with high mortality**
- ◆ **Strong association between hypotension, myocardial injury, MI, renal injury, and death**
- ◆ **Perioperative arterial blood pressure management was the basis of a Perioperative Quality Initiative**
- ◆ **Meeting featured a modified Delphi process in which groups address various aspects of perioperative arterial pressure**
  - **Three consensus statements on intraoperative blood pressure were established**



**Relationship between time weighted average (TWA), lowest intraoperative MAP, and 30-day postoperative mortality. Note: Y axis is logarithmic**



# Consensus Statements

- ♦ **1: Intraoperative mean arterial blood pressures below 60 – 70 mm Hg are associated with myocardial injury, acute kidney injury, and death.**
  - Injury is a function severity of hypotension and duration.
- ♦ **2: For adult non-cardiac surgical patients, there is insufficient evidence to recommend a general upper limit of arterial pressure at which therapy should be initiated.**
- ♦ **3: During cardiac surgery, intraoperative systolic arterial pressure above 140 mm Hg is associated with increased 30-day mortality.**



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# Treatment of Intraoperative Hypotension



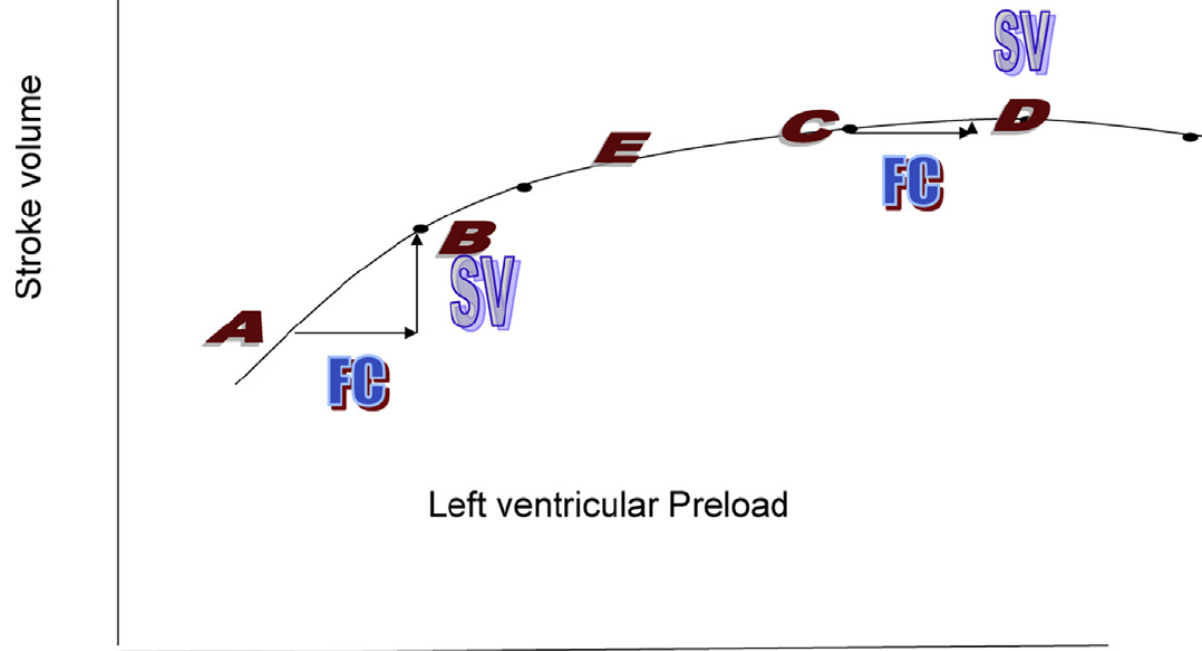
# Cause of Intraoperative Hypotension

- ♦ **Blood Pressure = SVR \* Cardiac Output**
  - **BP = SVR \* (HR \* Stroke Volume)**
- ♦ **Initial approach – treat the cause**
  - **Trendelenburg – increase preload**
    - » May not be clinically relevant - J. Anesth (2017) 31:692-702
  - **Fluids – increase preload**
  - **Lighten the anesthetic – increase cardiac output, SVR, venous tone**
    - » **Change to anesthetics that does not decrease BP *as much***
      - Nitrous oxide, ketamine, lidocaine, narcotic ...



