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ORIGINAL CLINICAL RESEARCH REPORT

Diastolic Versus Systolic or Mean Intraoperative Hypotension as Predictive of Perioperative Myocardial Injury in a White-Box Machine-Learning Model

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BACKGROUND: Intraoperative hypotension (IOH) and tachycardia are associated with perioperative myocardial injury (PMI), and thereby increased postoperative mortality. Patients undergoing vascular surgery are specifically at risk of developing cardiac complications. This study aimed to explore the association between different thresholds for IOH and tachycardia, and PMI. It also aimed to explore which threshold for IOH and tachycardia best predicts PMI.

METHODS: In this single-center prospective observational study, high-sensitivity cardiac troponin T was measured preoperatively and at 4, 24, and 48 hours after vascular surgery. Absolute and relative thresholds were used to define intraoperative systolic, mean, and diastolic arterial hypotension, measured every 15 seconds by invasive arterial pressure monitoring and heart rate using the Philips IntelliVue X3 monitor. Decision tree machine-learning (ML) models were used to explore which thresholds for IOH and tachycardia best predict PMI. Clinical utility and transparency were prioritized over maximizing the performance of the ML model and therefore a white-box model was used.

RESULTS: In all, 498 patients were included in the study. Ninety-nine patients (20%) had PMI. Significant associations were found between IOH and PMI using both absolute and relative thresholds for systolic, mean, and diastolic arterial pressure. Absolute thresholds based on diastolic arterial pressure had the strongest correlation with PMI and yielded greater statistical significance. The threshold that was most predictive of PMI was an absolute diastolic arterial pressure <44 mm Hg. The prediction model with the absolute threshold of diastolic arterial pressure <44 mm Hg had a macro average F1 score of 0.67 and a weighted average F1 score of 0.76. No association was found between tachycardia and PMI.

CONCLUSIONS: We found that an absolute, not relative, IOH threshold based on diastolic arterial pressure, and not systolic or mean arterial pressure, or tachycardia, was most predictive of PMI. (Anesth Analg 2025;141:5–15)

KEY POINTS

- **Question:** Which threshold for intraoperative hypotension and tachycardia best predicts perioperative myocardial injury (PMI)?
- **Findings:** In this explorative prospective observational trial in patients undergoing vascular surgery, we found that an absolute, not relative, threshold for intraoperative hypotension based on diastolic, and not systolic or mean arterial pressure, was most predictive of PMI.
- **Meaning:** Previous studies have established a relationship between mean arterial pressure and PMI; however, our findings suggest that diastolic pressure might be more predictive of PMI.

Each year, over 10 million adults have a cardiac complication within 30 days after noncardiac surgery.[1] Myocardial injury is the leading cause of 30-day mortality after noncardiac surgery.[2] Intraoperative hypotension (IOH) and tachycardia are both associated with PMI.[3,4] A recent Perioperative

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Quality Initiative Statement defined IOH as a mean arterial pressure (MAP) <60 to 70 mm Hg because lower values were associated with an increased risk of death, myocardial injury or acute kidney injury.[3]

Myocardial injury is universally defined as cardiac troponin above the 99th percentile upper reference limit.[5] The injury is acute if there is a rise or fall in cardiac troponin. The definition of myocardial injury after noncardiac surgery (MINS) or perioperative myocardial injury (PMI) varies. However, several studies have shown an association between PMI/MINS and postoperative mortality.[6–8] The distinction between PMI and MINS lies in the etiology of the myocardial injury, where PMI includes both cardiac and noncardiac causes, while MINS only includes cardiac causes.[6,8] The specific threshold used for IOH varies considerably in the literature, and may be based on the type of blood pressure (systolic, mean, or diastolic arterial pressure [DAP]), the absolute or relative threshold of IOH, and the duration of the hypotensive event.[9] Randomized control trials in the perioperative setting show conflicting results for the association between IOH and postoperative complications.[10–13] Intraoperative tachycardia, defined as a heart rate >100 beats per minute (BPM), has also been shown to be associated with PMI.[4]

Patients undergoing vascular surgery are at a greater risk of developing cardiac complications postoperatively because of a high prevalence of coronary artery disease.[14] Van Waes et al[15] used a combination of invasive and noninvasive blood pressure monitoring and postoperative troponin to define PMI in patients undergoing vascular surgery. They found a significant association between a 40% drop in MAP for >30 minutes and PMI. Whilst consensus exists regarding an association between IOH and PMI, it is difficult to precisely define the optimal threshold using the current definition of PMI.

The aim of this study was to explore the association between predefined thresholds for IOH (systolic, mean, and diastolic) and tachycardia, and PMI. Furthermore, we aimed to explore which thresholds for IOH and tachycardia best predict PMI.

METHODS

This study was approved by the appropriate Institutional Review Board. In this case, this was the Regional Ethical Committee in Stockholm (registration number: Dnr 2017/1178-31). Requirement for written informed consent was waived by the Regional Ethical Committee in Stockholm. The trial was registered before patient enrollment at ClinicalTrials.gov database (NCT03317561, principal investigator: A. Gupta, date of registration: October 18, 2017). Although the initial aim of this study was to determine postoperative myocardial injury using magnetic resonance imaging, this approach was abandoned after safety concerns in the early postoperative period. Therefore, this study focuses on the cohort as entered in part 1 of the ClinicalTrials.gov database. This was a prospective, single-center, cohort study.

Patients

All patients undergoing vascular surgery at Karolinska University Hospital, Stockholm, Sweden between November 2020 and December 2022 were screened for inclusion in the trial. The inclusion criteria were adult patients undergoing elective arterial vascular surgery including open or endovascular aortic repair (EVAR), peripheral vascular surgery, and carotid endarterectomy. The exclusion criteria were arteriovenous fistulas or surgery on veins, cognitive or communication difficulties, and patient inclusion in other ongoing studies. Written information was given to all patients and unless they wished to be excluded from the study, clinical data were gathered via the universal serial bus portal in the monitor as described below. The study was conducted according to Good Clinical Practice.

