PCRC Proposal Cover Sheet

Title of Study or Project:	**Automated Identification and Validation of Detecting Physiologically Implausible Pulsatile Blood Pressure Artifacts**
Principal Investigator:	Amy Shanks, PhD
Co-Investigators:	Amy Shanks PhD, Michael Burns MD PhD, Douglas Colquhoun MB ChB MSc MPH, Nicholas Douville MD PhD, Allison Janda MD, Aleda Thompson MS, John Vandervest MS, Michael Mathis MD, Leif Saager MD, and Sachin Kheterpal MD, MBA
Approved by Mentor:	Sachin Kheterpal MD, MBA
Type of Study:	Retrospective Observational
IRB Number and Status:	IRB HUM 24166
Hypothesis:	We hypothesize that a blood pressure artifact reduction algorithm using the Delphi method has good discrimination when compared to the gold standard of clinician review.
Number of Patients/Participants:	162 cases to review
Power Analysis:	To adequately determine the percentage of artifacts that should be reviewed we used data reported by Kool et al. Assuming that 4.6% of the NIBP would be artifacts, we would need a minimum 1,788 NIBP measurements with a two-sided 95% CI and the width of the CI should be 1% on either side maximum. Conservative total anesthesia time monitoring to have adequate power would be 8,940 minutes or 50 cases (1,788 measurements X 5 minute NIBP intervals). Assuming that 14% of the IBP would be artifacts as reported by Kool, we would need a minimum 4,724 IBP measurements with a two-sided 95% CI and the width of the CI should be 1% on either side maximum. IBP is documented every minute within the MPOG centralized database, however we do not anticipate the case having 100% IBP monitoring and will include cases with ≥ 80% IBP monitoring. Conservatively, we would need 5,669 minutes of anesthesia time monitoring or 31 cases.
Proposed statistical test/analysis:	Sensitivity and specificity will be reported for the overall artifact detection in each cohort comparing the BPAA and the gold standard reviewers as well as for each type of artifact. Gold standard reviewer's agreement will be assessed using Krippendorff's alpha.
Resources (Brief summary of resources for data collection, personnel, financial):	Amy will pull the data and do all analysis. The expert reviewers will hand review each record.

Automated Identification and Validation of Detecting Physiologically Implausible Pulsatile Blood Pressure Artifacts

Investigators: Amy Shanks PhD, Michael Burns MD PhD, Douglas Colquhoun MB ChB MSc MPH, Nicholas Douville MD PhD, Allison Janda MD, Aleda Thompson MS, John Vandervest MS, Michael Mathis MD, Leif Saager MD, and Sachin Kheterpal MD, MBA

Introduction

Anesthesia Information Systems (AIMS) have been exponentially adopted into clinical practice since their inception in the 1990's; by 2014, 75% of all academic anesthesia residency programs utilized one [1]. This increased use has allowed for an explosion of observational research studies investigating outcomes that are either rare or unethical to perform using a randomized control trial. AIMS data compiles manually-entered data, automatic machine-captured data, and other hospital-based systems into one usable interface. Aggregating these data types introduces the possibility for erroneous data elements or artifacts.

Hemodynamic stability is important during all operative cases. With the expansion of AIMS, several recent studies addressed whether hand-entered or automatic machine-captured blood pressure values are more accurate [2-5]. Observer bias has shown repeatedly that anesthesia providers do not adequately document extreme blood pressure values when compared to automated machine-capture [6-8]. These biases can feasibly lead to misleading research findings. Not surprisingly, compared to hand-entered values, machine-captured data had three times more blood pressure artifacts documented [9, 10]. Even with artifacts present, machine-captured data adequately documents the severity and variability of blood pressures and removes observer bias. However, it is imperative that algorithms must be developed to automatically detect and mark artifacts appropriately.