# Fluid Management

- ◆ **Patients require fluids for hypotension if they are volume depleted or vascular dilation**
- ◆ **Administration of a fluids will often increase BP.**
  - **If patient does not respond to fluid challenge then another treatment strategy should be pursued**
  - **Can be difficult to know patient's fluid status without introduction of further monitoring**
    - » **Central line, swan ganz, TEE, noninvasive CO**
    - » **Pulse pressure variation – available on many physiologic monitors**



- ◆ Response of stroke volume (SV) to a fluid challenge is a marker of position on the Frank-Starling curve.
- ◆ Where SV increases more than 10% in response to 200 mL of isotonic fluid (i.e. A to B), patients is fluid responsive.
- ◆ Where SV does not increase to this extent (i.e. C to D), then no further fluid challenge is given



# Hypotension Secondary to Anesthetic

- ◆ **Inhalation agents decrease MAP in a dose-dependent manner**
  - Decrease systemic vascular resistance (less with sevoflurane)
  - Decrease myocardial contractility
  - Increase heart rate
  - Increase vascular compliance
- ◆ **Intravenous anesthetic also decrease MAP**
  - Decrease SVR and contractility by decreasing sympathetic output
  - Propofol causes significant vascular dilatation
  - Ketamine increases sympathetic output, increasing MAP, HR, SVR
    - » Direct myocardial depressant, unmasked in patients in extremis
  - Opioids and benzodiazepines have no direct cardiovascular effects except when used together - can cause significant cardiovascular depression





# Lighten Anesthetic

## ♦ Ignore MAC value on anesthesia machine

- Patients do not require more than one simultaneous anesthetic
- Patients will buck on the endotracheal tube before anesthesia recall
  - » Careful attention to muscle relaxant (at least 1 twitch)
  - » Patients on significant doses of antihypertensives may not be able to respond to light anesthesia
    - Also, in elderly, trauma, and those with severe cardiovascular compromise

## ♦ Consider brain function monitoring (Processed EEG)

- Instills a degree of confidence that patient has adequate depth of anesthesia
- Some data suggests lighter anesthesia associated with decrease rate of postoperative delirium



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# Hemodynamic Management



# Patients with Central Access

- ◆ **Catecholamines remain the mainstay of treatment of low CO and/or low SVR**
- ◆ **Epinephrine**
  - **Direct Beta-1 agonist – increases HR, CO, BP**
  - **Direct Alpha-1 agonist – decreases renal and splanchnic perfusion**
  - **Direct Beta-2 agonist – bronchodilator, can decrease afterload**
- ◆ **Norepinephrine**
  - **Direct Alpha-1 agonist – intense vasoconstriction of arteries and veins**
  - **Minimal Beta-1 agonist**
- ◆ **Vasopressin**
  - **Stimulates VP1 receptor - Increase SVR, decrease mesenteric blood flow**
- ◆ **Calcium Chloride – increase contractility, SVR**
- ◆ **Dopamine and dobutamine less frequently used today**



# Norepinephrine Extravasation



- ◆ **Although some centers will infuse norepinephrine through a peripheral IV, one must balance risk and benefit to the patient**

**BMJ Case Reports 2012; doi:10.1136/bcr-2012-006836**

**<http://casereports.bmj.com/content/2012/bcr-2012-006836.full.pdf>**



# Vasoactive Drugs

- ◆ Unless patient has central access, choices are limited
- ◆ Ephedrine – indirect alpha and beta agonist
  - Increases myocardial contractility and SVR
  - Increases heart rate – increase in myocardial oxygen consumption
  - Decreases renal perfusion
  - Significant tachyphylaxis
- ◆ Phenylephrine – direct alpha-1 agonist
  - Increases SVR, decrease HR
  - Increase in myocardial oxygen consumption
  - Significant decrease in renal perfusion
- ◆ **Is the treatment worse than the disease?**
  - Scientific literature is mostly silent