Anesthesia and Surgery

Surgical procedures were performed in accordance with local routines and best clinical practices. The choice of anesthesia technique was left to the discretion of the attending specialist anesthesiologist. Regional anesthesia with or without sedation was used when applicable for patients undergoing peripheral vascular surgery, local anesthesia for patients undergoing carotid endarterectomy, and general anesthesia combined with epidural analgesia for open aortic surgery. Depending on the complexity of the procedure and the location of the aneurysm local or general anesthesia was used for patients undergoing EVAR.

Study Protocol and Data Collection

All patients included in the study had routine perioperative monitoring using a Philips IntelliVue X3 monitor. Additionally, hemodynamic data were collected using an arterial line placed in the radial artery and continuous **electrocardiogram** monitoring to register heart rate. Patients were continuously monitored from arrival in the operating theater until they left the postoperative high-dependency ward. Attending anesthesiology staff set blood pressure targets (usually MAP) depending on patient characteristics and hospital routines and responded appropriately to these targets. Hypotensive events were treated using fluids (balanced crystalloid solutions, albumin, or blood products) or vasopressors (ephedrine or phenylephrine given as single bolus doses intravenously or using a continuous infusion of norepinephrine). Patients were

monitored postoperatively in a high-dependency ward for at least 4 hours using the same monitoring equipment as in the operating room. All patients were followed-up via the electronic medical journal records (Take Care) for a period of 30 days after index surgery to register postoperative creatinine, duration of stay at a high-dependency ward, and mortality.

Before the induction of anesthesia, blood samples were taken after insertion of an arterial line for measurement of hs-cTnT and N-terminal pro–B-type natriuretic peptide (NT-proBNP), and repeated after 4 to 6, 24, and 48 hours postoperatively. Baseline SAP and DAP were calculated by taking the median of the most recent blood pressure values measured noninvasively and recorded in the patient's medical records within 1 year before the index surgery. In the rare event that 3 values were not recorded, the average of 2 or a single value was used as a baseline. All relevant parameter values from the Philips IntelliVue X3 monitor were sampled and stored at 15-second intervals in a central server and downloaded postoperatively in a CSV file format.

Definitions

Hypotension. A hypotensive episode was defined as a drop in blood pressure below predefined thresholds (see below) for >1 minute. The duration of the hypotensive episode, the magnitude of the fall in pressure and the threshold used to define hypotension were used to create an area under the target (AUT) for each episode. These values were then added to express a "dose" (quantity × time) of IOH for the intraoperative period for each individual patient during the operation (see Figure 1).

The formula below shows how the "dose" for a single hypotensive event was calculated:

$$UT = \frac{1}{60 \cdot F_s} \sum_{k=n_0}^{n_0+\Delta} T - m\,[k] \qquad (mmHg \cdot min)$$

where T is the target threshold in mm Hg, n_0 is the time of onset of hypotension (as sample index), Δ is the length of the hypotensive event (in number of samples), and F_s is the sampling frequency (in our case, F_s = 1/15s = 66.7 mHz, since we sampled the parameter values once every 15 seconds), and $m[k]$ is the sampled arterial pressure value in mm Hg at sample index k.

The total "dose" of hypotension was calculated for all patients during the intraoperative phase. The thresholds chosen were based on the most common thresholds used.[9]

- Absolute thresholds
- SAP: <80–100 mm Hg
- MAP: <50–70 mm Hg
- DAP: <40–60 mm Hg
- Relative thresholds
- A drop <10%, 20%, 30%, 40%, or 50% from baseline SAP
- A drop <10%, 20%, 30%, 40%, or 50% from baseline MAP
- A drop <10%, 20%, 30%, 40%, or 50% from baseline DAP

Tachycardia. The intraoperative "dose" (quantity × duration) of tachycardia was calculated, in the same way that the "dose" of IOH was calculated for each patient using several different absolute thresholds, > 80, 90, 100, 110, or 120 BPM (see Figure 1).

Primary Outcome

We defined PMI as a binary variable in line with published guidelines (as defined below) and not as a numeric variable based on absolute values of hs-cTnT. More specifically, PMI was defined pre hoc as normal preoperative hs-cTnT (≤14 ng·L^{-1}) or increased postoperative hs-cTnT (>14 ng·L^{-1}).[5] Chronic myocardial injury was defined as a hs- cTnT >14 ng·L^{-1}

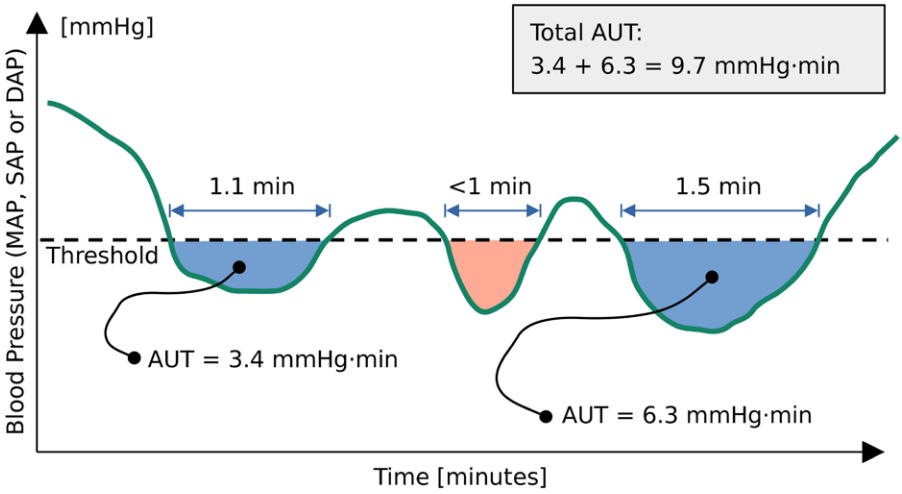


Figure 1. An illustration of how IOH was calculated, for each patient, using the sum of all AUT values where the duration of the hypotensive event was >1 min. Blue area: qualifies as IOH and pink area: does not qualify as IOH (see section about methods for definition). AUT indicates areas under the target; IOH, intraoperative hypotension.

