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Arterial Pressure Variation in Elective Non-cardiac Surgery: Identifying Reference Distributions and Modifying Factors

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Abstract

Background—Assessment of need for intravascular volume resuscitation remains challenging for anesthesiologists. Dynamic waveform indices, including systolic- and pulse-pressure variation (SPV/PPV), are demonstrated as reliable measures of fluid-responsiveness for mechanically ventilated patients. Despite widespread use, real-world reference distributions for SPV and PPV values have not been established for euvoletic intraoperative patients. The authors sought to establish SPV and PPV reference distributions and assess impact of modifying factors.

Methods—The authors evaluated adult patients undergoing general anesthetics for elective non-cardiac surgery. Median SPV and PPV over a 50-minute post-induction period were noted for each case. Modifying factors including body-mass index, age, ventilator settings, positioning, and hemodynamic management were studied via univariate and multivariable analyses. For SPV values, effects of data entry method (manually-entered versus automated recorded) were similarly studied.

Results—Among 1,791 cases, per-case median SPV and PPV values formed non-parametric distributions. For each distribution, median values, interquartile ranges, and reference intervals (2.5th-97.5th percentile) were respectively noted: these included manually-entered SPV (6.0, 5.0-7.0, 3.0-11.0 mmHg), automated SPV (4.7, 3.9-6.0, 2.2-10.4 mmHg), and automated PPV (7.0, 5.0-9.0, 2.0-16.0%). Non-supine positioning and preoperative beta blocker were independently associated with altered SPV and PPV, whereas ventilator tidal volume >8 mL/kg ideal body weight and peak inspiratory pressure >16 cm H₂O demonstrated independent associations for SPV only.

Conclusions—This study establishes real-world SPV and PPV reference distributions absent in the current literature. Through a consideration of reference distributions and modifying factors, our study provides further evidence for assessing intraoperative volume status and fluid management therapies.

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Conflicts of Interest: None

Introduction

Assessment of a patient's intravascular volume status is a vital component guiding an anesthesiologist's perioperative fluid management. Over the past decade, studies have demonstrated an association between fluid administration strategy and postoperative outcome.^{1,2} However, accurate assessment of intravascular volume remains challenging.

Many clinical signs of hypovolemia (e.g. skin turgor, capillary refill, nausea, and syncope) are unreliable and become masked during general anesthesia, historically leaving anesthesiologists with blood pressure, heart rate, and urine output as indicators of volume status.^{3,4} Static measures – including central venous pressure, pulmonary artery occlusion pressure, and “non-invasive” cardiac output – have been shown inadequate to guide volume resuscitation therapy.⁵⁻⁷ While echocardiography including inferior vena cava imaging may be useful,⁸ associated equipment and training costs pose barriers to widespread use. Recently, dynamic indices – derived from respirophasic variation of arterial pressure waveforms – have been developed, and are suggested for use in mechanically ventilated patients. These include systolic pressure variation (SPV)^{9,10}, pulse pressure variation (PPV)¹¹, and stroke volume variation (SVV)¹².

Systolic- and pulse-pressure variation have been studied in the perioperative setting to assess fluid-responsiveness, or the benefit of a fluid challenge. Compared to SVV, SPV and PPV have demonstrated similar or superior ability to predict fluid responsiveness without the need for specialized SVV measurement equipment,^{13,14} and eclipse other static measures.^{5,15} Limitations of SPV and PPV include requiring a regular heart rhythm^{16,17} and standardized ventilator settings,^{17,18} as well as sensitivity to confounding factors including positioning,¹⁹ intrathoracic pressure,¹⁶ intraabdominal pressure,^{16,20} and heart failure.²¹ Despite limitations, SPV and PPV have endured as commonly used measures of fluid-responsiveness, owing to literature support, clinical safety, lack of other cost-effective, reliable measures, and automatic near-continuous calculation by newer physiologic monitors.

Current studies examining SPV and PPV are confined to subpopulations with limited sample sizes. Meta-analyses and multicenter studies have been performed in attempt to overcome this limitation, including a “gray zone” analysis of PPV among cardiac, vascular, and abdominal surgeries.^{13,22} Through these studies, theoretical ranges of SPV and PPV values have been proposed for responders and nonresponders to volume expansion. In spite of advances, there is a persistent lack of data establishing baseline distributions of SPV and PPV values among a broad population of patients in a euvolemic state undergoing elective surgical procedures. Additionally, although univariate analyses have examined changes in SPV and PPV associated with specific factors – including patient positioning^{23,24}, obesity²⁵, ventilator settings^{26,27}, and hemodynamic management²⁸ – studies continue to be limited in clinical scope and size, and have been frequently performed outside the perioperative setting. Furthermore, no multivariable analysis has evaluated independent associations among these factors.

To characterize the distribution of SPV and PPV values during elective surgical procedures, we performed a retrospective observational study at an academic tertiary care hospital. We hypothesized that for adult patients undergoing a wide range of elective non-cardiac surgical procedures, distributions of median SPV and PPV values can be characterized for the euvolemic state. Additionally, we hypothesized that changes in distributions are associated with perioperative clinical factors including age, body-mass index (BMI), positioning, preoperative medications, ventilator settings, and hemodynamic management.