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# **A Systematic Review and Meta-Analysis on the Use of Preemptive Hemodynamic Intervention to Improve Postoperative Outcomes in Moderate and High-Risk Surgical Patients**

**Hamilton MA, Cecconi M, Rhodes A  
St. George's Healthcare  
NHS Trust, London, UK  
Anesth Analg 112,1392–402: 2011**



# Methods and Results

- ♦ **Meta-Analysis of 29 trials involved 4,805 moderate to high-risk surgical patients**
- ♦ **Overall mortality of 7.6%**
- ♦ **Preemptive hemodynamic interventions significantly reduced mortality – OR 0.48 (CI 0.33 - 0.78)  $p = 0.0002$  and surgical complications – OR 0.43 (CI 0.34 - 0.53)  $p < 0.0001$**
- ♦ **Subgroup analysis showed significant reduction in mortality in studies that used pulmonary artery catheters, supranormal hemodynamic targets, cardiac index, O<sub>2</sub> consumption, and the use of **fluids and inotropes as compared to fluids alone****
  - **Fluids and inotropes – OR 0.47 (CI 0.35 - 0.55)  $P < 0.01$**



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# **Effect of Individualized vs. Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery**

**Futier E, Lefrant JY, et al**

**Department of Anesthesia**

**Clermont-Ferrand, France**

***JAMA* 318(14), 1346-1357: 2017**





# Methods

- ◆ **Study of 298 pts at increased risk of post-op complications undergoing major surgery with general anesthesia**
- ◆ **Randomized to:**
  - **Individualized management strategy (IMS) to keep SBP within 10% baseline**
    - » **Low SBP treated with titration of norepinephrine infusion**
  - **Standard management strategy (SMS) to treat SBP < 80 mmHg or < 40% baseline**
    - » **Low SBP treated with 6 mg boluses of ephedrine (60 mg maximum)**
    - » **Norepinephrine rescue therapy**
  - **Baseline lactated ringers at 4 cc/kg/hr;**
  - **Additional fluid were given in 250 cc hydroxyethyl starch bolus to achieve maximal stroke volume (i.e. goal directed therapy)**
    - » **Did not identify how SV was determined**