preoperatively and an increase in postoperative troponin by < 14 ng·L^{-1}. Acute on chronic injury was defined *post hoc* as preoperative hs-cTnT >14 ng·L^{-1} and an increase in postoperative hs-cTnT by ≥14 ng·L^{-1}, which is in line with the current definition of PMI (and accounts for approximately 40% of patients in the vascular surgery cohort who have a preoperative hs- cTnT >14 ng·L^{-1}.[8,16,17]

Statistical Methods

The explorative nature of this study looking at multiple thresholds for IOH and tachycardia precluded the possibility of making an accurate pre hoc power calculation. In the Table, categorical values are presented as numbers (%) and continuous variables as median and interquartile range (IQR). *P*-values were calculated using the Kruskal-Wallis test or the χ^2 test, as appropriate. *P*-values <.05 were considered statistically significant. Baseline MAP was calculated using baseline SAP and DAP using the formula described below.

The formula for calculating baseline MAP is as follows:

$$\frac{1}{3} \cdot SAP + \frac{2}{3} \cdot DAP$$

where SAP is the baseline systolic arterial pressure and DAP is the baseline diastolic arterial pressure.

Association, Exploring Trends

Initially, the Kruskal-Wallis test was used to determine the trends in the associations between PMI and different thresholds for IOH and tachycardia. For each type of blood pressure (SAP, MAP, or DAP), a range of absolute thresholds and thresholds for relative drop (%) of pressure from the preoperative baseline was used. *P*-values were adjusted for multiple testing using the Benjamini and Hochberg procedure. Similarly, trends in the association between tachycardia and PMI were explored for a range of absolute thresholds for heart rate.

Spearman's correlation was then used to determine the trends in correlations between the thresholds mentioned above and PMI. It was used to verify the presence of possible significant trends between increasing or decreasing blood pressure or heart rate thresholds.

Prediction Using Machine Learning

A machine-learning (ML) approach was implemented. Several models were explored in pursuit of the aim of the study. Models based on different thresholds IOH and tachycardia were explored to find the threshold for IOH and tachycardia that is most predictive of PMI. Furthermore, a reference model using the conventional threshold, that is, IOH defined as MAP <65 mm Hg and tachycardia as heart rate >100 BPM, was explored. It was decided to opt for a decision tree, a type of model that step by step divides the dataset into smaller sets based on the satisfaction of a certain condition.[16] This white-box model offers a visualization that facilitates the understanding of the relationship between the predictor variables and the target. The goal was not to find the ML model that was most predictive of PMI but rather to create a model that allowed for visualization of how the different features in the model were being used in relation to each other to predict PMI. Within this framework, we designed a model with the objective of optimizing its F1 macro score without overfitting the model and preserving its clinical plausibility.

In addition to hypotension and tachycardia, perioperative characteristics in the Table were used as predictors in the models. The feature selection process started by considering perioperative characteristics deemed relevant by the Kruskal-Wallis and χ^2 tests (relevant if *P*-value <.05) and by domain knowledge. Despite preoperative hs-cTnT not meeting this *P*-value criterion, its inclusion was considered imperative since it is highly predictive of PMI.[17] Furthermore, features associated with hypotension threshold values (MAP, DAP, and SAP) were incorporated into the analysis, acknowledging their significance in the context of the study. The refinement of the feature subset was performed iteratively, with each subset subjected to rigorous testing within the decision tree model. This systematic approach involved evaluating various subset combinations to identify the specific feature group that maximized the F1 macro score of the models.

For the ML-based model training and testing, the dataset was split into 80% for a training set and 20% for a hold-out test set. In the training set, a 5-fold cross-validation was performed for each combination of selected features to ensure the generalizability of the model. Given the unbalanced dataset (~20% positive, ~80% negative) we used the F1-macro score as a metric.

The F1-macro score considers both precision and recall. Macro averaging gives equal importance to the positive and negative classes. The calculation of the F1-macro score and other relevant model performance parameters are listed in Supplemental Digital Content 1, Appendix A, http://links.lww.com/AA/F163. During the 5-fold cross-validation, we also searched for decision tree parameters that would optimize the prediction. Finally, having ascertained the generalizing capacity of the model, a further final test was performed on the 20% of hold-out data saved at the beginning of the experiment. Hyperparameters for the decision tree model are presented in Supplemental Digital Content 1, Appendix A, http://links.lww.com/AA/F163. Analyses were done using Python version 3.9 and the libraries used were numpy for numerical