Methods

This retrospective observational study was approved by the Institutional Review Board (HUM00052066; Ann Arbor, Michigan, USA). Patient consent was waived. Deidentified data were extracted from our local single-center Multicenter Perioperative Outcomes Group database, used for storage of our institution's electronic health record (EHR, Centricity® General Electric Healthcare, Waukesha, WI). Methodology for observational data collection, storage, and quality assurance within the Multicenter Perioperative Outcomes Group is described elsewhere.^{29,30} Per departmental policy, a detailed study protocol, including patient population, primary outcome, and planned statistical analyses, was presented at our local anesthesia clinical research committee on September 23, 2015 and registered on the department's internal research website.

At our hospital, physiologic monitoring is acquired via automated and validated interfaces at each anesthetizing location (CARESCAPE™ B850 or Solar 9500®; General Electric Healthcare). For cases including an arterial blood pressure monitor, SPV and PPV measurements are automatically recorded into the EHR from the CARESCAPE™ B850 monitor; anesthesiologists can also choose to manually calculate and record SPV values as a distinct EHR database concept. Both manually-entered and automated recorded values were calculated as the difference between the maximum and minimum systolic arterial pressures (SAP_{max} and SAP_{min} , respectively) observed on the arterial waveform throughout phases of the respiratory cycle, expressed in mmHg:³¹

$$SPV = SAP_{max} - SAP_{min}$$

PPV values, expressed as a percentage, were calculated in automated fashion using the established formula:

$$PPV = (PP_{max} - PP) / [(PP_{max} + PP_{min}) / 2] * 100$$

PP_{max} and PP_{min} represent the maximum and minimum pulse pressures observed on the arterial waveform throughout phases of the respiratory cycle.³¹

Patient Population

All adult patients (> 18 years) undergoing elective surgical procedures with general anesthesia, tracheal intubation, and invasive arterial blood pressure monitoring from January

1, 2009, to June 10, 2016, were included for analysis. To minimize the effect of prolonged preoperative fasting on intravascular volume status, cases were restricted to first-case morning start times, determined by documentation of anesthetic induction end between 07:30 and 08:30. Additional exclusion criteria for the study were (1) cardiac or cardiothoracic operating room procedures, (2) open-chest procedures, (3) laparoscopic procedures, (4) procedures utilizing a double-lumen endotracheal tube or one-lung ventilation, (5) patients receiving regional or spinal anesthetics to supplement general anesthesia pre-induction, (6) inpatient admission status prior to date of procedure, (7) American Society of Anesthesiologists (ASA) physical status class 5 and 6 patients, (8) blood product transfusion during SPV/PPV measurement, (9) vasopressor or inotropic infusion during SPV/PPV measurement, and (10) patients with significant cardiopulmonary comorbidities. Cardiopulmonary comorbidity exclusion criteria were heart failure, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), sleep apnea, low functional capacity, or dysrhythmia other than sinus tachycardia/bradycardia, occasional premature ventricular or atrial contractions, or first-degree heart block. Inclusion/exclusion criteria are illustrated in Figure 1; cardiopulmonary comorbidity diagnoses were established by the pick-list variables within the preoperative History & Physical electronic documentation described in Appendix 1.

To account for a shift in measurement practices at our institution during the study period, patients were stratified by data entry method: those with manually-entered SPV values only (PPV data unavailable) and those with automated recorded SPV and PPV values. This shift in practice was attributable to updated physiologic monitors capable of automated SPV/PPV recording (CARESCAPE™ B850). For cases in which manually-entered and automated recorded SPV values were both available, automated recorded values were used. Validation of arterial blood pressure values – and subsequently derived SPV/PPV values – was performed by manual review of a simple random sample of 125 patient intraoperative records. Through this manual review, an algorithm for removing possible artifactual arterial line values (e.g. dampened waveform, arterial line flushing for blood draws) was developed and subsequently applied to all cases. These included values for which the systolic blood pressure (SBP) was >200 mmHg and pulse pressure (PP) <50 mmHg, SBP >150 mmHg and PP <30 mmHg, SBP 100 mmHg and PP <20 mmHg, or SBP <100 mmHg and PP <10 mmHg. Automated SPV and PPV values concurrently recorded at time of possible arterial line artifact were also removed.

For all cases, SPV and PPV measurements were obtained starting 10 minutes after anesthetic induction end and concluding 60 minutes after anesthetic induction end, or at surgical procedure end if earlier. This measurement period was selected to minimize the effects of confounders on SPV and PPV values (e.g. anesthetic induction agents prior to measurement period, and blood loss, insensible loss, and fluid shifts after the measurement period). For automated recorded values, measurements were obtained once per minute; for manually-entered values, measurements were obtained as frequently as recorded by the anesthesiologist – most commonly once every 15 minutes, per institutional practice. For each case meeting inclusion criteria, median SPV values (and PPV values when available) were calculated within the measurement period. To derive a standard distribution of arterial

pressure variation values, histograms were developed for SPV values (manually-entered and automated recorded) and PPV values.

