PCRC Proposal Cover Sheet

Title of Study or Project:	Is Anesthesia Caregiver Specialization Associated With Improved Postoperative Adverse Outcomes?
Primary Institution:	University of Michigan
Principal Investigator:	Leif Saager
Co-Investigators:	M. Burns, M. Housey, and Colleagues
Type of Study:	Retrospective Observational Outcomes Study
Hypothesis:	We propose to test the hypothesis that operative teams with specialized anesthesia caregivers are associated with better patient outcomes following surgery when compared to teams of non-specialized anesthesia caregivers.
Number of Patients/Participants:	All eligible cases recorded in the MPOG database
Power Analysis:	We would need up to 50,346 patients to detect an odds ratio from 0.8 to 0.9 for the expert group as compared to the control group with 90% power, assuming an incidence rate of 8.6% in the control group at the significance level of 0.05
Proposed statistical test/analysis:	Matched expert team cases and control team cases will be compared using a logistic regression. We will assess an average relative effect of receiving anesthesia care from an expert team across the components of the collapsed composite outcome using a multivariate (i.e., multiple outcomes) generalized estimating equation (GEE) model with unstructured covariance matrix.
Resources (Brief summary of resources for data collection, personnel, financial):	Data query and statistical analysis to be performed by University of Michigan / MPOG personnel.

DO IT OFTEN, DO IT BETTER. DOES ANESTHESIA CAREGIVER SPECIALIZATION AFFECT POSTOPERATIVE OUTCOMES?

BACKGROUND

The anesthesia team, consisting of a medically directed provider and a faculty anesthesiologist in a supervisory/teaching role, is part of the operating room team, also including nurses, surgeons, techs and others. This operating room team frequently faces critical situation with rapidly declining health of the patient. Patients with multiple co-morbidities, patients brought to the operating room from the intensive care unit or sudden deterioration in otherwise healthy patients can challenge the team and require immediate and appropriate responses to avoid lasting patient harm.

Due to ever increasing medical knowledge and complexity of procedures that can be performed, physicians specialize in specific areas of expertise. “Trauma Surgeons” or “Neuro-anesthesiologists” are only two examples. This sub-specialization presumably leads to deeper expertise and proficiency. While surgeons specialized in colon-rectal surgery nearly exclusively perform such surgeries, anesthesiologists, even when subspecialized, will cover a broad range of cases in various operating rooms. Frequently cases where sub-specialization is available are covered by non-specialized anesthesiologists due to scheduling conflicts.

It seems intuitive that anesthesia provider familiar with specific operating rooms, surgeons and procedures can utilize their expertise to improve patient outcomes as compared to anesthesia providers who only infrequently face this specific combination of patients, surgeons and procedure.

While in other high-performance scenarios teamwork and specialization is well studied, there is a paucity of data on intraoperative team factors and patient outcome.

A recent study of 849 patients by Hofer et al. found that patients undergoing liver transplantation and being cared for by an anesthesiologists with an incremental case number of ≤ 5 liver transplants experienced a significantly increased 30-day mortality.[1] This data clearly supports sub-specialization of anesthesiologists into often called “liver teams”. Similar, Walsh et al. investigated a retrospective cohort of 1155 patients undergoing major vascular surgery. They

found that care from a "vascular anesthetist" was associated with a reduced 30-day mortality, as well as medium-term mortality.[2]

Silber et al. found that mortality in patients undergoing general or orthopedic surgery was higher in patients cared for by non-board-certified anesthesiologists.[3]

We propose to test the hypothesis that operative teams with specialized anesthesia caregivers are associated with better patient outcomes following surgery when compared to teams of non-specialized anesthesia caregivers.

METHODS

Members of the Multicenter Perioperative Outcomes Group utilize fully digitalized Anesthesia Information Management Systems, which register manually entered as well as monitor generated data (vital signs, ventilator settings etc.) in real time. This data is stored locally at each institution, validated and processed. After removal of patient identifiers, the anesthetic record as well as comprehensive perioperative and administrative data is uploaded to a central MPOG repository at the University of Michigan. Currently, the MPOG registry has about 9 million patient records and grows at a rate of 100,000 cases per month. The MPOG registry, data entry process and validation of data has been described in detail previously.[4,5]

For this retrospective observational analysis, we will extract patient, provider and procedure characteristics, intraoperative fluids and medications administered, as well as administrative data to determine outcomes. For our secondary analysis we will stratify patients by surgical service. The study will be conducted in adherence to the STROBE statement for observational research. [6]

PATIENT POPULATION

The study population will consist of all adult patients (age ≥18 years) who underwent non-cardiac surgery documented in the MPOG database between January 1, 2012 and February 28, 2018.

EXCLUSION CRITERIA

Emergency cases will be excluded. Cases started during call times (Monday to Friday 17:00 to 7:00, or anytime Saturday to Sunday) will be excluded as they are assigned based on call schedule and not on routine basis. Short cases (< 30 minutes) will be excluded. Cases that did not have faculty anesthesiologist and CRNA provide care will be excluded.