Table. Perioperative Characteristics

	No PMI (n = 396)	PMI (n = 99)	*P* value
Preoperative characteristics			
Age (median [IQR]), y	74 [67–79]	77 [70–81]	.028
Sex, male (%)	303 (76.5)	74 (74.7)	.812
Weight (median [IQR]), kg	80 [70–91]	77 [67–86]	.070
Height (median [IQR]), cm	176[169–182]	174 [166–182]	.104
Comorbidities			
Hypertension (%)	304 (76.8)	84 (84.8)	.107
Heart failure (%)	87 (22.0)	22 (22.2)	1.000
Ejection fraction (median [IQR]), %	52.5 [50.0–57.0]	55 [50.0–57.5]	.200
Regional hypokinesia (%)	49 (12.4)	15 (15.2)	.569
Atrial fibrillation (%)	85 (21.5)	15 (15.2)	.208
Coronary heart disease (%)	111 (28.0)	30 (30.3)	.746
Percutaneous coronary intervention (PCI) (%)	61 (15.4)	17 (17.2)	.781
PCI within 6 mo (%)	4 (1.0)	0 (0.0)	.707
Stroke/transient ischemic attack (%)	72 (18.2)	27 (27.3)	.060
Peripheral vascular disease (%)	218 (55.1)	61 (61.6)	.287
Pacemaker (%)	23 (5.8)	8 (8.1)	.547
Diabetes mellitus (%)	93 (23.5)	27 (27.3)	.512
Insulin-dependent diabetes mellitus (%)	28 (7.1)	11 (11.1)	.260
Chronic obstructive pulmonary disease (%)	111 (28.0)	35 (35.4)	.192
Cancer (%)	35 (8.8)	8 (8.1)	.968
Medication			
Angiotensin-converting enzyme inhibitor (%)	101 (25.5)	29 (29.3)	.523
Angiotensin receptor blocker (%)	130 (32.8)	26 (26.3)	.256
Calcium channel blocker (%)	164 (41.4)	44 (44.4)	.665
Beta blocker (%)	191 (48.2)	46 (46.5)	.840
Diuretics (%)	87 (22.0)	26 (26.3)	.438
Nonsteroidal anti-inflammatory drugs (%)	8 (2.0)	1 (1.0)	.799
Statin (%)	303 (76.5)	80 (80.8)	.436
Aspirin (%)	275 (69.4)	74 (74.7)	.362
Clopidogrel (%)	30 (7.6)	7 (7.1)	1.000
Direct-acting oral anticoagulants (%)	59 (14.9)	13 (13.1)	.774
Warfarin (%)	15 (3.8)	4 (4.0)	1.000
Low-molecular-weight heparin, high dose (%)	36 (9.1)	9 (9.1)	1.000
MET >4 (%)	260 (69.0)	59 (64.1)	.443
Hemoglobin (median [IQR]), $g.L^{-1}$	132 [120–146]	133 [117–146]	.968
Creatinine (median [IQR]), $\mu mol.L^{-1}$	85 [72–102]	85 [72–112]	.422
Preop hs-cTnT (median [IQR]), $ng.L^{-1}$	16 [10–23]	14 [12–24]	.615
Preop NT-proBNP (median [IQR]), $ng.L^{-1}$	246 [85–678]	255 [99–785]	.266
Baseline SAP (median [IQR]), mm Hg	136 [124–148]	140 [125–150]	.269
Baseline DAP (median [IQR]), mm Hg	76 [70–83]	77 [70–83]	.867
ASA physical status classification (%)			.083
I	1 (0.3)	2 (2.0)	
II	69 (17.4)	11 (11.1)	
III	289 (73.0)	74 (74.7)	
IV	37 (9.3)	12 (12.1)	
Intraoperative characteristics			
Open aortic surgery (%)	42 (10.6)	19 (19.4)	.029
Endovascular aortic repair (%)	145 (36.6)	44 (44.4)	.187
Peripheral vascular surgery (%)	147 (37.1)	26 (26.3)	.056
Carotid surgery (%)	62 (15.7)	11 (11.1)	.326
General anesthesia (%)	134 (33.8)	42 (42.4)	.139
Regional anesthesia (%)	288 (72.7)	71 (71.7)	.940
Duration of anesthesia (median [IQR]), min	255 [188–330]	310 [238–404]	<.001
Hemorrhage (median [IQR]), mL	200 [50–400]	300 [100–737]	.006
Lactate max (median [IQR]) $mmol.L^{-1}$	0.80 [0.60–1.20]	0.90 [0.70–1.58]	.036
Postoperative characteristics			
Creatinine (median [IQR]), $\mu mol.L^{-1}$	84 [69–102]	91.50 [76–126]	.003
Duration of stay in a High-dependency ward (median [IQR]), d	1 [1–1]	2 [1–2]	<.001
30-d mortality (%)	3 (0.8)	7 (7.1)	<.001

All results are presented as n (%), unless otherwise stated.

Abbreviations: ASA, American Society of Anesthesiologists; DAP, diastolic arterial pressure; PMI, perioperative myocardial injury; hs-cTnT, high-sensitivity cardiac Troponin T; IQR, interquartile range; MAP, mean arterial pressure; MET, metabolic equivalent of task; NT-pro BNP, N-terminal-pro-B-type natriuretic peptide; Preop, preoperative; SAP, systolic arterial pressure.

calculations, pandas for data preprocessing, sklearn for ML, and matplotlib for visualization. R version 4.1.2 (R Core Team (2021) was also used in creating the Table. R: A language and environment for statistical computing, R Foundation for Statistical Computing).

RESULTS

A total of 498 patients were included. Of these, 3 patients had missing data for preoperative hs-cTnT and were therefore excluded. A further 98, 101, 96, and 88 patients were excluded in the SAP, MAP, DAP, and heart rate analysis, respectively, due to some missing data from the intraoperative period. A total of 397 patients were analyzed for SAP, 394 patients for MAP, 399 patients for DAP, and 407 patients for heart rate to determine thresholds for IOH and tachycardia, respectively (see **strengthening the reporting of observational studies in epidemiology** diagram, Figure 2; Supplemental Digital Content 1, Appendix A, Tables A1–A4, http://links.lww.com/AA/F163).

