

# HYPOTENSION AND ANESTHESIA OUTCOMES

*AAAA ANNUAL MEETING  
AUSTIN, TEXAS*

JEFFREY S. PLAGENHOEF, M.D.  
CHAIRMAN, DEPARTMENT OF ANESTHESIOLOGY  
BAYLOR SCOTT & WHITE HILLCREST MEDICAL CENTER  
ASA PRESIDENT-ELECT

# INTRAOPERATIVE HYPOTENSION

- Recent studies reporting relationship between intraoperative hypotension and adverse outcomes:
  - Acute kidney injury
  - Myocardial injury
  - Mortality

## BUT WHAT TARGETS FOR BP CONTROL?

- Systematic review of the literature reveals 130 studies and 140 definitions of intraoperative hypotension
- And which organ system – lows of autoreg at diff BP values
  - Myocardial perfusion – DBP (30-50)
  - Brain perfusion – MAP (lower limits for autoreg variable – 30-80)
  - Kidney perfusion – MAP & flow sensitive – mammalian kidney loses autoreg at 80mmHg, and the pressure-flow relationship for the kidney appears to follow a steeper slope

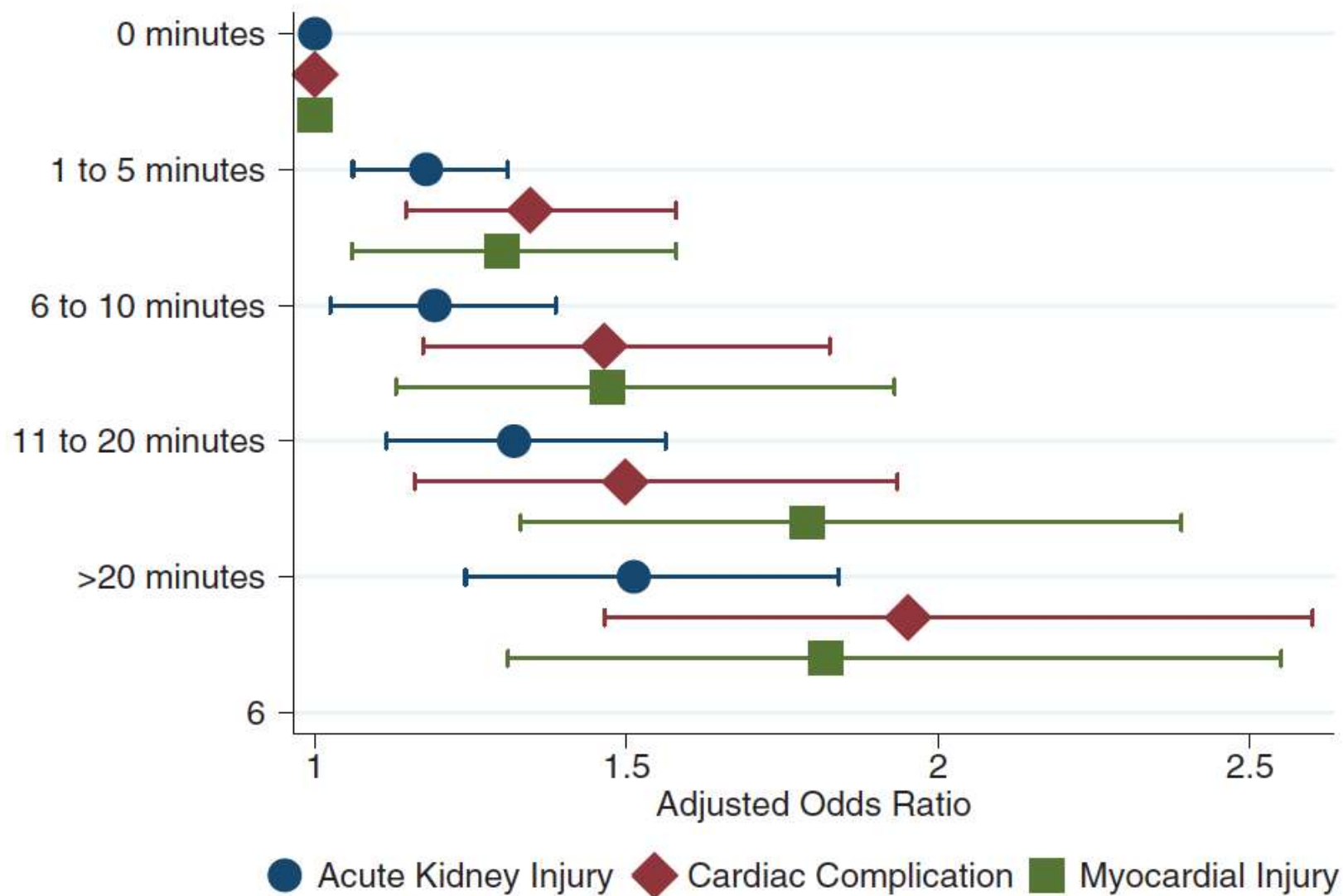
# RELATIONSHIP BETWEEN INTRAOPERATIVE MAP AND CLINICAL OUTCOMES

WALSH M, DEVEREAUX PJ, ET AL, ANESTHESIOLOGY, 119(3), 2013

- 33,330 noncardiac surgeries at Cleveland Clinic
- Evaluated the association between an intraoperative MAP from <55 to 75 mmHg and postoperative acute kidney injury (AKI), myocardial injury, and cardiac complications
  - AKI (= rise of serum creatinine 1.5 fold or more than 0.3 mg/dl) seen in 7.5% of noncardiac surgery patients & associated with increased mortality
  - Myocardial injury (rise in cardiac biomarkers, troponin T greater than necrosis limit, and CK-MB greater than upper limit of normal) in 11.6% of surgical patients
  - Cardiac complications – myocardial infarction, heart failure, arrest