After characterizing SPV and PPV distributions, associations between clinical factors and altered SPV and PPV measurements were analyzed. These factors included patient age and BMI, preoperative medications (preoperative angiotensin converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB), beta blocker, or diuretic), ventilator settings, decreased mean arterial pressure (MAP) >20% below baseline, and total fluid administration at the end of SPV/PPV measurement period. For purposes of statistical analysis, continuous study variables were collapsed to binary variables. BMI, tidal volume, peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and MAP cutoffs were chosen as used in prior literature.^{12,26,32-35} A patient age cutoff was chosen based upon median age of the study population. Fluid administration was converted to crystalloid equivalents (colloids multiplied by a factor of 1.5),³⁶ with a 1000 mL binary cutoff. MAP values were obtained concurrently for all SPV/PPV measurements; a majority of MAP values >20% below initial intraoperative baseline defined hypotension as a binary variable for each case.

Statistical Analysis

Analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC) and SPSS version 21.0 (IBM, Somers, NY). Basic descriptive statistics were calculated for demographic and relevant intraoperative data. Pearson chi-square or Fisher exact tests (for categorical variables) and independent two-tailed t-tests or Mann-Whitney U tests (for continuous variables) were used to assess baseline univariate clinical differences between patients with manually-entered SPV values versus those with automated recorded SPV (and PPV) values (Table 1). Each distribution of median SPV/PPV values was tested against the normal, lognormal, gamma and Weibull distributions using the Kolmogorov-Smirnov goodness-of-fit test within the SAS univariate procedure. A p-value of <0.05 denoted statistical significance.

Univariate clinical differences between median SPV/PPV value distributions were next assessed using Mann-Whitney U tests for all modifying factors studied. To assess for independent predictors of SPV and PPV values, separate full-fit multivariable linear regression models were derived for three study cohorts: cases with manually-entered SPV values, cases with automated recorded SPV values, and cases with automated recorded PPV values. Before developing a prediction model to determine independent risk factors, all variables were tested for collinearity by investigating the correlations. Pairwise Pearson and Spearman correlation matrices were constructed to determine high correlation between variables, with a correlation coefficient of 0.70 as the threshold for high collinearity. If the correlation coefficient was less than 0.70, then no collinearity was detected and all variables were eligible for multivariable model entry. Residual plots were tested for homoscedascity and presence of a non-linear relationship. Finally, to assess for an independent association between SPV and data entry method (manually-entered versus automated recorded), a multivariable model including all univariate analysis variables that met collinearity criteria, plus a variable for method of SPV data entry, was constructed for all patients.

Given the lack of prior studies describing multivariable independent associations between shifts in SPV and PPV value distributions and clinical modifying factors, our sample size was selected based on availability of reliable clinical data. Based upon study inclusion/exclusion criteria and procedural volume at our tertiary care center, we projected 1,000-2,000 patients included in analysis. To assess for robustness of study results, three sensitivity analyses were performed: (1) a study population excluding cases with epidurals dosed intraoperatively to supplement general anesthesia (spinal and regional supplemental anesthetics previously excluded), (2) a study population restricting SPV/PPV measurements to 15 minutes after anesthetic induction end and before surgical incision, and (3) a separate population of cases with an anesthetic induction end time documented between 09:00 and 13:00.

Results

We studied 1,791 cases, 1,323 with manually-entered SPV values and 468 with automated SPV and PPV values (Figure 1). Patients' perioperative characteristics are described in Table 1. Compared to patients with manually-entered SPV values, patients with automated recorded values were older, taller, less likely to be positioned supine, ventilated with lower tidal volumes and higher PEEP levels, and less likely to have general surgery. Prior to artifact removal, arterial line data quality assessment demonstrated that on a per-case basis, a mean of 95% and minimum of 90% of values were non-artifactual.

The 2.5 – 97.5 percentile reference interval as recommended by the Clinical and Laboratory Standards Institute^{37,38} for manually-entered SPV was 3.0-11.0 mmHg, automated recorded SPV 2.2-10.4 mmHg, and PPV 2.0-16.0% (Table 2). Interquartile ranges were 5.0-7.0 mmHg, 3.9-6.0 mmHg, and 5.0-9.0%, respectively (Table 2). Manually-entered values were higher than values in the automated recorded cohort (6.0 median [5.0-7.0 interquartile range (IQR)] mmHg versus 4.7 [3.9-6.0] mmHg, $p < 0.001$), (Table 1). To adjust for the differences in patient characteristics between the manually and automated SPV, we used multivariable linear regression and found that manually-entered values were slightly higher than automated values ($0.76 \text{ mmHg} \pm 0.13 \text{ standard error}$, $p < 0.001$).