Perioperative Characteristics

Perioperative characteristics are presented in the Table. No significant difference was noted between the group with and without PMI regarding preoperative characteristics except for age, which was higher in group PMI. No other significant differences in comorbidities were seen between the groups in the total cohort (n = 495). However, there were significantly more patients with stroke/transient ischemic attack and a higher American Society of Anesthesiologists (ASA) class in the PMI group when studying only patients included in the analysis of SAP, MAP, DAP, and heart rate (Supplemental Digital Content 1, Appendix A, Tables A1–A4, http://links.lww.com/AA/F163). Regarding intraoperative characteristics, a greater number of patients underwent open aortic surgery in the PMI group and the duration of anesthesia was longer and bleeding was more common. Furthermore, patients in the PMI group had higher postoperative creatinine, stayed longer in a high-dependency ward, and had higher 30-day mortality.

Associations Between Thresholds for Both IOH and Tachycardia, and PMI

The associations and correlations between the patients' total "dose" using different absolute IOH thresholds (based on SAP, MAP, and DAP) and PMI are shown in Figures 3 and 4, exact values are presented in Supplemental Digital Content 1, Appendix A, Tables A5 and A6, http://links.lww.com/AA/F163. Most absolute thresholds based on MAP and DAP, but not SAP, were significantly associated with PMI. DAP-based absolute thresholds were most strongly correlated with PMI, with the strongest correlation and statistical significance observed at a DAP <46 mm Hg (correlation = 0.164, P = .021). When comparing relative thresholds, based on a drop in blood pressure from a preoperative baseline value, more SAP and DAP-based thresholds were significantly associated with PMI, see Figures 3 and 4. The SAP-based threshold and DAP-based threshold with a 50% drop from baseline were most strongly correlated with PMI and yielded a greater statistical significance (correlation = 0.119, P = .044 and correlation = 0.119, P = .043, respectively) compared to other relative thresholds. When comparing the results from both absolute and relative

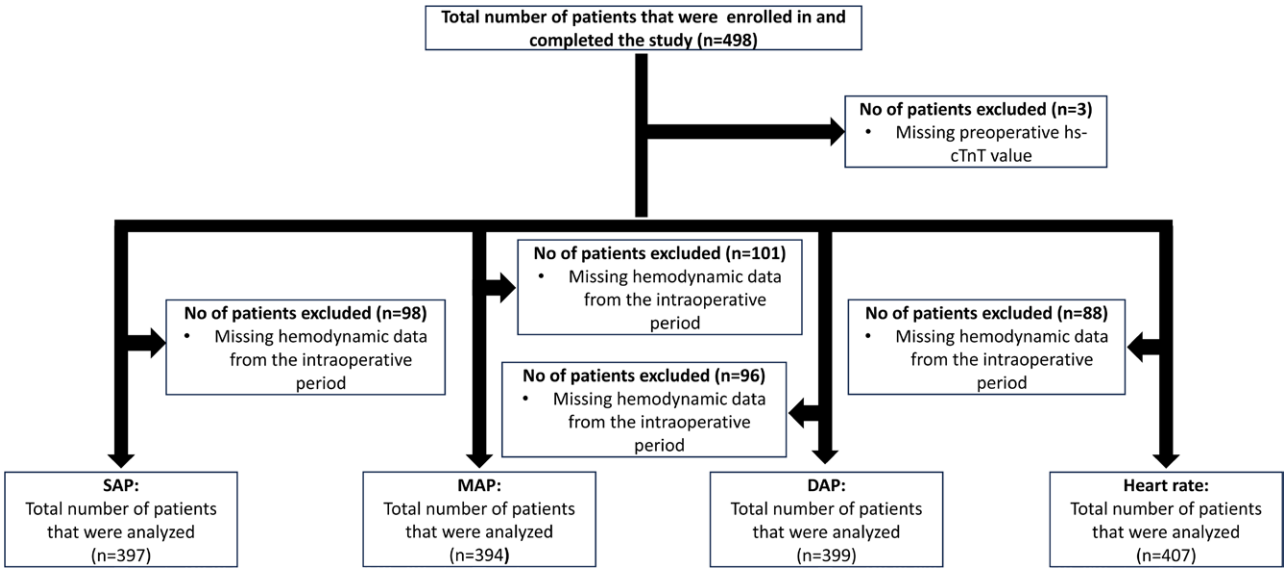


Figure 2. STROBE diagram. DAP indicates diastolic arterial pressure; HR, heart rate; hs-cTnT, high-sensitivity cardiac Troponin T; MAP, mean arterial pressure; SAP, systolic arterial pressure; STROBE, strengthening the reporting of observational studies in epidemiology.