- Determined the threshold of MAP where risk is increased
  - < 55, < 60, < 65, < 70, < 75 mmHg; 0, 1-5, 6-10, 11-20, > 20 mins

# RESULTS

- Independent graded relationship between the length of time spent with a MAP < 55 mmHg and AKI and cardiac complications
  - Similar magnitude but less graded relationship for myocardial injury
  - Those with the longest periods of a MAP < 55 mmHg had about a 1.5-fold increased risk of AKI or myocardial injury and an almost 2-fold increase in cardiac complications ( $p < 0.001$ ).
  - Interestingly, there was no evidence of interaction between preoperative BP and time with a MAP < 55 mmHg
  - As time increased with MAP < 55 mmHg, there was a trend to a higher 30-day mortality (>20 mins. was statistically significantly)



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

**Table 2.** Adjusted Odds Ratios for Acute Kidney Injury, Myocardial Injury, and Cardiac Complications for Intraoperative Time Spent with a MAP <55 mmHg

Time MAP <55 mmHg (min)	Adjusted Odds Ratio (95% CI)			
	Acute Kidney Injury	Myocardial Injury	Cardiac Complication	30-day Mortality
0		Referent		
1-5	1.18 (1.06-1.31)	1.30 (1.06-1.58)	1.35 (1.15-1.58)	1.16 (0.91-1.46)
6-10	1.19 (1.03-1.39)	1.47 (1.13-1.93)	1.46 (1.17-1.83)	1.16 (0.84-1.60)
11-20	1.32 (1.11-1.56)	1.79 (1.33-2.39)	1.50 (1.16-1.94)	1.26 (0.89-1.80)
>20	1.51 (1.24-1.84)	1.82 (1.31-2.55)	1.95 (1.46-2.60)	1.79 (1.21-2.65)

Estimates adjusted for patient age, sex, Charlson comorbidity index, emergency procedure status, type of surgery, preoperative hemoglobin, decrement in hemoglobin concentration, estimated blood loss, and volume of erythrocyte transfusions.

MAP = mean arterial pressure.