Median SPV and PPV values for all cases included in the study formed distributions as shown in Figures 2 and 3. The three sensitivity analyses (exclusion of cases with epidurals used to supplement general anesthesia, exclusion of SPV/PPV measurements after surgical incision, and a separate population of cases with anesthetic induction end time documented between 09:00 and 13:00) yielded distributions with median/IQR values within 1.0 mmHg for SPV values and within 1.0% for PPV values (Supplemental Digital Content 1-3).

By univariate analysis, factors associated with differences in SPV values included tidal volume, positioning (manually-entered only), median PIP, preoperative beta blocker, and preoperative diuretic (Table 3). Statistically significant differences in PPV values were associated with age and preoperative ACE inhibitor/ARB, beta blocker, and diuretic (Table 4).

No variables included in the univariate analysis were shown to have high collinearity. After adjustment for other factors using multivariable linear regression, non-supine positioning and lack of preoperative beta blockade were independently associated with increased SPV and PPV values, whereas elevated median ventilator tidal volume and elevated median PIP were each independently associated with increased SPV values only (Supplemental Digital Content 4-6). MAP >20% below intraoperative baseline was independently associated only with PPV. Finally, a lack of preoperative diuretic was independently associated with increased SPV among manually-entered values only. Although statistically significant, all independent associations identified were small (1 mmHg or 2%). All other clinical factors demonstrated no significant independent associations.

Discussion

Among 1,791 general anesthetics at our tertiary care academic institution, per-case median SPV and PPV values formed non-parametric distributions with medians of 4.7 mmHg (automated), 6.0 mmHg (manually-entered), and 7.0% respectively. Non-supine positioning and lack of preoperative beta blocker were independently associated with increased SPV and PPV, whereas elevated median ventilator tidal volume and elevated median PIP were each independently associated with increased SPV only. Based upon 25th-to-75th percentiles, we conclude a “normal” range of manually-entered SPV 5.0-7.0 mmHg, automated recorded SPV 3.9-6.0 mmHg, and PPV 5.0-9.0% among adult patients undergoing general anesthetics for elective non-cardiac surgery. The SPV/PPV histograms derived from this study establish essential real-world reference distributions lacking in current perioperative literature. These measurements allow for validation of prior studies, and provide a prerequisite reference distribution for use in future studies assessing SPV/PPV-driven goal-directed therapies, as called for in prior literature.^{21,39-41}

In contrast to analyses of patients in the post-cardiac surgery or ICU setting, our mean SPV and PPV values obtained were generally lower. In a meta-analysis of PPV among cardiac surgical and ICU patients, mean baseline PPV values of 7.1% for fluid challenge non-responders and 16.6% for responders were observed.¹³ In studies analyzing SPV in cardiac surgical/ICU patients, mean baseline values were 8-14 mmHg.⁴²⁻⁴⁴ Compared to these patients, our elective general surgical population may have possessed factors (e.g. euvolemic state, absence of cardiopulmonary comorbidities, absence of vasoactive infusions) predisposing to lower SPV/PPV values. Further studies are needed to investigate these differences; however, this difference illustrates the context-sensitivity of SPV/PPV values, and the value of our study investigating a broader, generally healthier elective surgical population.

Our study reports no independent association between obesity (BMI ≥30) and SPV/PPV values obtained intraoperatively; this finding sheds new light on a currently controversial concept. A theory which challenges measurement validity in the setting of obesity relates to increased intra-abdominal pressure in the supine position for obese patients, for which a decrease in venous return results in an increase in arterial waveform pressure variation (rightward shift of SPV/PPV distributions). This relationship between intra-abdominal pressure and arterial waveform pressure variation has been described in prior studies.^{20,45}

Despite this relationship in controlled settings, our results question the impact of obesity on the SPV/PPV normal range. However, given that few patients had a BMI > 40, we cannot draw conclusions about what extreme levels of obesity may have on SPV and PPV.

The statistically significant association between elevated tidal volumes and small increases in SPV values agree with prior literature.⁴⁶⁻⁴⁸ We were unable to demonstrate an association between tidal volumes >8 mL/kg IBW and increased PPV values, in contrast to prior studies.^{47,48} While elevated PEEP failed to demonstrate any association, elevated median PIP demonstrated a stronger independent association compared to tidal volumes, with small increases in SPV values but not PPV values. Recent studies note similar findings, placing a stronger emphasis on the relationship between driving pressure and dynamic waveform indices compared to tidal volumes.^{16,49} In an era of lung-protective ventilation favoring lower tidal volumes and plateau pressures, our findings suggest a similar trend in SPV and PPV values which anesthesiologists may need to consider; indeed, the utility of an arterial pressure variation indexed to tidal volume has been demonstrated.⁴⁸ Despite this association, a study also demonstrates that the ability of dynamic waveform indices to predict fluid-responsiveness remains intact even at lung-protective ventilation levels and continues to greatly exceed predictive capabilities of static measures.¹⁸