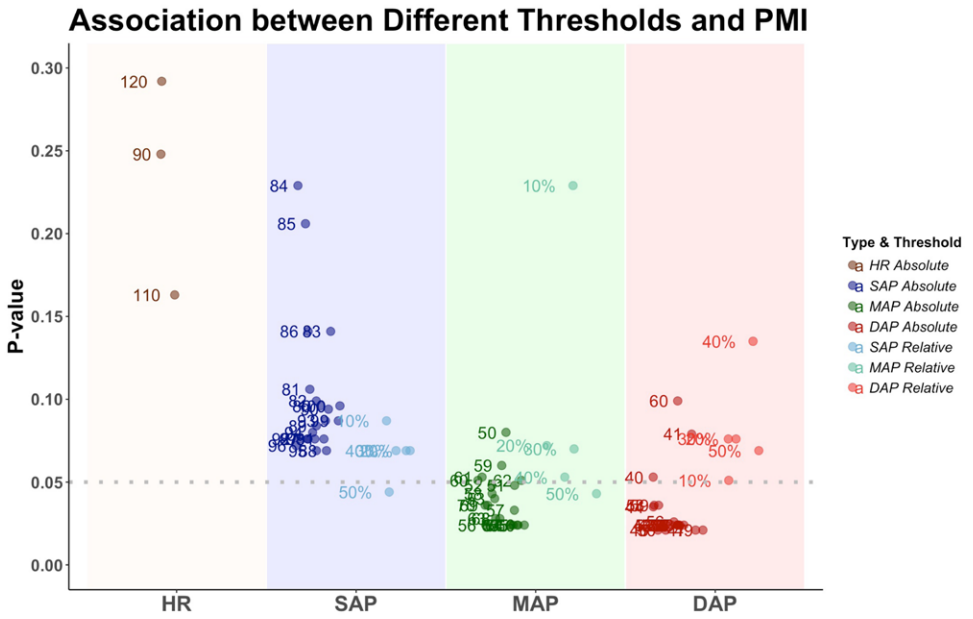


Figure 3. The association between the total "dose" using different thresholds for both intraoperative hypotension (both absolute and relative drop from baseline) and tachycardia, and PMI. A hypotensive event based on an absolute threshold (in mm Hg) is defined as a drop in blood pressure below the above-mentioned threshold for >1 min. A hypotensive event based on a relative threshold is defined as a % fall in blood pressure (10%, 20%, 30% …%) below baseline blood pressure for >1 min. A tachycardia event is defined as an increase in heart rate (in beats per minute) above a certain threshold for >1 min. *P*-values: Calculated using the Kruskal-Wallis test. *P*-values are adjusted for multiple testing using the Benjamini and Hochberg procedure. The dotted line represents the alpha level of .05. *P*-values for absolute HR > 80 and 100 were 0.51 and 0.93, respectively. They were excluded because they were outliers. DAP indicates diastolic arterial pressure; HR, heart rate; MAP, mean arterial pressure; PMI, perioperative myocardial injury; SAP, systolic arterial pressure.

thresholds, DAP-based absolute thresholds had the strongest correlation with PMI and yielded the greatest statistical significance, which can be visualized in Figures 3 and 4. No significant association was found between any threshold for tachycardia and PMI, see Figures 3 and 4 (exact values are presented in Supplemental Digital Content 1, Appendix A, Table A7, http://links.lww.com/AA/F163). The distribution of PMI was calculated for patients with IOH for each threshold of DAP (Supplemental Digital Content 1, Appendix A, Table A8, http://links.lww.com/AA/F163). The incidence of tachycardia, calculated for each threshold, is shown in Supplemental Digital Content 1, Appendix A Table A9, http://links.lww.com/AA/F163, and provides context for the negative results.

Prediction of PMI Using Machine Learning

Amongst all the preoperative and intraoperative features presented in the Table, preoperative hs-cTnT, age, and ASA were most predictive of PMI. These features were combined with every individual threshold for IOH and tachycardia (described above) one by one to define different decision tree models for predicting PMI. The models that performed best were the ones based on absolute thresholds for IOH. Furthermore, models based on absolute thresholds for DAP performed better than those based on MAP and SAP. Universally, in all models explored, preoperative hs-cTnT was the best predictor of PMI. Models combining tachycardia with other relevant predictors (preoperative hs-cTnT, etc) were not predictive of PMI. An attempt was made to create a reference model using the IOH threshold of MAP <65 mm Hg and tachycardia threshold of >100 BPM. However, none of these models were able to predict PMI well when tested on new unseen data. The best ML model found, where IOH had the highest feature importance, was one using an absolute DAP threshold of 44 mm Hg. The decision tree shows how each feature contributed to predicting PMI (see Figure 5A). The involvement of each feature in the decisions made within the decision tree model is shown as a percentage in Figure 5B. IOH was involved in approximately 5% of all the decisions made in the decision tree. ASA did not contribute to any of the decisions in the model. The performance of the model is presented in the confusion matrix (n = 81) in Figures 5C, 5D. The model had a macro average F1 score of 0.67. This score assigns equal importance to the model's ability to predict PMI as no PMI. The model had a weighted average F1 score of 0.76. This score assigns more importance to the model's ability to predict no PMI reflecting the imbalance between the proportion of patients with and without PMI in the study population. When the model predicted no PMI, it was correct 91% of the

