PCRC Proposal Cover Sheet

Title of Study or Project:	Association between Intraoperative Hypotension and Patient Outcomes following Non-cardiac Surgery: A Multicenter Retrospective Observational Study
Primary Institution:	University of Michigan
Principal Investigator:	Nirav Shah
Co-Investigators:	Patrick McCormick, MD, Sachin Kheterpal, Leif Saager, Mike Mathis, Shelley Vaughn, Graciela Mentz, Ken Cummings, Kamal Maheshwari, Rob Schonberger, and others
Type of Study:	Retrospective Observational
IRB Number/Status:	HUM00160134
Hypothesis:	Prolonged intraoperative hypotension is associated with AKI (primary outcome) and myocardial injury, in-hospital mortality, and hospital length of stay are associated (secondary outcomes.) For this analysis we will consider a combination of 5 different MAP nadirs (<55, 55- 59, 60-64, 65-69 and ≥ 70) with time events derived using time as a continuous variable.
Number of Patients/Participants:	Approximately 207,000 patients (225,000 cases)
Power Analysis:	With 150,000 patients and the incidence of AKI of 2% or more, we had good statistical power (80% or more) to detect reductions of 10% or more on AKI prevalence.
Proposed statistical test/analysis:	Using exploratory data analysis techniques (EDA) we will assess the distribution of outcomes as well as exposure and covariates. For each selected MAP threshold, inspection of the association curves of AKI prevalence versus the cumulative distribution of time at or below the MAP threshold will allow us to determine relevant time thresholds. Generalized linear mixed models (GLMM) will be considered for the analysis testing the effects of hypotension on selected outcomes.
Resources (Brief summary of resources for data collection, personnel, financial):	Sponsored by Edwards Lifesciences

Introduction

What is the significance of the clinical problem being addressed?

Previous studies have demonstrated associations between low mean arterial pressure (MAP) and organ injury following non-cardiac surgery, with hypotension defined in terms of cumulative minutes or integrated pressures below various absolute thresholds. Recently, Salmasi and colleagues assessed the relationship between myocardial injury after noncardiac surgery (MINS) and acute kidney injury (AKI) and intraoperative absolute (intraoperative MAP) and relative (reduction from preoperative pressure) MAP thresholds using retrospective data from a single institution. Prolonged hypotension was independently associated with increased incidence of AKI and MINS, when adjusted for previously studied risk factors.

This study will analyze the relationships between several commonly used definitions of intraoperative hypotension and post-operative outcomes. Our primary hypothesis is that intraoperative hypotension – defined in a variety of ways - is associated with increased adjusted rates of postoperative AKI.

What current gaps exist in the understanding of this problem?

Prior studies developing prediction models for postoperative AKI following non-cardiac surgery have either: (i) been limited to single-center data, (ii) been limited to highly specified surgical subpopulations, or (iii) lacked robust intraoperative blood pressure data to be included in multivariable analyses.

How will this project address this gap and advance clinical care and/or research knowledge?

This multicenter study will provide robust intraoperative data to support or refute earlier findings, in a more generalizable, multicenter non-cardiac surgical population.