## SUMMARY

- MAP < 55 mmHg associated with AKI, myocardial injury, and cardiac complications
- Risk escalates rapidly and there was no safe duration for a MAP < 55 mmHg
- AKI 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 OF INTRAOPERATIVE HYPOTENSION WITH ACUTE KIDNEY INJURY AFTER ELECTIVE NONCARDIAC SURGERY

SUN LY, ET AL, ANESTHESIOLOGY 123(3), 2015

- Retrospective cohort study of all non cardiac surgery patients with A-lines from Nov 2009 - 2011 (5,127)
  - ◆ Seen in preoperative clinic
  - ◆ At least one day as hospital in-patient
- Primary outcome AKI (= rise of serum creatinine 1.5 fold or more than 0.3 mg/dl) during the first 2 postop days
- Examined MAP < 60 mmHg for 11-20 mins and MAP < 55 mmHg for more than 10 mins

# RESULTS

- Of the 5,127 patients, 324 (6.3%) developed AKI
- Graded relationship between IOH (both magnitude and duration > 10 mins) and odds of postoperative AKI
  - e.g. stage I AKI associated with MAP < 55 and < 60 for 11 to 20 mins
  - Graded relationship between incremental durations of MAP < 55 and odds of stage I AKI
- Compared to patients without IOH, the adjusted OR of AKI in pts with MAP < 55 mmHg was: 2.34 (1.51-4.05) for 11-20 mins and 3.52 (1.51-8.25) for > 20 mins
- MAP < 60 mmHg for 11-20 mins had 2-fold increase in AKI
- Male gender, Hx of hypotension, preop renal insufficiency, anemia, and surgical duration also associated with AKI
- **\*Preoperative HTN had no association with AKI**

**Table 2.** Proportion Experiencing AKI, Stratified by Hypotension Duration for MAP Thresholds of 55, 60, and 65 mmHg

IOH Duration (min)	MAP < 55 mmHg		MAP < 60 mmHg		MAP < 65 mmHg	
	N	AKI	N	AKI	N	AKI
1-5	2,807	189 (6.7%)	2,490	137 (5.5%)	1,474	64 (4.3%)
6-10	637	63 (9.9%)	1,030	64 (6.2%)	1,252	79 (6.3%)
11-20	63	7 (11.1%)	579	67 (11.6%)	1,182	80 (6.8%)
>20	23	4 (17.4%)	274	30 (11.0%)	903	92 (10.2%)

AKI = acute kidney injury; IOH = intraoperative hypotension; MAP = mean arterial pressure.

**Table 5.** Comparison of Odds Ratios of Acute Kidney Injury across Mean Arterial Pressure “Bands” (i.e., MAP <55, 55–59, and 60–64 mmHg)

Mean Arterial Pressure Band (mmHg)	Duration of Intraoperative Hypotension (min)				
	0	1–5	6–10	11–20	>20
<55	Reference	1.23 (0.87–1.74)	1.51 (1.00–2.30)	1.44 (0.94–2.19)	2.09 (1.40–3.11)
55–59	Reference	1.04 (0.67–1.62)	1.13 (0.69–1.84)	1.23 (0.77–1.97)	1.74 (1.13–2.69)
60–64	Reference	1.43 (0.68–3.00)	1.15 (0.53–2.50)	1.69 (0.83–3.43)	2.00 (1.01–3.95)

MAP = mean arterial pressure.

**Table 6.** Comparison of Odds Ratios of Acute Kidney Injury across Primary and Sensitivity Analyses in Patients with Mean Arterial Pressure < 55 mmHg

Analysis	Duration of Intraoperative Hypotension (min)				
	0	1–5	6–10	11–20	>20
Primary analysis	Reference	1.35 (0.98–1.86)	1.45 (0.94–2.22)	2.34 (1.35–4.05)	3.53 (1.51–8.25)
AKIN stage II	Reference	0.79 (0.44–1.43)	1.29 (0.61–2.72)	0.79 (0.22–2.87)	4.86 (1.38–17.10)
Adjusted for intraoperative blood loss	Reference	1.24 (0.90–1.71)	1.28 (0.83–1.97)	2.04 (1.17–3.56)	3.11 (1.31–7.40)
Excluded patients without postoperative Cr measurement	Reference	1.33 (0.97–1.84)	1.41 (0.92–2.16)	2.10 (1.21–3.65)	3.53 (1.50–8.26)
Restricted to patients with preoperative eGFR > 60 ml/min	Reference	1.22 (0.85–1.77)	1.44 (0.88–2.35)	1.96 (0.99–3.88)	3.49 (1.25–9.74)

All models are age, gender, comorbidity, and surgery adjusted.