To date, there has been one peer-reviewed article documenting the incidence of intraoperative blood pressure artifacts using AIMS data. Kool et al. sought to identify the reliability of blood pressure

values and quantify the number of artifacts [11]. They determined the overall percentage of non-invasive (NIBP) blood pressure artifacts were 3.3% (95% confidence interval (CI) 2.5-87.2) and for invasive arterial line (IBP) blood pressure artifacts were 27% (95% CI 24-31) [11]. A sensitivity analysis on values between surgical incision and closure demonstrated NIBP artifacts during 4.4% (95% 3.1-6.1) of the case and IBP artifacts during 13.9% (95% CI 10.7-18.1) [11]. Intraoperative blood pressure management has been studied in recent years using retrospective AIMS methodologies to address a variety of outcomes and recommend targeted blood pressure ranges in major anesthesiology peer-reviewed journals [12-26]. These research studies have either not removed artifacts or have not validated an artifact algorithm prior to interpretation, even though Kool et al. has established that intraoperative blood pressure artifacts occur and occur often for IBP monitoring [11-26]. Interestingly, these studies also include recommendations for appropriate blood pressure management techniques.

With the growing expansion of AIMS and the concurrent increase in anesthesia-related observational outcomes studies, it is imperative that proper artifact reduction algorithms be developed, validated, and used prior to analysis and interpretation of research findings. The proper blood pressure artifact reduction algorithm should allow for detection of physiological implausible values, inaccurate invasive arterial line measurements, and known artifacts as documented by the clinical provider within the AIMS. We hypothesize that a blood pressure artifact reduction algorithm derived using the Delphi method has good discrimination when compared to the gold standard of clinician review. Such an algorithm could be used by all researchers when performing analyses of intraoperative blood pressure data.

Methods

Development of Blood Pressure Artifact Algorithm

A team of experienced anesthesiologists (SK, MM, MB, DC, LS) developed the blood pressure artifact algorithm (BPAA) using Delphi Methodology through an iterative process. First, a consensus was taken to identify physiologically implausible ranges for systolic (SBP) and diastolic (DBP) blood pressure (Table 1, Artifacts #2-6). The BPAA was then retrospectively applied to a random subset of 500 cases and manually reviewed (AS, AT) for accuracy in detecting non-physiologically plausible values for both NIBP and IBP. Through the first iteration, it was determined that mean arterial pressure (MAP) should be included in the algorithm, and after the case review was finished three new rules were applied to the BPAA (Table 1, Artifacts #7-9). Multiple iterations were then retrospectively queried and manually reviewed (AS, AT, MB, MM) to determine the accuracy of the algorithm in identifying artifacts. Through the iterative process, the pulse pressure (SBP minus DBP) and MAP thresholds were changed to their current values (Table 1). In addition, if any artifact #1-9 for a specific time-stamped blood pressure value was marked for SPB, DPB, or MAP, all of the corresponding blood pressure values were also designated as artifacts. Our BPAA was developed for adult patients with pulsatile blood flow and is not accurate for patients with left ventricular assist devices or during cardio-pulmonary bypass.

Table 1 – Blood Pressure Artifact Reduction Logic

Artifact Code	Rules/Logic
1	Marked as artifact in real-time by the provider
2	SBP > 150 and PP < 30
3	SBP ≥ 100 AND SBP ≤ 150 AND PP < 15
4	SBP < 100 AND PP < 10
5	SBP > 200 AND PP < 50
6	SBP ≤ 10 OR DBP ≤ 10
7	SBP = DBP = MAP
8	MAP < 0
9	MAP ≥ 140
10	If any BP is marked as artifact #1, 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) Note: If artifact code #2-9 is marked for systolic, diastolic, or mean arterial pressure for a specific reading, then all three blood pressure values are marked as an artifact.

Data Acquisition

Retrospective data will be queried using the Multicenter Perioperative Outcomes Group (MPOG) centralized database housed at the University of Michigan. Since no care interventions are being investigated, a waiver of informed patient consent was granted by the institutional review board (HUM 24166). The MPOG database includes individual anesthetic records from over 50 US and European hospitals. The database includes patient demographics, preoperative history and physical information, intraoperative physiologic monitoring data, medications administered, procedure notes, laboratory values, and discharge/billing codes. To validate our BPAA we will only use cases that have all machine captured blood pressure values. For those cases, every NIBP is electronically captured and IBP values are captured in the database at q1-minute intervals.

To address our study hypothesis, we will query the MPOG database for a random selection of cases across all the participating institutions to retrospectively apply the BPAA from January 1 to March 31, 2017. For each case, basic patient demographics, type of surgery, length of anesthetic time (anesthesia induction start to surgery end), intraoperative medications used, and time-stamped individual blood pressure (SBP, DBP, MAP) measurements will be extracted.