Methods

IRB statement

HUM00160134

Study type

Retrospective observational

Exposure Variable

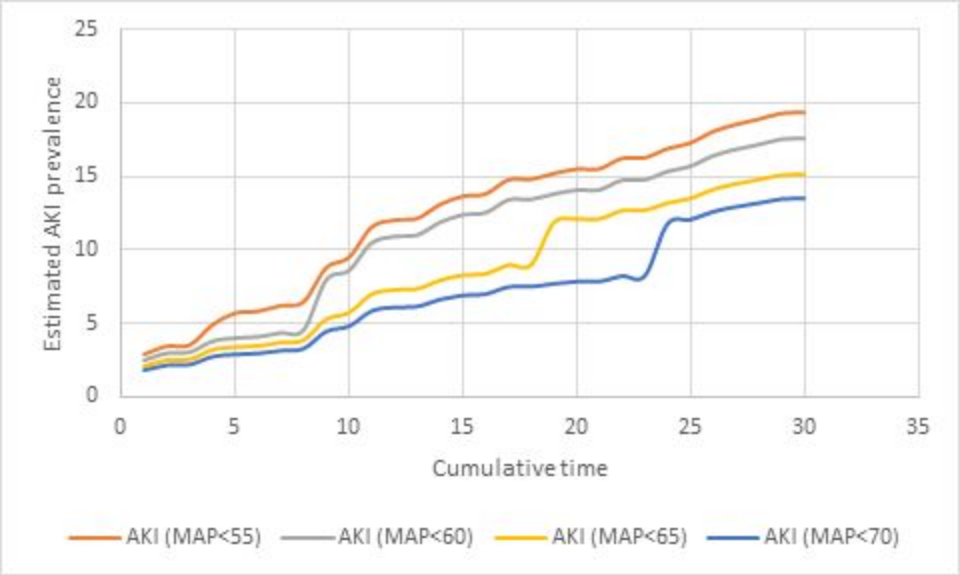
Intraoperative Hypotension, measured via mean arterial blood pressure *(MAP).*

Four different MAP thresholds were selected for this analysis: 55, 60, 65 and 70 mmHg.

Time Events.

For each selected MAP threshold, we will first visually inspect the association curves of AKI prevalence versus the cumulative time at or below the MAP threshold. Using segmented regression modeling techniques for each MAP threshold, we aim to identify an inflection point. The highest inflection point across MAP thresholds will be the upper bound of time thresholds and the lowest inflection point across MAP thresholds will be the lower bound of time thresholds. Additionally, equal intervals of time from the lower bound time threshold to the upper bound time threshold will be considered for this analysis. In total, we expect to choose approximately 3-5 time thresholds.

Example Figure



If analysis becomes intractable, then we will revert to pre-established time events to improve clarity and comprehension of the manuscript.

Intraoperative Hypotension

A combination of the four MAP ranges and the time thresholds will be considered as the intraoperative hypotension measure primary exposure for this analysis. These binary measures take the value of 1 if the cumulative time spent within the MAP range exceeds the time threshold. Note that these measures account for an 'interaction' effect of MAP and duration.

For this study we will define clinically relevant MAP(t) buckets as the lowest range of MAPs for a cumulative of t-minutes were recorded (nadir MAP). Using a cumulative time of 5 minutes of hypotension as an example, each case will be classified into one and only one of the following clusters:, <55, 55-59, 60-64, 65-69, or no hypotension depending on the lowest MAP values recorded for a cumulative time of 5 minutes.

We will make this determination for each time duration. Example distribution for 1000 cases and time duration of 5 and 10 minutes.

Time Duration: 5 minutes of hypotension

MAP nadir < 55	MAP nadir 55 to 59	MAP nadir 60 to 64	MAP nadir 65 to 69	No Hypotension MAP > 70	Total cases
50 cases	100 cases	150 cases	250 cases	450 cases	1000

Time Duration: 10 minutes of hypotension

MAP < 55	MAP < 60	MAP < 65	MAP < 70	No Hypotension	Total cases
25 cases	50 cases	100 cases	200 cases	675 cases	1000

The analysis will be conducted for each time duration separately

Primary outcome

Postoperative acute kidney injury (AKI). AKI will be defined as either A) a serum creatinine within 7 postoperative days that is increased by ≥1.5 times the baseline serum creatinine or B) a serum creatinine within 48 hours after anesthesia end that is increased by ≥0.3 mg/dL. Baseline serum creatinine is the most recent serum creatinine within the 60 days prior to the anesthetic. This definition matches the ASPIRE AKI 01 measure.