Our finding of a positive association between non-supine positioning and SPV values offers insight into currently contrasting literature, which have examined alterations in dynamic arterial waveform indices associated with variations in surgical positioning, including prone,^{19,24,32} Trendelenburg,^{23,50} and reverse Trendelenburg.⁵⁰ SVV and PPV demonstrated increases when prone,¹⁹ whereas SPV demonstrated no association.³² With regards to table positioning (e.g. Trendelenburg) as opposed to patient position, a lack of standardized documentation in our intraoperative record precluded this analysis, and thus was a limitation to our study. Although the anesthesiologist must be aware of the possible effects of surgical positioning on SPV and PPV, current literature is promising in that such indices remain effective measures of predicting fluid-responsiveness in these settings.^{19,23,24,32}

Our study demonstrated an independent association between hypotension and increased PPV values but not SPV values. These results elucidate prior conflicting studies, which have either shown a decrease in PPV associated with a MAP augmented via norepinephrine infusion,⁵¹ or no association between MAP and PPV – and conversely, an association between MAP and SPV.²⁸ Compared to prior studies, our analysis was performed retrospectively using clinical data, rather than in a controlled experimental environment, and thus unmeasured confounders associated with hypotension may have influenced our results. Nonetheless, the observed associations represent valuable information for the anesthesiologist assessing SPV and PPV values in a clinical setting. As with other variables studied, it should also be noted that the independent effect size of hypotension on dynamic waveform indices was small (<1 mmHg for PPV).

Finally, our study noted lower SPV and PPV values for patients receiving preoperative beta blockers, and lower manually-entered SPV values for patients receiving diuretics. Although the response of SPV/PPV measurements from medications altering vascular tone (e.g. phenylephrine, adenosine) have been investigated in the acute setting,^{28,52} no study to the

authors' knowledge has assessed the independent association between chronic cardiovascular medical therapies and SPV/PPV measurements. It is possible that such medical therapies are markers for underlying cardiovascular disease responsible for these associations, however it should be noted that patients with heart failure diagnoses (among other comorbidities) as well as patients requiring vasopressor/inotrope infusions were excluded from the study. Further prospective studies are needed to investigate this relationship. Nonetheless, chronic cardiovascular medical therapies serve as an important covariate in our multivariable analysis, enabling adjustment for other variables studied.

We also found a small difference (0.3 – 1.5 mmHg, Table 2) in the distribution of SPV values between manually and automated entry (Figure 2). As the measurements were not made simultaneously in the same patients and persisted after multivariable analysis (0.76 + 0.13 mmHg), these small differences may have reflected other unmeasured patient characteristics or differences between human calculations and computer algorithms. Further study is needed to clarify this issue.

Comparing SPV to PPV, PPV values in general were less affected by confounding factors. This finding in favor of PPV as a more robust measure aligns with current literature, which supports PPV as a better predictor of fluid responsiveness.¹³ A limitation of our study was a lack of SVV measurement analysis. However, while studies have shown that SVV has a similar accuracy at predicting fluid responsiveness as SPV, it is less accurate than PPV.²¹⁻²⁴

Our study possessed several additional limitations. Our study was performed retrospectively, and was subject to limitations inherent to study design. Data were available as charted within the perioperative database; additional details beyond the scope of clinical care were unavailable. Similarly, given our study design, patient responses to therapeutic interventions were not assessed; this warrants future prospective study investigation. In addition, although standard clinical practices were employed, no specific study protocols – including standard methods for manually-entered SPV measurement – were utilized. Despite anesthesiologist training on data entry, manual auditing of sample cases, and the use of data validation algorithms, no standard of data quality assurance could be applied at the point of care. All PPV values were obtained via the algorithm employed by the CARESCAPE™ B850 monitor; automated PPV calculation variations may exist across different manufacturers. Though our study identified a reference distribution of SPV/PPV values lacking in current literature, potential confounders – including those used as exclusion criteria, those studied in univariate analyses, and those remaining unidentified – limit the generalizability of our results. Conversely, the reference intervals identified by our study were generated by a broad surgical population, and despite consideration of modifying factors, application to individual surgical cases with multiple modifying factors must be made with caution. Additionally, although measures to target a euvolemic patient population included restricting to a morning case time, elective procedures, and patients with minimal cardiopulmonary comorbidities, no rigorous measures were implemented to confirm a particular patient volume status. We performed our study at a single academic tertiary care center, and institutional variations, scope of practice, and geographic region may bias our results. Our study population drawing from convenience samples for SPV and PPV measurements represents the largest population currently studied for this purpose and was able to detect clinically meaningful associations

between SPV/PPV values and clinical factors. However, a larger sample size may be required to uncover smaller, yet statistically significant associations for other factors.