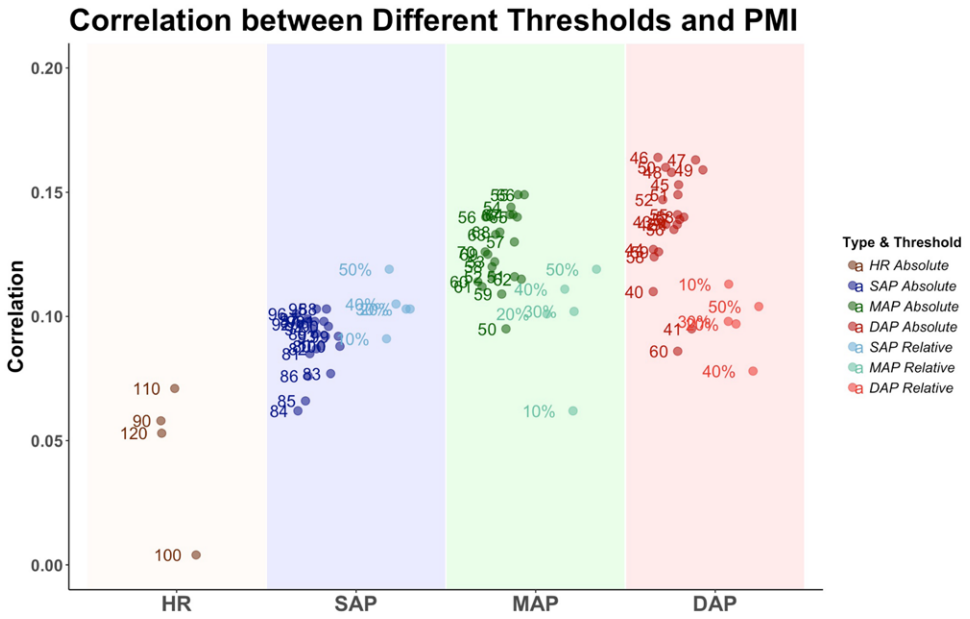


Figure 4. The correlation between the total "dose" using different thresholds for both intraoperative hypotension (both absolute and relative drop from baseline) and tachycardia, and PMI. A hypotensive event based on an absolute threshold (in mm Hg) is defined as a drop in blood pressure below the above-mentioned threshold for >1 min. A hypotensive event based on a relative threshold is defined as a % fall in blood pressure (10%, 20%, 30%…%) below baseline blood pressure for >1 min. A tachycardia event is defined as an increase in heart rate (in beats per minute) above a certain threshold for >1 min. Correlations: calculated using Spearman's correlation. #Correlation for absolute HR > 80 was −0.03. It was excluded because it was an outlier. DAP indicates diastolic arterial pressure; HR, heart rate; MAP, mean arterial pressure; PMI, perioperative myocardial injury; SAP, systolic arterial pressure.

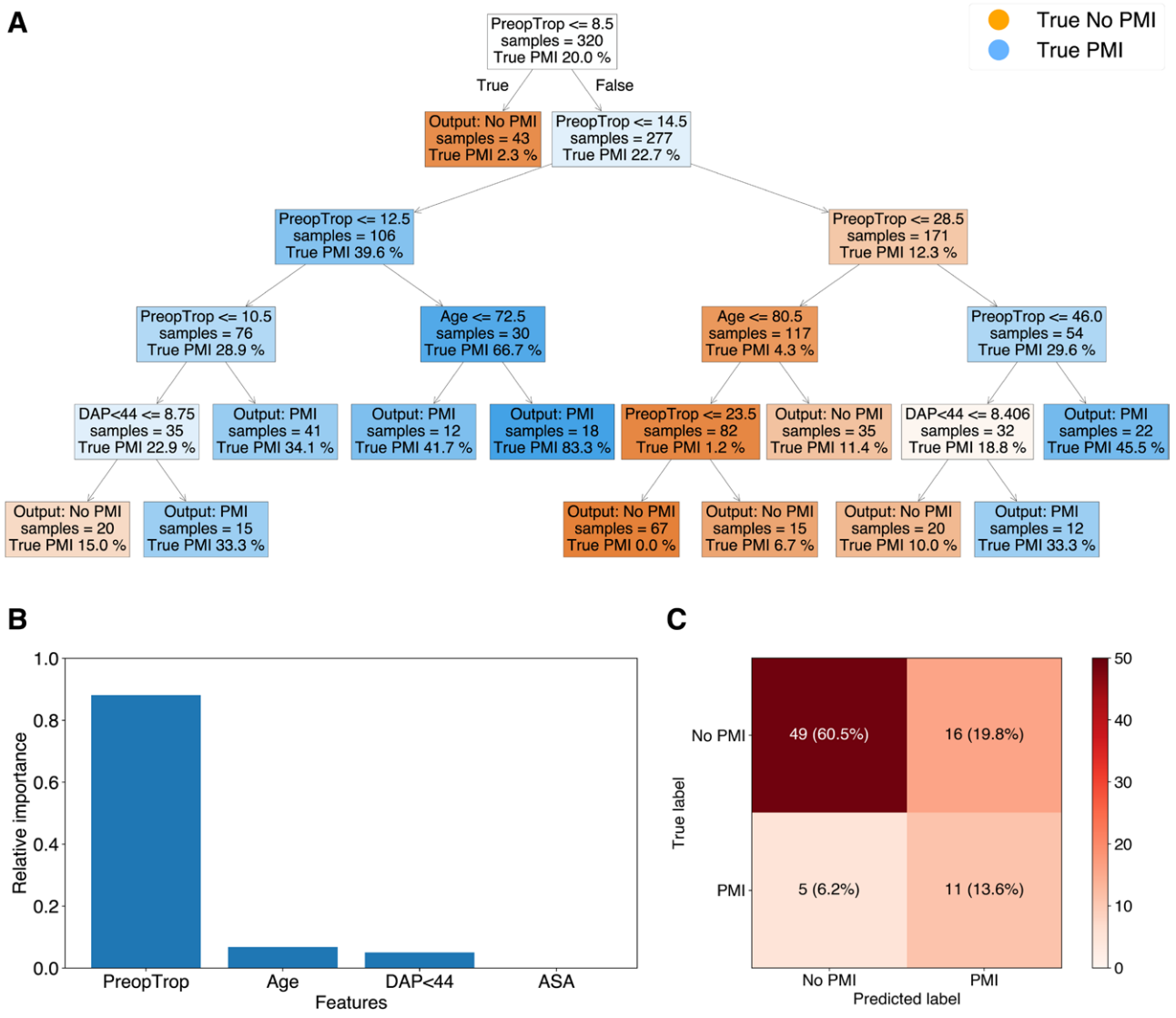
time (precision). Among the actual patients with no PMI, the model identified 75% of them (recall). When the model predicted a PMI, it was correct 41% of the time (precision). Among the actual patients with PMI, the model could identify 69% of episodes (recall/sensitivity).

DISCUSSION

We found that absolute thresholds for IOH were more consistently associated with PMI as opposed to relative thresholds (change in blood pressure from baseline). We also found that absolute thresholds based on diastolic blood pressure were more strongly correlated with PMI than systolic or MAP. Furthermore, we found that an absolute DAP <44 mm Hg was most predictive of PMI. However, we found no significant association between tachycardia and PMI.