Secondary outcome(s), where applicable

- **Myocardial injury in non-cardiac surgery (MINS):** Postoperative troponin I within 72 hours after anesthesia finish with a value over 0.6 ng/dL. (will also assess if other troponin assays are used)
- **In-hospital mortality**
- **Hospital length of stay**

Patient inclusion criteria

- Adult patients (greater than 18 years of age)
- Non-cardiac cases
- Elective same day admission or inpatient
- Surgical time ≥ 3 hours
- Cases with arterial lines, including those placed during anesthesia induction (aline for 75% case)
- Creatinine within 60 days before surgery and 7 days postoperatively

Patient exclusion criteria

- ASA 5 or 6
- Emergency case
- Outpatient case
- Patients with pre-existing renal (stage 4 or 5) failure based upon BSA-indexed EGFR less than 30 mL/min/1.73 m^2
- Patients undergoing procedures affecting kidneys:
    - Urologic surgery on kidney/ureter – CPT 00862, 00864, 00870, 00872, 00873, 00865, 00908, 00910, 00912, 00914, 00916, 00918, 00860, 00942
    - Renal & Liver Transplants – CPT 00868, 00796
- Patient undergoing multiple surgeries within the same admission will have cases after the index case (defined as the first case) excluded to avoid bias
- Cardiac operations will be excluded
    - Anesthesia CPTs 00560, 00561, 00562, 00563, 00566, 00567, 00580
    - All cases with cardiopulmonary bypass will be excluded
        - 50399 Cardiopulmonary bypass - aortic clamp on/off note
        - 50409 Cardiopulmonary bypass terminated
        - 50410 Cardiopulmonary bypass initiated (full)
        - 50416 Cardiopulmonary bypass - crossclamp and circulatory arrest time totals
        - 50417 Cardiopulmonary bypass - Access cannula removed note
        - 50714 Cardiopulmonary bypass - Bypass start / stop event
    - Cases performed by cardiac surgical service (Concept 80005)
- Lung and liver transplant surgery excluded:
    - Anesthesia CPT 00796 (liver), 00580 (lung)
- Estimated blood loss over 1000 mL
- PRBC transfusion total over 4 units (1000 mL)
- Use of inotropic infusions (epinephrine, dobutamine, milrinone, isoproterenol, dopamine)
- Baseline MAP less than 65 (baseline MAP is holding room MAP or first MAP in OR if holding room not available)

- Cases without documented ICD 9/10 codes

Covariate Data

To adjust for confounding variables associated with postoperative AKI, we will include multiple covariates. Preoperative variables include an array of patient, procedural, and institution characteristics). We collect patient medical history data as classified by the Elixhauser Comorbidity Enhanced ICD-9-CM/ICD-10 CM Algorithm. Additional study variables include age, preoperative hemoglobin, preoperative blood pressure, American Society of Anesthesiologists (ASA) physical status classification, vasopressor infusion (yes/no), procedure urgency, and surgical procedure type, characterized by body region on the basis of primary anesthesiology Current Procedural Terminology (CPT) code.

We may conduct a sensitivity analysis for patients with pre-operative anemia.

Data source

MPOG Registry

Statistical analysis

The primary clinical outcome will be AKI, as defined by baseline creatinine increase more than 1.5 times within 7 postoperative days or the baseline creatinine level increase by ≥0.3 mg/dL within 48 hours postoperatively. Secondary outcomes will be MINS, as defined by troponin I elevation greater than 0.6 within 72 hours postoperatively, in hospital mortality, and hospital length of stay (using administrative data.)

Exploratory Data Analysis (EDA) techniques (i.e histograms, QQ-Plots, box-plots, scatterplots, means, medians, IQR) will be used to assess the distribution of dependent measures. These will identify the distribution of outcomes to inform appropriate modeling strategies. In addition, these techniques will explore the most informative transformations for covariates, confounders and relevant predictors considered in the analysis. To address the problem of multicollinearity, we propose to use the variance inflation analysis (VIF) to determine potential co-linear measures. If collinearity is detected, then one of the collinear covariates will be removed from the analysis.

Segmented regression models will be used to estimate piecewise line slopes within predetermined intervals of time . These slopes will be compared and when a significant change in trend is identified, that time interval will be considered the ‘initial time event” interval. Using 5-minute intervals, we will run segmented regressions with in each 5-minute interval. As an example, if a significant change in the slope of these regressions was determined in the interval from 10 - 15 minutes, then we will identify 10 minutes as the baseline time event. In addition, we may also consider other time events for analysis as well.