AKIN = Acute Kidney Injury Network; Cr = serum creatinine; eGFR = estimated glomerular filtration rate, as determined by the Cockcroft-Gault formula.

## DISCUSSION POINTS

- AKI was associated with intraoperative MAP < 55 mmHg for more than 10 min, and MAP < 60 mmHg for 11-20 mins
- Results may help develop goal-directed hemodynamic management strategies because BP is one of very few modifiable intraoperative risk factors
- Consistent with results in Walsh study
- The magnitude and duration of IOH are an important risk factor for both stage I and II AKI
  - Physiologically reasonable since MAP of 65-75 mmHg is the lower limit of human renal auto regulation

# ASSOCIATION BETWEEN INTRAOPERATIVE HYPOTENSION AND HYPERTENSION AND 30-DAY POSTOPERATIVE MORTALITY IN NONCARDIAC SURGERY

MONK TG ET AL, ANESTHESIOLOGY 123(2); 2015

- 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
- The deviations in BP were assessed using 3 methods:
  - Population thresholds (individual pt. sum of area under or over threshold (2 ST's 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 hypotension (MAP < 49 mmHg for > 4 mins) [OR 2.8 (1.9-4.3)], and diastolic hypotension (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)] Remember ~70/50/30mmHg as targets!
  - 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 POINTS

- Results of this study are consistent with both the findings reported in Walsh and Sun
  - Significant intraoperative hypotension (both magnitude and duration) is associated with adverse outcomes – AKI, cardiac injury/complications and 30-day mortality
- Both Walsh and Monk are large studies of about 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, at a greater risk to begin with because of unmeasured variable?

# RELATIONSHIP BETWEEN INTRAOPERATIVE HYPOTENSION, DEFINED BY EITHER REDUCTION FROM BASELINE OR ABSOLUTE THRESHOLDS, AND ACUTE KIDNEY AND MYOCARDIAL INJURY AFTER NONCARDIAC SURGERY

VA SALMASI, M.D., KAMAL MAHESHWARI, M.D., M.P.H., DONGSHENG YANG, M.A., EDWARD J. MASCHA, PH.D., ASHA SINGH, M.D., DANIEL I. SESSLER, M.D., ANDREA KURZ, M.D.; ANESTHESIOLOGY 2017; 126:47-65

- The authors characterized hypotension by the lowest MAP below various absolute and relative thresholds for cumulative 1, 3, 5, or 10 min and also time-weighted average below various absolute or relative MAP thresholds.
- **Results:** MAP below absolute thresholds of 65 mmHg or relative thresholds of 20% were progressively related to both myocardial and kidney injury.
- There were no clinically important interactions between preoperative blood pressures and the relationship between hypotension and myocardial or kidney injury at intraoperative mean arterial blood pressures less than 65 mmhg.
- **Conclusions:** The associations based on relative thresholds were no stronger than those based on absolute thresholds. Furthermore, there was no clinically important interaction with preoperative pressure. Anesthetic management can thus be based on intraoperative pressures without regard to preoperative pressure.