To come to a generalizable and consistent conclusion, we first need to come to an agreeable definition of PMI and IOH. Unfortunately, the definition of PMI is inconsistent in the literature.[6–8] Some studies use postoperative values of hs-cTnT to define myocardial injury while others use a change from preoperative to postoperative values.[6,8] It has been shown that patients with an acute on chronic myocardial injury have the highest mortality.[8] However, approximately 40% of patients undergoing vascular surgery have preoperative hs- cTnT >14 ng·L^{-1}, which makes the diagnosis of PMI indefinite without preoperative values.[18] Additionally, it is recommended that high-sensitivity troponin assays be used to determine PMI.[19] However, previous trials studying the relationship between IOH and PMI have rarely used hs-cTnT assays and have not defined PMI as a *change* in troponin between the preoperative and postoperative values.[4,15,20]

Regarding IOH, although its relationship with PMI is well established, thresholds for IOH that are associated with PMI vary considerably.[3] Furthermore, it has been shown that relative thresholds are not more predictive of PMI compared to absolute thresholds.[21] In a recent study, the authors found that the magnitude of the drop in pressure was more predictive of PMI than the duration of the hypotensive event.[22] However, it remains unclear whether SAP, MAP, or DAP best predict PMI in the perioperative setting[3] and most studies have used IOH thresholds based on MAP.[4,15,20] We found a greater correlation between DAP and PMI compared with MAP in the present study. This may be logical since coronary blood flow to the left ventricle occurs primarily during diastole,[23] and raises the question of whether DAP rather than MAP should be further evaluated in future randomized studies. We also found that the threshold for DAP that best predicted PMI was <44 mm Hg. This corresponds closely to thresholds that were most strongly correlated with PMI. Presumably, even lower thresholds should be more strongly correlated with and more predictive of PMI. However,



D

	Precision	Recall	F1-score
No PMI	0.91	0.75	0.82
PMI	0.41	0.69	0.52
Accuracy			0.74
Macro average	0.66	0.72	0.67
Weighted average	0.81	0.74	0.76

Figure 5. The best machine learning decision tree model found where intraoperative hypotension had the highest feature importance. A, The decision tree model. Orange is negative for PMI, and blue is positive for PMI. White represents a situation where the model is uncertain. The color gradient indicates the chance of predicting a positive or negative outcome, a more intense color indicates a higher chance and vice versa. B, The importance of each feature as determined by the decision tree model. C, The confusion matrix for the model. D, The performance of the model. The F1-score considers both precision and recall. DAP <44 indicates the absolute diastolic arterial pressure threshold of 44 mm Hg; PMI, perioperative myocardial injury; Preop trop, preoperative high-sensitivity cardiac Troponin T.

this was not reflected in our results, presumably because pressures below those thresholds were seldom observed.

ML models, that maximize predictive power, have previously been used to determine risk factors associated with PMI, using the model as a risk assessment

tool.[17,24] We opted to use a different approach, focusing on 2 specific risk factors for PMI (IOH and tachycardia) and using ML as a tool to visualize the relationship between the optimal thresholds and perioperative characteristics that were predictive of PMI. Therefore, we choose a white-box ML model that can easily be tracked and visualized in contrast to a black-box ML model that maximizes predictive power.

Previous studies have found that perioperative characteristics, such as preoperative troponin, are a more important variable in predicting PMI compared with intraoperative hemodynamic factors,[17,24] which was similar to our findings. It is possible, indeed likely, that a raised preoperative hs-cTnT combined with IOH sets the stage for an ischemic event, which may be critical in a group of patients undergoing vascular surgery. Therefore, aggressive intraoperative hemodynamic management would minimize the occurrence of IOH and thereby also PMI. The only preoperative characteristic, besides preoperative hs-cTnT, that differed between the groups was age. This difference was due to 12 patients who were younger than 45 years and who all had no PMI.

There are several different thresholds used to define tachycardia.[25] One study found no association between PMI and thresholds of 100 BPM or less.[3] However, other studies have shown an association between thresholds >100 BPM and PMI.[4,25] Despite having high-resolution data where even short episodes of tachycardia could be detected, we did not find any significant association between tachycardia and PMI.

One major strength of our study is that we used invasive arterial blood pressure monitoring in all patients. This is important since noninvasive techniques tend to underestimate the magnitude of the drop in pressure.[26] Moreover, we used high-resolution data where blood pressure and heart rate were registered frequently, every 15 seconds, in contrast to most other large trials.[4,15,20,27] This facilitated a more accurate estimation of the length and depth of each episode of IOH. Our primary focus was acute myocardial injury, which may be prevented by modifiable perioperative factors. Another strength of this study is the homogenous group of patients included who underwent vascular surgery and had a high prevalence of cardiovascular disease. Optimizing hemodynamic management in this group may be important in preventing PMI. There are some weaknesses in this study. We had to exclude many patients with missing hemodynamic data and lacking invasive arterial pressure monitoring. Another limitation is that we did not measure postoperative hs-cTnT at 48 hours in all patients since they were discharged home earlier, meaning that some cases of late onset of PMI may potentially have gone undetected. Finally, it is difficult to generalize our findings to patients undergoing other types of surgery.

In this exploratory prospective cohort study in patients undergoing vascular surgery with a high burden of cardiovascular comorbidities, we found that the optimal threshold to predict PMI was DAP <44 mm Hg for ≥1 minute. Using ML models, we demonstrated that DAP-based thresholds were consistently more predictive of PMI compared to SAP and MAP-based thresholds. An absolute threshold for IOH was superior to a relative threshold for predicting PMI. No association was found between tachycardia and PMI. Future studies should focus on further evaluating diastolic blood pressure thresholds in predicting PMI in other groups of patients undergoing nonvascular surgery. ■

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DISCLOSURES

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