Generalized linear mixed models (GLMM) will be considered for the analysis testing the effects of hypotension on selected outcomes. These models account for different levels of clustering of the data within centers. We will consider exchangeable correlation matrix with binary link.

Recognizing potential 'overlapping' of patients we propose a specific time event non-overlapping classification approach by assigning each patient into one of 5 categories: <55, 55-59, 60-64, 65-69, non-hypotensive using the nadir MAP. Using >5 minute as example of time frame, the 5 level categorical variable we would construct will take the values of 0 if Non-Hypotensive, 1 if MAP<55, 2 if $55 \leq$ MAP<60, 3 if $60 \leq$ MAP<65 and 4 if $65 \leq$ MAP<70 for 5 minute or more. Then we would include 4 dummy variables representing 4 levels of interest and used the non-hypotensive as reference. Then model considered for testing our research questions can be expressed as:

$$log(\frac{P(AKI=1)}{P(AKI=0)}) = \beta_0 + \beta_1 D1 + ... + \beta_4 D4 + covariates \quad [1]$$

Where $\beta_i \, for \, i = 1, 2, 3 \, and \, 4$ are estimates of the effect of each level of hypotension on AKI within a given time frame. Model [1] will allow us to test the 'relative' importance of each of these categories of hypotension. This model will be use for each identified time frame separately. Thus, if 4 time frames were of interest, then we would run model [1] four separate times.

Statistical models will account for basic demographics such as age, gender, race ethnicity. In addition, we will adjust for ASA status, preop hemoglobin, procedure type, and comorbidities. Goodness of fit statistics will be used to determine the appropriateness of the model. To adjust for multiple testing of our primary outcome against various exposure thresholds, p-values will be corrected using a weighted testing correction method proposed by Changchun Xie in 2013 for correlated binary endpoints.

As there is risk for overestimating the risk of AKI due to exclusion of cases without postoperative creatinine, we will perform a sensitivity analysis where we assume no AKI for patients without postoperative creatinine.

Descriptive Statistics

Table 1. Patients Characteristics. This table will include patient demographics as well as mean time-weighted lowest MAP and outcome distribution. (Overall and per site?)

Table 2a

Descriptive	MAP < 55			MAP < 60			MAP < 65			MAP < 70		
	>Time^1	>Time^2	>Time^3	>Time^1	>Time^2	>Time^3	>Time^1	>Time^2	>Time^3	>Time^1	>Time^2	>Time^3
Number of patients with hypotensive events												
Total number of hypotensive events												
Average number of hypotensive events												
Total duration of hypotensive events per patient												
Average duration of each hypotensive event												
Percentage of monitoring time (between patient in room and patient out of room) that patient was hypotensive												

Table 2b				

Descriptive	MAP < 55	MAP < 60	MAP < 65	MAP < 70
AUC for specified MAP values (average mmHg*min/patient)				
Number of patients with time weighted average MAP less than specified threshold				

Table 2c

Descriptive
Mean MAP under 65 per pt mmHg for all sites

Power analysis

Sample Size Considerations. With 150,000 patients and the incidence of AKI of 2% or more, we will have good statistical power (80% or more) to detect reductions of 10% or more on AKI prevalence.

Handling of Missing or Invalid Data

Preoperative creatinine is not obtained for all patients or resulted in systems that do not link with the MPOG registry. We will determine the number of cases with missing creatinine values and report the proportion of patients that were excluded due to missing creatinine.

Intraoperative Blood Pressure Monitoring, Signal Processing, and Arterial Blood Pressure Artifact Reduction Algorithm

We will include cases with arterial line waveform data for this study; however, as there are cases when arterial lines are placed during anesthesia induction, we will include non-invasive blood pressure monitoring data for these cases; when simultaneous values were recorded, the higher of the two MAP values will be used. When blood pressure monitoring is non-continuous during a case (e.g. non-invasive blood pressure measurements, or arterial line disconnected), blood pressure will be assumed constant and equal to the previous measurement if within five minutes from the most recent measurement; if five minutes or greater from any blood pressure measurement value, blood pressure will be presumed unknown and treated as missing data for analysis purposes. Valid arterial line pressures will trump valid non-invasive pressures.