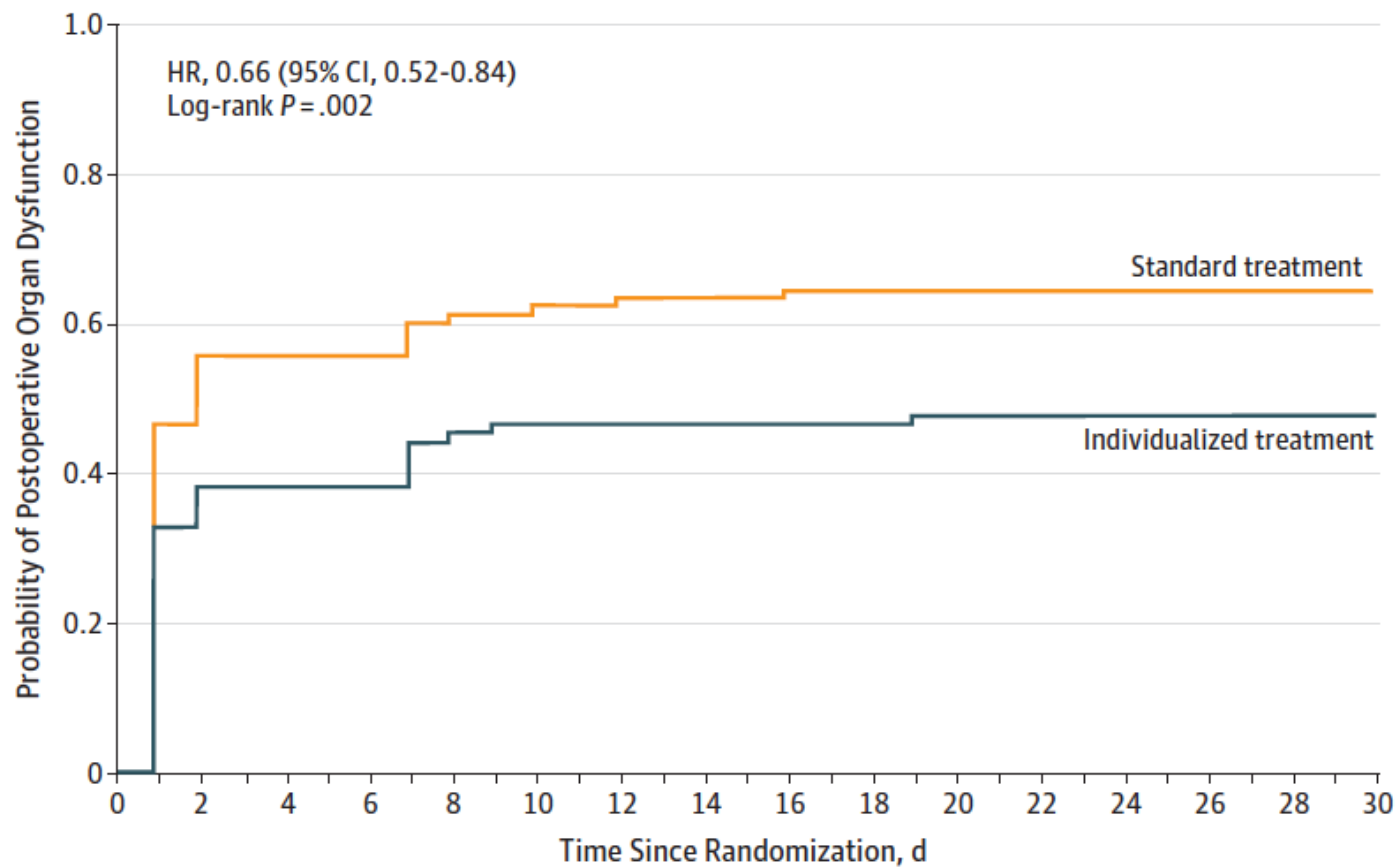


# Results

- ♦ **Composite of systemic inflammatory response syndrome and dysfunction of at least 1 organ system (i.e. renal, pulmonary, cardiovascular, coagulation, neurologic)**
  - **7 days, 56/147 (38.1 %) of IMS vs. 75/145 (51.7 %) of SMS patients had organ dysfunction;**
    - » **Relative risk 0.73; CI 0.56 - 0.94, P = 0.02**
  - **30 days, 63/147 (46.3 %) of IMS vs. 92/145 (63.4 %) of SMS patients had organ dysfunction;**
    - » **Relative risk 0.66; CI, 0.52 - 0.84, P = 0.001**
  - **30 day mortality, 9/147 (6.1 %) of IMS vs. 8/145 (5.5 %);**
    - » **Relative risk 1.11; CI, 0.44 – 2.81, P = 0.82**



Figure 3. Kaplan-Meier Estimates of the Probability of Postoperative Organ Dysfunction by Day 30 After Surgery



No. at risk

Standard treatment	145	78	65	58	54	53
Individualized treatment	147	99	91	82	80	79



# Conclusion

- ◆ **Even brief periods of hypotension (MAP < 55 mmHg) associated with increased AKI, myocardial injury, and death**
- ◆ **Low blood pressure should be avoided and if it occurs promptly treated. Goal should be MAP > 65 mmHg**
- ◆ **Treat first with fluids and decrease depth of anesthesia, avoid full paralysis**
  - **Switch to anesthetic technique the minimizes cardiac depression and vasodilatation**
- ◆ **Use of vasoactive medications may be associated with improved outcomes in critical care and surgical patients**
  - **Norepinephrine and epinephrine drugs of choice with central line**
  - **Ephedrine and phenylephrine with peripheral IV**



# Questions

<https://youtu.be/FFaRVy-1zuo>