# SO, DO WE ALTER OUR ANESTHETIC MANAGEMENT?

- Appears that the internists who recommend that anesthesia “avoid hypoxia and hypotension” are not so silly after all
- We’ve always treated “hypotension,” but there is great variation in the trigger to treat, how long to wait before treating, and aggressiveness in treating
  - Appears that treating before MAP < 60 mmHg would be reasonable
- Initial approach – treat the cause ( $BP = (SV * HR) * SVR$ ):
  - Increase preload – Trendelenberg, leg lift, IV Fluids – colloid vs. crystalloid
  - **Lighten the anesthetic** – increase cardiac output and/or SVR
    - **Decrease inhaled anesthetic**, & don’t fully paralyze – “patients will move before they remember”
    - Add anesthetics that don’t decrease BP

# VASOACTIVE DRUGS

- Unless patient has a PICC or central line, choices are reduced
  - Peripherally - ephedrine, phenylephrine, vasopressin
  - Centrally - epinephrine, norepinephrine, dopamine
- Ephedrine
  - Increases contractility and SVR
  - Increases heart rate – increase in myocardial oxygen consumption
  - Significant tachyphylaxis
- Phenylephrine
  - Increases SVR, decrease HR
  - Significant decrease in renal perfusion
  - Increase in myocardial oxygen consumption
- Vasopressin
  - Increases SVR, decreased mesenteric blood flow
- Is the treatment worse than the disease?

# OTHER CAUSES OF AKI AND MYOCARDIAL INJURY

- GA for total joints (9,171 pts.) risk factor for AKI
  - Weingraden, et al Can J Anesth, 59:2012
- Total vasopressor dose, vasopressor infusion, and diuretics are risk factors for AKI
  - Kheterpal, et al Anesthesiology, 107:2007
- Tachycardia, hypoxemia, and hypertension associated with myocardial injury
  - Reich, et al Anesth Analgesia, 95:2002
- Review article concludes the use of vasopressors (primarily norepinephrine) in hypotension secondary to vasodilatation is associated in improved outcomes (i.e. sepsis in ICU)
  - Bellomo, et al Crit Care Med, 36(4):2008

# META-ANALYSIS OF PREEMPTIVE HEMODYNAMIC INTERVENTIONS TO IMPROVE POSTOPERATIVE OUTCOMES

HAMILTON, ET AL ANESTH ANALG 112(6): 2011

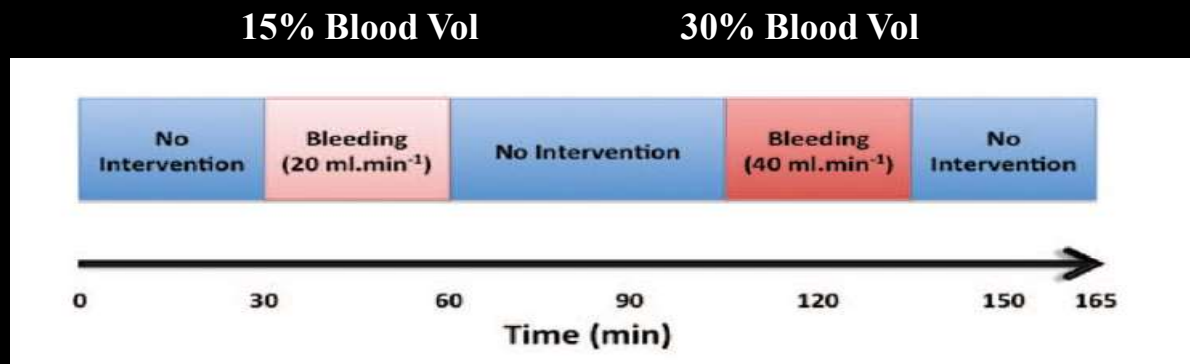
- Meta-Analysis of 29 trials involved 4,805 moderate to high-risk surgical patients
- Overall mortality of 7.6%
- Preemptive hemodynamic interventions significantly reduced mortality – OR 0.48 (0.33-0.78)  $p = 0.0002$  and surgical complications – OR 0.43 (0.34-0.53)  $p < 0.0001$
- Subgroup analysis 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 (0.35-0.55)  $p < 0.01$

## The “*Learning Intravenous Resuscitator (LIR)*”

- Designed for automated optimization of cardiac output (CO) in patients in OR or ICU
- Computer simulation shows LIR maintained a higher and more stable CO as compared to physician management
- Hypothesis of this study - LIR would maintain a higher and more stable stroke volume (SV) and CO than anesthesiologists throughout the 2-phase hemorrhage pig model protocol