Example Scenarios:

1. no aline (induction)
2. aline dampens, eventually becomes invalid; in the meantime provider switches to using NIBP, places new aline, then stops using NIBP

To minimize the impact of blood pressure monitoring artifact, we used an artifact reduction algorithm:

Artifact Elimination Strategy	**Rules/Logic**
Provider Marked Artifacts	Marked as artifact in real-time by the provider
Artifact from arterial line clamping, damping, or flushing; or cuff under external pressure	SBP > 200 AND PP < 50
	SBP > 150 and SBP ≤200 AND PP < 30
	SBP ≥ 100 AND SBP ≤ 150 AND PP < 15
	SBP < 100 AND PP < 10
Artifact from arterial line or cuff transducing signal but disconnected from patient	SBP ≤ 10 OR DBP ≤ 10
	SBP = DBP = MAP
	MAP < 0
	MAP ≥ 140
	If any BP is marked as artifact, then all BP measurements for that time will be marked as artifact

SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; MAP = Mean Arterial Pressure; PP = Pulse Pressure (SBP-DBP). If artifact other than provider-marked, is detected for SBP, DBP, or MAP for a specific reading, then all three blood pressure values are marked as an artifact.

The algorithm was created using modified Delphi methodology. Systolic, diastolic, and mean blood pressures as well as pulse pressures are set at specific thresholds and if the data element violates the thresholds, the timestamped value is marked as artifact. Within the MPOG database, each blood pressure value is reported as it was captured in the AIMS system and a separate artifact code is also given to indicate which rule of the algorithm was violated. If either the systolic, diastolic or mean blood pressure for a specific timestamp was marked as artifact, then the other two blood pressure values for that timestamp were also marked as artifact.

Areas for discussion/known limitations

The AKI primary outcome definition does not include postoperative renal replacement therapy or urine output per complete KDIGO guidelines; we relied upon creatinine values alone. For uncomplicated surgical procedures, postoperative creatinine values may not be measured, and the exclusion of such cases can lead to an overestimation of AKI. Conversely, a sensitivity analysis performed assuming that such patients did not develop AKI may underestimate AKI incidence. While measures were taken to

maximize data quality, including careful participating site selection and artifact reduction algorithms, our study analysis and results remained subject to a level of data quality derived from routine clinical care, rather than a controlled experimental setting. Additionally, associations between IOH and AKI within preoperative risk strata are conditional on the accuracy of preoperative risk model developed.

There may be variation in practice of troponin ordering across sites, where sites that routinely order troponin based on patient comorbidity or surgical characteristics (surveillance troponins) have higher MINS rates than sites that order troponin based in patient symptoms or physiologic changes (ST elevations or hypotension). We will distribute a survey to all sites to understand troponin ordering practices.

Data Query Specification (see attached sheet)

References

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Intraoperative Blood Pressure, Risk and Outcomes for Elective Surgery." British Journal of Anaesthesia. Published electronically February 27, 2019. doi: 10.1016/j.bja.2019.01.013

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STROBE Statement

Checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time

		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Inclusion Criteria			
Variable	**Location (Concept ID or Phenotype)**	**Data Type**	**Data Direct Category**
Anesthesia Start	Phenotype	Numeric	Cases
Age	Phenotype	Integer	Demographics
Admission Type	Phenotype	String	Cases
Cardiac	Phenotype	Boolean	Cases
Case Duration	Phenotype	Integer	Cases
Surgery Duration	Phenotype	Integer	Cases
Arterial Line Used	Phenotype	Boolean	n/a
Creatinine	Concept	5002	Laboratory