Despite these limitations, our study successfully addresses a shortcoming in current literature through establishing reference distributions of SPV and PPV values for patients undergoing elective surgical procedures. By providing a means of validation for prior studies, as well as a platform for assessing impact of subsequent interventions as well as goal-directed therapies, our study furthers the knowledge of two widely-used clinical measures associated with fluid-responsiveness, and offers a standard reference range to the anesthesiologist for volume assessment and intraoperative fluid management therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix 1: Preoperative comorbidity pick-list choices

Preoperative Comorbidity	Pick-list Choices
Functional Capacity	Low (1-4 METs): Self Care, Walk indoors, 1-2 blocks outside, light housework Medium (4-10 METs) : Climb 1 flight of stairs, run short distance High (>10 METs) : Strenuous sports
Heart Failure	Currently Active Class 1: no limitation of physical activity Class 2: ordinary activity produce cardiac symptoms Class 3: less than ordinary activity produces symptoms Class 4: symptoms at rest
Chronic obstructive pulmonary disease	Severity: Mild Severity: Moderate (chronic bronchodilator use) Severity: Severe (oxygen use) Severity: Very severe (oxygen dependent)
Sleep Apnea	Treated by BiPAP/CPAP Prescribed BiPAP / CPAP but not using Treated by surgery Diagnosed by sleep study, untreated Symptomatic, untreated
ARDS	Acute Respiratory Failure: Respiratory Distress Syndrome
Heart Rhythm*	NSR / Sinus Tachy / Sinus Brady / PVCs / PACs / 1 st Degree Block AFib / 2 nd Degree Block Type 1 / 2 nd Degree Block Type 2 / 3 rd Degree Block / SVT / Paced Rhythm / Junctional / AFlutter / Torsades de Pointes / VFib / VTach / Asystole

MET = metabolic equivalent, BiPAP = bilevel positive airway pressure, CPAP = continuous positive airway pressure, ARDS = acute respiratory distress syndrome, NSR = normal sinus rhythm, PVC = premature ventricular contraction, PAC

= premature atrial contraction, AFib = atrial fibrillation, SVT = supraventricular tachycardia, AFlutter = atrial flutter, VFib = ventricular fibrillation, VTach = ventricular tachycardia

* As routinely charted within 15-minute intervals within the intraoperative record. Dysrhythmia characterized as any rhythm other than NSR, sinus tachycardia/bradycardia, occasional PVCs/PACs, or 1st degree block.

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Summary Statement

Systolic- and pulse-pressure variation are well-studied measures of fluid-responsiveness in mechanically ventilated patients. Our study establishes reference distributions – and analyzes clinical modifying factors – for these parameters in adult patients undergoing elective non-cardiac surgery.

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Figure 1. Study inclusion/exclusion criteria

* Exclusion counts non-mutually exclusive, e.g. cases may have multiple exclusion criteria
 SPV = systolic pressure variation; COPD = chronic obstructive pulmonary disease; ARDS = acute respiratory distress syndrome; OSA = obstructive sleep apnea; MET = metabolic equivalent; PPV = pulse pressure variation; ASA = American Society of Anesthesiologists; ETT = endotracheal tube

Figure 2. Per-case median systolic pressure variation distributions

* Distributions determined to be non-parametric; each failed to fit a normal, lognormal, gamma, or Weibull distribution. Percentile ranks illustrated across figure headers. SPV = systolic pressure variation.

Figure 3. Per-case median pulse pressure variation distribution

* Distribution determined to be non-parametric; failed to fit a normal, lognormal, gamma, or Weibull distribution. Percentile ranks illustrated across figure header. PPV = pulse pressure variation.

Table 1
Study cohort characteristics

Category	Descriptor	Manually-Entered Values (N = 1,323), n (%)	Automated Recorded Values (N = 468), n(%)	p-value
Anthropometric Data	Age (years)	57.0 [47.0 to 66.0]	58.0 [50.0 to 67.0]	0.018
	Height (cm)	170.2 [162.6 to 177.8]	172.7 [162.6 to 180.3]	0.030
	Weight (kg)	81.2 [68.0 to 95.0]	82.0 [68.0 to 96.0]	0.261
	BMI	27.8 [24.2 to 31.7]	28.1 [24.5 to 32.2]	0.702
	<i>WHO Classification</i>			
	Underweight <18.5	19 (1.5)	10 (2.1)	
	Normal 18.5-24.9	384 (29.3)	121 (25.9)	
Surgical Data	Overweight 25-29.9	452 (34.4)	174 (37.3)	
	Obese 30	458 (34.9)	162 (34.7)	
	Gender			
	Male	706 (53.4)	268 (57.3)	0.145
	Female	617 (46.6)	200 (42.7)	
	Primary Procedural Service			
	General	246 (18.6)	63 (13.5)	<0.001
	Neurosurgery	400 (30.2)	164 (35.0)	
	Obstetrics/Gynecology	20 (1.5)	3 (0.6)	
	Ophthalmology	1 (0.1)	0 (0)	
Surgical Data	Oral/Maxillofacial	69 (5.2)	27 (5.8)	
	Orthopedics	66 (5.0)	8 (1.7)	
	Otolaryngology	294 (22.2)	139 (29.7)	
	Plastics	26 (2.0)	4 (0.9)	
	Transplant	43 (3.3)	19 (4.1)	
	Unknown	38 (2.9)	3 (0.6)	
	Urology	120 (9.1)	38 (8.1)	
	Patient Positioning			
	Supine	983 (78.2)	298 (67.7)	<0.001
	<i>Non-supine:</i>			
Surgical Data	Prone	140 (11.1)	45 (10.2)	
	Lateral Decubitus	59 (4.7)	46 (10.5)	
	Beach Chair/Sitting	23 (1.8)	28 (6.4)	
	Lithotomy	52 (4.1)	23 (5.2)	
Anesthetic Data	ASA Physical Status			
	1	18 (1.4)	8 (1.7)	0.568
	2	569 (43.0)	185 (39.5)	
	3	717 (54.2)	269 (57.5)	