# HEMORRHAGE PIG MODEL

- 16 anesthetized and ventilated pigs – randomized to anesthesiologist group or closed-loop control group
  - Fentanyl and isoflurane
  - RR 13/min, TV 10 cc/kg
  - Monitored with arterial line, CCO PAC, & LiDCO (noninvasive CO)
- Each animal underwent:



- Anesthesiologist brought into room after setup and asked to manage as if pig was an 18yr old human for abdominal surgery
  - Fluids, vasoactive drugs, anesthetic at discretion of the physician



# CLOSED-LOOP CONTROL METHODOLOGY

- LIR system was in charge of fluid management
  - Supervised by a technician
- Technician started with colloid until a total of 33 mL/kg
  - Colloid was given first in accordance with GDFT protocols
  - Then alternated between crystalloid and colloid, per liter
- LIR alone determined the rate and timing of fluid delivery through control of the pumps
- i-STAT tests were performed once every 45 minutes to record pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, base excess, and Hb.
  - The technician was not allowed to give any vasopressors or to change the study protocol based on i-STAT tests.
  - Whole blood was hung when Hemoglobin < 7 g/dl

# RESULTS

- CI and SVI higher in CL vs. AP group
  - 3.7 [3.4 - 4.1] vs. 3.5 [3.2 - 3.9], CI -0.5 to -0.2,  $P < 0.0005$
  - 40 [34 - 45] vs. 36 [31 - 38], CI -5.9 to -3.1,  $P < 0.0005$
- HR was significantly lower in CL vs. AP group
  - 92 [89 - 93] vs. 95 [91 - 97], CI 1.4-5.0;  $P = 0.001$
- No difference in total fluid, or volume of blood, colloid, or crystalloid between groups
- Hemoglobin concentration was lower in CL group
  - 6.0 [5.3 - 7.3] vs. 7.3 [6.3 - 8.2], CI 0.0 to 2.4;  $P = 0.04$
- Urine flow greater in CL group
  - 10.0 [5.6 - 14.7] vs. 6.0 [2.0 - 11.1], CI -2.5 to 0.2;  $P = 0.04$

# DISCUSSION POINTS

- Closed-loop fluid management of in vivo fluid resuscitation during mild and severe hemorrhages maintains higher CO and reduced hemodynamic variability as compared to physicians
- Recent studies suggest:
  - Intraoperative hemodynamics affect postoperative outcome
  - CO and SV optimization can decrease postoperative morbidity and length of stay in the hospital in high-risk surgery
  - Blood pressure variability can increase postoperative mortality
- These results suggest that the LIR has potential to help physician anesthesiologists optimize hemodynamics and decrease perioperative morbidity and mortality

# RELEVANCE

- These results should come at no surprise, in other aspects of our lives this kind of technology is routine
  - Antilock brakes, thermostats, autopilot
- In our own practice today, technologies that were once done by anesthesiologists are now automated
  - Ventilators vs. hand-and-bag ventilation
  - Noninvasive blood pressure vs. cuff and stethoscope
  - Infusion pump vs. microdrip and stop-watch
  - Electronic anesthesia machines vs. copper kettle vs. open drop
- Closed-loop control of hemodynamics is just the next logical step.
- **A tool we can use to provide better care to our patients**

# CONCLUSION

- It is clear that even brief periods of hypotension (MAP < 55 mmHg) are associated with increased AKI, myocardial injury, and death
- Low blood pressure should be avoided, and if it occurs it should be promptly treated. Goal should be MAP > 70 mmHg
- Treat first by increasing preload, and decrease depth of anesthesia, avoid full paralysis whenever unnecessary
  - Pharmacy supplied “Nitro (200mcg/ml) & Neo (80mcg/ml) Sticks”
  - Modify anesthetic technique to minimize cardiac depression and vasodilatation
- Use of vasoactive medications associated with improved outcomes in critical care and surgical patients
  - Central access: norepinephrine (#1) and epinephrine(#2)
  - Peripheral access: ephedrine, phenylephrine, vasopressin