To be included in the study and be assigned to a group, the respective team is required to have provided care for at least the entire first 50% of the case duration, or the first two consecutive hours, as during this period fundamental decisions on patient management are made, and later

decisions are unlikely to completely change the anesthetic plan, but rather adopt to dynamic clinical situations. In other words, cases with transitions of anesthesia care (defined by sign in/out of providers) during either the first half of case, or the first two hours of the case (whichever occurs first) will be excluded (*breaks* of <40 minutes will be included, *handovers* of >40 minutes will be excluded). We will extract pre-, intra- and post-operative data to describe our patient population including: demographics, comorbidities and significant preoperative testing as well as weight, height, ASA status, start and duration of anesthesia and surgical procedure (CPT code and ICD-9 code), estimated blood loss, transfusion of blood products, amount of fluids, use of any type of vasoactive or anesthetic drug (duration of infusion and dose). Also, we will extract MPOG institution identifier, and providers information including role of provider (attending / CRNA / resident) and sign in / out times of provider.

BUILDING TEAMS

Cases will be grouped into surgical specialties by surgical, or if not available, by anesthesia CPT code (orthopedic, colorectal, gynecology, urology, neurological, and vascular surgery). Per institution we will identify the top faculty anesthesiologists who provided care for most of the cases per each surgical specialty based on the frequency distribution (Top quartile). These will be considered the "expert" faculty. Similarly, we will identify "expert" certified registered nurse anesthetists (CRNA). We will then identify all cases that received care from a "expert" faculty as well as a "expert" CRNA. This will be considered the "expert team" group.

Additionally, we will identify the faculty anesthesiologists who provided care in the least number of cases in a specific surgical service (Bottom quartile). They will be considered the "control" faculty anesthesiologists who cover a broad range of procedures with few dedicated assignments to one specialty. Similarly, we will identify a "control" CRNA group of certified registered nurse anesthetists. We will then identify all cases that received care from a "control" faculty as well as a "control" CRNA. This will be considered the "control team" group.

To investigate a potential "dose-response" relationship, we will create a third group consisting of cases that received care from either a "expert" faculty and a "control" CRNA or a "control" faculty and a "expert" CRNA. This will be considered the "mixed team" group.

As residents are frequently assigned according to a rotation schedule to allow for maximum exposure over the full scope of anesthesiology during their training, they will not have had the opportunity to develop a special interest and we will therefore exclude them from the analysis.

PRIMARY OUTCOME

We will assess the association of receiving anesthesia care from an "expert team" vs. a "control team" with a collapsed composite (any versus none) of 6 major morbidities including serious

cardiac, respiratory, gastrointestinal, urinary, bleeding, and infectious complications, based on the U.S. Agency for Healthcare Research and Quality's (AHRQ) single-level Clinical Classifications Software (CCS) categories for International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes.

Morbidity	AHRQ CCS category*	ICD-9 code	ICD-9 code description
Cardiac	16.10.2.1	429.4	Functional disturbances following cardiac surgery
		458.21	Hypotension of hemodialysis
		458.29	Other iatrogenic hypotension
		997.1	Cardiac: arrest during or resulting from a procedure insufficiency during or resulting from a procedure
Respiratory	16.10.2.2	518.7	Transfusion related acute lung injury (TRALI)
		997.3	Respiratory complications
		997.31	Ventilator associated pneumonia
		997.32	Postprocedural aspiration pneumonia
		997.39	Other respiratory complications
		518.7	Transfusion related acute lung injury (TRALI)
Gastrointestinal	16.10.2.3	539.01	Infection due to gastric band procedure
		539.09	Other complications of gastric band procedure
		539.81	Infection due to other bariatric procedure
		539.89	Other complications of other bariatric procedure
		564.2	Postgastric surgery syndromes
		564.3	Vomiting following gastrointestinal surgery
		564.4	Other postoperative functional disorders
		569.6	Colostomy and enterostomy complications
		569.71	Pouchitis
		569.79	Other complications of intestinal pouch

		579.3	Other and unspecified postsurgical nonabsorption
		997.4	Digestive system complications
		997.41	Retained cholelithiasis following cholecystectomy
		997.49	Other digestive system complications
Urinary	16.10.2.4	596.81	Infection of cystostomy
		997.5	Urinary complications
Bleeding	16.10.2.5	998.1	Hemorrhage or hematoma or seroma complicating a procedure
		998.11	Hemorrhage complicating a procedure
		998.12	Hematoma complicating a procedure
		998.13	Seroma complicating a procedure
Infectious Complications	16.10.2.6	519.01	Infection of tracheostomy
		536.41	Infection of gastrostomy
		530.86	Infection of esophagostomy
		997.62	Infection (chronic)
		998.5	Postoperative infection
		998.51	Infected postoperative seroma
		998.59	Other postoperative infection
		999.3	Other infection
AHRQ = U.S. Agency for Healthcare Research and Quality			
ICD = International Classification of Diseases			
*** Multi-level Clinical Classifications Software for International Classification of Diseases, 9th Revision, Clinical Modification diagnosis codes.**			

Secondary Outcomes

We will use the following intraoperative variables to characterize anesthetic management between the groups:

- Type and amount of blood transfusion (PRBC, FFP, Platelets)

- Type and amount of fluids (crystalloid, colloid, albumin)
- Type and amount of muscle relaxant (Depolarizing, Non-depolarizing)
- Type and amount of vasopressor (Phenylephrine, Ephedrine, Norepinephrine, Epinephrine, Vasopressin)
- Type and amount of anesthetic drug (Propofol, volatile, nitrous oxide)
- Total amount of opioids (morphine equivalent)
- Time from emergence to extubation (in min.)