Exclusions, Covariates, Outcomes, and Exposure Variables				
Concept/Phenotype Display Name	**Concept ID/Phenotype Name**	**Concept Type**	**Data Characteristic**	**Comment**
Age		Phenotype	Integer	
Sex		Phenotype	String	
ASA Class		Phenotype	Integer	
Emergency Status		Phenotype	Boolean	
Weight		Phenotype	Number	
Height		Phenotype	Number	
Admission Type		Phenotype	String	
Date of service (Anesthesia Start)		Phenotype	Integer	
Procedural service	Surgical Service Concept Type	Providers	String	Column AIMS_Primary_Procedural_Service
Primary Anesthesia CPT		Phenotype	Integer	Use as covariate Also use to exclude kidney transplant, urologic procedures involving kidneys
ProcedureTypeTransplantLiver		Phenotype		Exclude Liver transplants
ProcedureTypeTransplantLung		Phenotype		Exclude Lung transplants
Cardiac		Phenotype	Boolean	
Procedure Text		Phenotype	String	
Anesthesia Technique - General		Phenotype	Boolean	
Anesthesia Technique - Block		Phenotype	Boolean	
Anesthesia Technique - Neuraxial		Phenotype	Boolean	
Anesthesia Start		Phenotype	String	
Anesthesia End		Phenotype	String	
Patient in Room		Phenotype	String	
Patient out of Room		Phenotype	String	
Case Duration		Phenotype	Integer	
Arterial Line Used		Phenotype	Boolean	This is a yes/no answer
Preoperative BP (Systolic)	70211	Physiologic	Integer	Phenotype: Baseline Blood Pressure: Systolic
Preoperative BP (Diastolic)	70212	Physiologic	Integer	Phenotype: Baseline Blood Pressure: Diastolic
Baseline Blood Pressure: Mean		Phenotype		Phenotype: Baseline Blood Pressure: Mean
Preoperative BP (combined)	71120	Physiologic	String	
BP Sys Invasive Unspecified Site 1	3011	Physiologic	Integer	
BP Dias Invasive Unspecified Site 1	3012	Physiologic	Integer	
BP Mean Invasive Unspecified Site 1	3013	Physiologic	Integer	
BP Sys Invasive Unspecified Site 2	3041	Physiologic	Integer	
BP Dias Invasive Unspecified Site 2	3042	Physiologic	Integer	
BP Mean Invasive Unspecified Site 2	3043	Physiologic	Integer	
BP Sys Invasive Unspecified Site 3	3046	Physiologic	Integer	
BP Dias Invasive Unspecified Site 3	3047	Physiologic	Integer	
BP Mean Invasive Unspecified Site 3	3048	Physiologic	Integer	
BP Sys Invasive Unspecified Site 4	3026	Physiologic	Integer	
BP Dias Invasive Unspecified Site 4	3027	Physiologic	Integer	
BP Mean Invasive Unspecified Site 4	3028	Physiologic	Integer	
BP Sys Arterial Line (Invasive, Peripheral)	3030	Physiologic	Integer	
BP Dias Arterial Line (Invasive, Peripheral)	3035	Physiologic	Integer	
BP Mean Arterial Line (Invasive, Peripheral)	3040	Physiologic	Integer	
Systolic BP (non-invasive)	3015	Physiologic	Integer	
Diastolic BP (non-invasive)	3020	Physiologic	Integer	