Category	Descriptor	Manually-Entered Values (N = 1,323), n (%)	Automated Recorded Values (N = 468), n(%)	p-value
	4	19 (1.4)	6 (1.3)	
	Median Tidal Volume (mL/kg IBW)	8.1 [7.2 to 9.1]	7.0 [6.4 to 7.7]	<0.001
	8	232 (17.5)	237 (50.6)	
	>8	1,091 (82.5)	231 (49.4)	
	Median PEEP (cm H ₂ O)	5.0 [4.0 to 5.0]	5.0 [5.0 to 5.0]	<0.001
	5	1,178 (89.0)	408 (87.2)	
	> 5	145 (11.0)	60 (12.8)	
	Median PIP (cm H ₂ O)	17.0 [15.0 to 20.0]	17.0 [15.0 to 20.0]	0.409
	16	517 (39.1)	335 (71.6)	
	> 16	806 (60.9)	133 (28.4)	
	MAP during SPV Values			
	Majority >20% below baseline	641 (48.5)	204 (43.6)	0.070
	Normotensive	682 (51.6)	264 (56.4)	
Arterial Waveform Data	SPV (mmHg)	6.0 [5.0 to 7.0]	4.7 [3.9 to 6.0]	<0.001
PPV (%)	N/A	7.0 [5.0 to 9.0]	N/A	

Data presented as median [25th percentile to 75th percentile].

ASA = American Society of Anesthesiologists; SPV = systolic pressure variation; PPV = pulse pressure variation; BMI = body mass index; WHO = World Health Organization; IBW = ideal body weight; PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure; MAP = mean arterial pressure; N/A = Not applicable

Table 2
Percentile ranks for systolic pressure variation & pulse pressure variation value distributions

	Percentile										
	1 st	2.5 th	5 th	10 th	25 th	50 th	75 th	90 th	95 th	97.5 th	99 th
SPV, Manually-Entered (mmHg) N = 1,323	2.0	3.0	4.0	4.0	5.0	6.0	7.0	9.0	10.0	11.0	13.0
SPV, Automated Recorded (mmHg) N = 468	1.7	2.2	2.5	3.0	3.9	4.7	6.0	7.7	9.0	10.4	12.4
PPV, Automated Recorded (%) N = 468	1.0	2.0	2.0	3.0	5.0	7.0	9.0	12.0	13.5	16.0	20.0

SPV = systolic pressure variation, PPV = pulse pressure variation

Table 3

Study results – systolic pressure variation values

	Manually-Entered SPV Values (N = 1,323)			Automated Recorded SPV Values (N = 468)		
	Median SPV (mmHg)	Frequency (%)	p-value	Median SPV (mmHg)	Frequency (%)	p-value
All cases	6.0 [5.0 to 7.0]	1,323 (73.9)	--	6.0 [5.0 to 7.0]	468 (26.1)	--
BMI						
<30	6.0 [5.0 to 7.0]	865 (65.4)	0.090	4.8 [3.9 to 6.1]	306 (65.4)	0.558
30	6.0 [5.0 to 7.0]	458 (34.6)		4.6 [3.7 to 6.0]	162 (34.6)	
Median Tidal Volume (mL/kg IBW)						
8	5.5 [4.0 to 7.0]	232 (49.5)	<0.001	4.4 [3.7 to 5.7]	237 (50.6)	0.005
>8	6.0 [5.0 to 7.0]	1,091 (82.5)		4.9 [4.0 to 6.3]	231 (49.4)	
Positioning						
Supine	6.0 [5.0 to 7.0]	983 (78.2)	<0.001	4.6 [3.8 to 5.9]	298 (67.7)	0.053
Non-supine	6.5 [5.0 to 8.0]	274 (21.8)		4.9 [3.9 to 6.5]	142 (32.3)	
Crystalloid equivalent fluid volume received						
1,000 mL	6.0 [5.0 to 7.0]	1,055 (79.7)	0.231	4.7 [3.9 to 6.1]	382 (81.6)	0.348
> 1,000 mL	6.0 [5.0 to 8.0]	268 (20.3)		4.5 [3.8 to 5.7]	86 (18.4)	
Median PIP (cm H ₂ O)						
16	6.0 [4.5 to 7.0]	517 (39.1)	<0.001	4.6 [3.7 to 5.7]	335 (71.6)	0.012
> 16	6.0 [5.0 to 7.0]	806 (60.9)		4.9 [4.0 to 6.4]	133 (28.4)	
Median PEEP (cm H ₂ O)						
5	6.0 [5.0 to 7.0]	1,178 (89.0)	0.884	4.7 [3.8 to 6.0]	408 (87.2)	0.850
> 5	6.0 [5.0 to 7.0]	145 (11.0)		4.5 [3.9 to 6.2]	60 (12.8)	
Age (years)						
57	6.0 [5.0 to 7.0]	691 (52.2)	0.165	4.8 [4.0 to 6.0]	223 (47.7)	0.419
> 57	6.0 [5.0 to 7.0]	632 (47.8)		4.6 [3.7 to 6.1]	245 (52.4)	