STATISTICAL ANALYSIS

CONTROL FOR OBSERVED CONFOUNDING VARIABLES

To control for observed confounding variables, each case receiving anesthesia care from an expert team will be matched to a case receiving anesthesia care from a control team using exact and propensity score matching.[7] First, we will estimate the probability of receiving anesthesia care from an expert team (i.e., the propensity score) for each case using logistic regression with expert team as the outcome and the following potential confounding variables - demographics, comorbidities, preoperative tests, body mass index, ASA status, type of anesthesia, duration of procedure, start time of surgery, total number of anesthesia handovers per case. We will then 1 to 1 match expert team and control team cases using a greedy distance matching algorithm (SAS macro: gmatch), restricting successful matches to those within the same institution and for the same surgical procedure (orthopedic, colorectal, gynecology, urology, neurological, and vascular surgery) and using a caliper width within 0.2 of the pooled standard deviation of the logit of the propensity score.[8] All the analyses will use this subset of matched patients.

Assessment of balance on the covariates used for the propensity score matching will be performed using standardized differences (i.e., difference in means or proportions divided by the pooled standard deviation). Imbalance is defined as an absolute standardized difference (STD) greater than $1.96 \times \sqrt{\frac{2}{n}}$ (n: number of cases per group) in absolute value;[9] any such covariates will be entered into the models comparing expert team cases and control team cases on outcomes to reduce potential confounding.

PRIMARY ANALYSIS

Matched expert team cases and control team cases will be compared on the composite of mortality and 6 major morbidities using a logistic regression that adjusts for imbalanced covariates after the matching.

Furthermore, we will assess an average relative effect of receiving anesthesia care from an expert team across the components of the collapsed composite outcome using a multivariate (i.e., multiple outcomes) generalized estimating equation (GEE) model with unstructured covariance matrix. The association between expert team and each individual component will be reported regardless of the existence of the interaction. The significance criterion will be 0.007 for each of the 7 components of the composite (i.e., 0.05/7).

SECONDARY ANALYSIS

If a significant difference in the composite outcome is found between expert and control teams, we will further investigate a potential "dose-response" relationship. We will do 1 to 1 to 1 match between the expert team, the mixed team, and the control team. The same statistical methods will be used as in the above analysis with a caliper width of 0.2. Additionally, to assess balance of covariates among the three treatment groups, pairwise comparisons will be calculated for the standardized differences. A standardized difference less than 0.1 indicates sufficient balance among the three groups.[8]

Descriptive statistics will summarize the following intraoperative characteristics - type and amount of blood transfusion, type and amount of fluids, type and amount of muscle relaxant, amount of opioids, type and amount of vasopressor, type and amount of anesthetic drug and time from emergence to extubation. Standardized differences between expert and control teams will be evaluated. SAS software version 9.4 (SAS Institute, Cary, NC, USA) will be used for all statistical analysis.

SAMPLE SIZE CONSIDERATION

The sample size consideration is based on our primary outcome of the collapsed composite of in-hospital mortality and 6 major morbidities. In a retrospective analysis previously performed at the Cleveland Clinic based on 25,546 adults who had non-cardiac surgery between 2005 and 2009, we observed an incidence rate of 8.6% for the collapsed composite of in-hospital mortality and major morbidities.[10]

We would need from 11,810 to 50,346 patients to detect an odds ratio from 0.8 to 0.9 for the expert team as compared to the control team with 90% power, assuming an incidence rate of 8.6% in the control team at the significance level of 0.05. We will utilize all available patients accrued in the MPOG database and would have adequate power.

HUMAN SUBJECTS' RISKS AND DATA PROTECTION

Data analysis will be restricted to aggregated group data. Data will be de-identified regarding individual hospitals and providers. While hospital and hospital characteristics might be part of

the analysis to account for practice variation, no individual hospitals will be identifiable in the results or publication. Each group will contain a sufficient number of hospitals, providers and cases to ensure de-identification or no group analysis will be performed. Again, data analysis and results will not allow identification of individual contributing sites.

Data will be maintained on a password protected secure MPOG server hosted. The study data will be accessible only to the statistical team directly involved with analyzing the data. The system fully meets all applicable HIPAA privacy and security rules. Access to the database and backups are strictly monitored according to need.

The final dataset will contain no patient or caregiver identifier. No protected health information or identifying information about individual patients, caregivers or hospitals will be part of a publication.

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