Exclusions, Covariates, Outcomes, and Exposure Variables				
Concept/Phenotype Display Name	**Concept ID/Phenotype Name**	**Concept Type**	**Data Characteristic**	**Comment**
Mean BP (non-invasive)	3025	Physiologic	Integer	
Formal lab - Hemoglobin	5005	Laboratory / Testing	Numeric	
POC - Blood gas - Hemoglobin	5081	Laboratory / Testing	Numeric	
POC - Coulter counter - Hemoglobin	3440	Laboratory / Testing	Numeric	
POC - Coulter counter - Hematocrit	3450	Laboratory / Testing	Numeric	
Formal lab - Hematocrit	5006	Laboratory / Testing	Numeric	
POC - hematocrit spun	3435	Laboratory / Testing	Numeric	
BUN	5012	Laboratory / Testing	Numeric	
Creatinine	5002	Laboratory / Testing	Numeric	
Troponin I	5011	Laboratory / Testing	Numeric	
POC - Blood gas - Lactate (unknown sample type)	3410	Laboratory / Testing	Numeric	
Formal lab - Lactate, Serum/Plasma	5018	Laboratory / Testing	Numeric	
Formal lab - Blood gas - Lactate (unknown sample type)	5040	Laboratory / Testing	Numeric	
Formal lab - Blood gas - Lactate (arterial)	5086	Laboratory / Testing	Numeric	
Epinephrine	10176	Medication Administration	Numeric	Infusions only
Dobutamine	10162	Medication Administration	Numeric	Infusions only
Milrinone	10302	Medication Administration	Numeric	Infusions only
Isoproterenol	10235	Medication Administration	Numeric	Infusions only
Dopamine	10165	Medication Administration	Numeric	Infusions only
Norepinephrine	10326	Medication Administration	Numeric	Infusions only
Vasopressin	10445	Medication Administration	Numeric	Infusions only
Phenylephrine	10354	Medication Administration	Numeric	Infusions only
Vasopressor Infusion		Phenotype	Boolean	Phenotype not started, spec ready; note that this phenotype treats epinephrine and dopamine as vasopressors
Mortality (In hospital)		Phenotype	Integer	Days from Date of Surgery to Date of Death
Total PRBC		Phenotype	Integer	
Total EBL		Phenotype	Integer	
Discharge Diagnosis Code		Diagnoses	Boolean	Phenotype: DishargeDiagnosisCount
Comorbidity - Aids \ HIV		Comorbidity	Boolean	
Comorbidity - Alcohol Abuse		Comorbidity	Boolean	
Comorbidity - Blood Loss Anemia		Comorbidity	Boolean	
Comorbidity - Cardiac Arrhythmias		Comorbidity	Boolean	
Comorbidity - Chronic Pulmonary Disease		Comorbidity	Boolean	
Comorbidity - Coagulopathy		Comorbidity	Boolean	
Comorbidity - Congestive Heart Failure		Comorbidity	Boolean	
Comorbidity - Deficiency Anemia		Comorbidity	Boolean	
Comorbidity - Depression		Comorbidity	Boolean	
Comorbidity - Diabetes (complicated)		Comorbidity	Boolean	
Comorbidity - Diabetes (uncomplicated)		Comorbidity	Boolean	
Comorbidity - Drug Abuse		Comorbidity	Boolean	
Comorbidity - Fluid/Electrolyte Disorders		Comorbidity	Boolean	
Comorbidity - Hypertension (complicated)		Comorbidity	Boolean	
Comorbidity - Hypertension (uncomplicated)		Comorbidity	Boolean	
Comorbidity - Hypothyroidism		Comorbidity	Boolean	
Comorbidity - Liver Disease		Comorbidity	Boolean	

Exclusions, Covariates, Outcomes, and Exposure Variables				
Concept/Phenotype Display Name	**Concept ID/Phenotype Name**	**Concept Type**	**Data Characteristic**	**Comment**
Comorbidity - Lymphoma		Comorbidity	Boolean	
Comorbidity - Metastatic Cancer		Comorbidity	Boolean	
Comorbidity - Obesity		Comorbidity	Boolean	
Comorbidity - Other Neurological Disorders		Comorbidity	Boolean	
Comorbidity - Paralysis		Comorbidity	Boolean	
Comorbidity - Peptic Ulcer Disease, Excluding Bleeding		Comorbidity	Boolean	
Comorbidity - Peripheral Vascular Disorders		Comorbidity	Boolean	
Comorbidity - Psychoses		Comorbidity	Boolean	
Complication - Acute Kidney Injury (AKI)		Phenotype	Numeric	
ComplicationMyocardiacInfarctionAdministrative		Phenotype		
CARD 02		Phenotype		QI measure
HospitalLOSDays		Phenotype	Number	This should be a phenotype