Study Population and Analysis Groups

Data across all participating institutions for adult ASA I-IV patients undergoing non-cardiac surgery with a general anesthetic, and who have a minimum of three hours of anesthesia monitoring (anesthesia induction start to surgery end) will be randomly sampled. Cases without valid intraoperative time-stamps for operative events (anesthesia start, patient in room, induction start, surgery start, surgery end and anesthesia end) and IBP monitoring cases where IBP is used <80% of the case will be excluded. Data

acquisition will start from first valid blood pressure past the patient in room timestamp. Intraoperative blood pressure responds very rapidly to blood pressure support medications; therefore, the study population will be divided into four different cohorts as described below to allow investigation into the accuracy of the BPAA for cases with and without medications used for blood pressure support. Each study cohort will have a minimum of 5 different participating institutions represented.

1. Operative cases with only NIBP used and *no* documented use of the following medications: Phenylephrine, Norepinephrine, Vasopressin, Epinephrine, Ephedrine, Nitroglycerin
2. Operative cases with only NIBP used and *with* documented use of the following medications: Phenylephrine, Norepinephrine, Vasopressin, Epinephrine, Ephedrine, Nitroglycerin
3. Operative cases with IBP used the majority of the case (>80%) and *no* documented use of the following medications: Phenylephrine, Norepinephrine, Vasopressin, Epinephrine, Ephedrine, Nitroglycerin
4. Operative cases with IBP used the majority of the case (>80%) and *with* documented use of the following medications: Phenylephrine, Norepinephrine, Vasopressin, Epinephrine, Ephedrine, Nitroglycerin

Gold Standard Review

Using the case viewer developed by MPOG, each case included in the analysis will be hand-reviewed by expert clinicians (MB, DC, ND, AJ) to determine if a blood pressure value is an artifact. The MPOG case viewer is a de-identified visual schematic of the patient's anesthetic record. All data from the AIMS record is displayed for review including physiologic monitoring data, medication administration with times and doses, as well as time-stamps for operative events. The expert reviewers will be blinded to the artifacts that were triggered using the BPAA, though they will be able to see clinician-designated artifacts (Table 1, Artifact #1).

Data Aggregation and Analysis

Within each study cohort, for each case, the percentage of artifacts captured (BPAA and gold standard review) will be calculated, as well as the individual frequency of each artifact type (Table 1). The data will be reported as an average frequency and percentage across all cases. In addition, data will also be analyzed independently for each study cohort for each type of artifact detected. Sensitivity and specificity will be reported for the overall artifact detection in each cohort comparing the BPAA and the gold standard reviewers as well as for each type of artifact (Table 1). Gold standard reviewer's disagreement will be assessed using Krippendorff's alpha. Krippendorff's alpha measures the degree of *disagreement* between raters instead of agreement that is used with Cohen's kappa statistic and can be used regardless of missing data, number of reviewers, and sample sizes [27]. Artifacts already documented by the clinician at the point of care will be excluded from the analysis (Table 1, Artifact #1).

Power Analysis

To adequately determine the percentage of artifacts that should be reviewed we used data reported by Kool et al [11]. Assuming that 4.6% of the NIBP would be artifacts, we would need a minimum 1,788 NIBP measurements with a two-sided 95% CI and the width of the CI should be 1% on either side maximum. Conservative total anesthesia time monitoring to have adequate power would be 8,940 minutes or 50 cases (1,788 measurements X 5 minute NIBP intervals). Assuming that 14% of the IBP would be artifacts as reported by Kool, we would need a minimum 4,724 IBP measurements with a two-sided 95% CI and the width of the CI should be 1% on either side maximum. IBP is documented every minute within the MPOG centralized database, however we do not anticipate the case having 100% IBP monitoring and will include cases with ≥ 80% IBP monitoring. Conservatively, we would need 5,669 minutes of anesthesia time monitoring or 31 cases. Power was calculated using PASS 15 (PASS 15 Power Analysis and Sample Size Software (2017). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass).

Sensitivity Analysis

Previous research has demonstrated that the greatest amount of artifacts is seen during induction of anesthesia [11, 28]. Therefore, a sensitivity analysis will be performed for the same four cohorts explained above but excluding the induction period of anesthesia (anesthesia induction start to surgery start).

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