	Manually-Entered SPV Values (N = 1,323)			Automated Recorded SPV Values (N = 468)		
	Median SPV (mmHg)	Frequency (%)	p-value	Median SPV (mmHg)	Frequency (%)	p-value
Preoperative ACE Inhibitor/ARB	No	6.0 [5.0 to 7.0] 1,143 (86.4)	0.627	4.8 [3.9 to 6.0]	325 (69.4)	0.359
	Yes	6.0 [5.0 to 7.0] 180 (13.6)		4.5 [3.5 to 6.1]	143 (30.6)	
Preoperative Beta Blocker	No	6.0 [5.0 to 7.0] 1,105 (83.5)	0.011	4.8 [4.0 to 6.1]	351 (75.0)	<0.001
	Yes	5.5 [5.0 to 7.0] 218 (16.5)		4.2 [3.1 to 5.6]	117 (25.0)	
Preoperative Diuretic	No	6.0 [5.0 to 7.0] 1,202 (90.9)	0.032	4.8 [4.0 to 6.1]	364 (77.8)	0.001
	Yes	5.5 [4.5 to 7.0] 121 (9.2)		4.1 [3.2 to 5.9]	104 (22.2)	
MAP	>20% below baseline	6.0 [5.0 to 7.0] 641 (48.5)	0.673	4.7 [3.7 to 6.1]	204 (43.6)	0.573
	Normotensive	6.0 [5.0 to 7.0] 682 (51.6)		4.8 [3.9 to 5.9]	264 (56.4)	

Data are presented as either frequency (percent) or median [25th percentile to 75th percentile].

SPV = systolic pressure variation; PPV = pulse pressure variation; BMI = body mass index; IBW = ideal body weight; PIP = peak inspiratory pressure; PEEP = positive end-expiratory pressure; ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; MAP = mean arterial pressure

Table 4
Study results – pulse pressure variation values

		Automated Recorded PPV Values (N = 468)		
		Median PPV (%)	Frequency (%)	p-value
All cases		7.0 [5.0 to 9.0]	468 (100.0)	---
BMI				0.615
	<30	7.0 [5.0 to 9.0]	306 (65.4)	
	30	6.8 [5.0 to 9.0]	162 (34.6)	
Median Tidal Volume (mL/kg IBW)				0.512
8	7.0 [5.0 to 9.0]	237 (50.6)		
>8	7.0 [5.0 to 9.0]	231 (49.4)		
Positioning				0.069
	Supine	7.0 [5.0 to 9.0]	298 (67.7)	
	Non-supine	8.0 [5.0 to 10.0]	142 (32.3)	
Crystalloid equivalent fluid volume received				0.302
1,000 mL	7.0 [5.0 to 9.0]	382 (81.6)		
> 1,000 mL	6.0 [5.0 to 9.5]	86 (18.4)		
Median PIP (cm H ₂ O)				0.101
16	7.0 [5.0 to 9.0]	335 (71.6)		
>16	7.0 [5.0 to 10.0]	133 (28.4)		
Median PEEP (cm H ₂ O)				0.221
5	7.0 [5.0 to 9.0]	408 (87.2)		
> 5	7.3 [5.0 to 10.0]	60 (12.8)		
Age (years)				<0.001
	57	8.0 [5.5 to 9.0]	223 (47.7)	
	> 57	6.0 [4.0 to 8.5]	245 (52.4)	
Preoperative ACE Inhibitor/ARB				0.019
No	7.0 [5.0 to 9.0]	325 (69.4)		
Yes	6.0 [4.0 to 9.0]	143 (30.6)		
Preoperative Beta Blocker				<0.001
No	7.0 [5.0 to 9.5]	351 (75.0)		
Yes	5.0 [3.0 to 8.0]	117 (25.0)		
Preoperative Diuretic				<0.001
No	7.0 [5.0 to 9.0]	364 (77.8)		
Yes	5.5 [4.0 to 8.3]	104 (22.2)		
MAP				0.016

	Automated Recorded PPV Values (N = 468)		
	Median PPV (%)	Frequency (%)	p-value
>20% below baseline	7.0 [5.0 to 9.0]	264 (56.4)	
Normotensive	6.0 [4.0 to 9.0]	204 (43.6)	

Data are presented as either frequency (percent) or median [25th percentile to 75th percentile].

SPV = systolic pressure variation; PPV = pulse pressure variation; BMI = body mass index; IBW = ideal body weight; PIP = peak inspiratory pressure; PEEP = positive end-expiratory pressure; ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; MAP = mean arterial pressure