ORIGINAL CLINICAL RESEARCH REPORT

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Preoperative Identification of Patient-Dependent Blood Pressure Targets Associated With Low Risk of Intraoperative Hypotension During Noncardiac Surgery

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BACKGROUND: Intraoperative hypotension (IOH) is strongly linked to organ system injuries and postoperative death. Blood pressure itself is a powerful predictor of IOH; however, it is unclear which pressures carry the lowest risk and may be leveraged to prevent subsequent hypotension. Our objective was to develop a model that predicts, before surgery and according to a patient's unique characteristics, which intraoperative mean arterial pressures (MAPs) between 65 and 100 mm Hg have a low risk of IOH, defined as an MAP <65 mm Hg, and may serve as testable hemodynamic targets to prevent IOH.

METHODS: Adult, noncardiac surgeries under general anesthesia at 2 tertiary care hospitals of the University of Pittsburgh Medical Center were divided into training and validation cohorts, then assigned into smaller subgroups according to preoperative risk factors. Primary outcome was hypotension risk, defined for each intraoperative MAP value from 65 to 100 mm Hg as the proportion of a value's total measurements followed by at least 1 MAP <65 mm Hg within 5 or 10 minutes, and calculated for all values in each subgroup. Five models depicting MAP-associated IOH risk were compared according to best fit across subgroups with proportions whose confidence interval was <0.05. For the best fitting model, (1) performance was validated, (2) low-risk MAP targets were identified according to applied benchmarks, and (3) preoperative risk factors were evaluated as predictors of model parameters.

RESULTS: A total of 166,091 surgeries were included, with 121,032 and 45,059 surgeries containing 5.4 million and 1.9 million MAP measurements included in the training and validation sets, respectively. Thirty-six subgroups with at least 21 eligible proportions (confidence interval <0.05) were identified, representing 92% and 94% of available MAP measurements, respectively. The exponential with theta constant model demonstrated the best fit (weighted sum of squared error 0.0005), and the mean squared error of hypotension risk per MAP did not exceed 0.01% in validation testing. MAP targets ranged between 69 and 90 mm Hg depending on the subgroup and benchmark used. Increased age, higher American Society of Anesthesiologists physical status, and female sexindependently predicted ($P < .05$) hypotension risk curves with less rapid decay and higher plateaus.

CONCLUSIONS: We demonstrate that IOH risk specific to a given MAP is patient-dependent, but predictable before surgery. Our model can identify intraoperative MAP targets before surgery predicted to reduce a patient's exposure to IOH, potentially allowing clinicians to develop more personalized approaches for managing hemodynamics. (Anesth Analg 2023;136:194–203)

KEY POINTS

- **Question:** Blood pressures commonly maintained during noncardiac surgery possess inherently different risks of intraoperative hypotension (IOH); can those with the lowest risks be predicted before surgery to reduce exposure to intraoperative hypotension?
- **Findings:** Using 7.3 million intraoperative blood pressure measurements from 166,091 surgeries, we developed an IOH prediction model, which showed that IOH risk is patient-dependent, but predictable preoperatively using an exponential decay algorithm.

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- **Meaning:** Our model identifies, before surgery and according to a patient's individual characteristics, which intraoperative mean arterial pressures (MAPs) between 65 and 100 mm Hg possess a low risk of hypotension, thus predicted to reduce IOH compared to others in this clinically acceptable range, potentially allowing clinicians to develop more personalized approaches for managing hemodynamics.

GLOSSARY

ASA = American Society of Anesthesiologists; **CI** = confidence interval; **HPI** = hypotension prediction index; **INPRESS** = Intraoperative Norepinephrine to Control Arterial Pressure; **IOH** = intraoperative hypotension; **MAP** = mean arterial pressure; **SE** = squared error; **SSE** = sum of squared errors; **TRIPOD** = transparent reporting of a multivariable prediction model for individual prognosis or diagnosis; **UPMC** = University of Pittsburgh Medical Center

Intraoperative hypotension (IOH) in noncardiac surgery is a major risk factor for organ system injuries and postoperative death.[1,2] Mean arterial pressure (MAP) values of <65 mm Hg are typically used to define IOH and are strongly associated with poor postoperative outcomes.[3–8] Clinically, IOH is avoided by attempting to maintain pressures above these levels; however, a wide range of pressures are possible whose risks of adverse events or poor outcomes are poorly differentiated,[9] making it unclear if one pressure, or a particular range of pressures, should be maintained over others.

Growing evidence demonstrates that blood pressure itself is a powerful predictor of IOH, suggesting individual pressures have distinct risks that impact a patient's hypotension exposure.[10–13] The hypotension prediction index (HPI) is a novel algorithm that uses the arterial pressure waveform to accurately predict IOH up to 15 minutes before it occurs.[10,11] In a gradient boosting machine-learning model predicting postinduction hypotension, the initial MAP was most critical to accurate prediction compared to other physiological features,[12] while preinduction systolic blood pressure is an independent risk factor for IOH.[13] Despite these advances, the IOH risk associated with individual intraoperative blood pressures in a patient remains undefined. If defined, new blood pressure targets can be identified as those that (1) do not constitute IOH per se and (2) possess a low risk of subsequent IOH occurrence. Targets would then represent blood pressure(s) with the lowest overall IOH risk for patients during surgery.

A new predictive model, designed to perform preoperatively, will allow risk information to be assessed before surgery unlike HPI and similar models that are used intraoperatively. Here, we generate a preoperative MAP-IOH risk model by first comparing a pool of candidate models according to their fit across a wide range of patient subgroups, each characterized by unique IOH risk factors. The primary outcome was to define the IOH risk associated with individual intraoperative MAP values between 65 and 100 mm Hg, a range including common, clinically acceptable blood pressures with poorly differentiated risks. The best fitting model was selected for performance validation using a time-separated dataset. Finally, MAP targets associated with low IOH risk were identified for each patient subgroup using absolute and historical risk benchmarks.

METHODS

Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines were followed, where applicable, in this article.[14] The institutional review board at the University of Pittsburgh approved this study and waived the informed consent requirement. The R statistical software (R Foundation for Statistical Computing, version 3.5.3, Austria) was used for all described analyses.[15]

Study Population

Patients' age 18 years or older undergoing noncardiac surgery with general anesthesia at the University of Pittsburgh Medical Center (UPMC) Presbyterian and UPMC Montefiore hospitals between June 2011 and August 2020 were selected for study.

Training and Validation Datasets

Data from the following variables were extracted from the Cerner electronic health record system for each study surgery: patient age, American Society of Anesthesiologists (ASA) physical status, sex, emergent surgery, primary surgical procedure, and intraoperative MAP with measurement timestamp. MAPs <10 and >250 mm Hg were considered artifacts and removed. This range was selected to maximize the amount of MAP data available for analysis and eliminate possible artifacts based on MAP value alone. MAPs in the dataset were derived from both invasive and noninvasive monitoring techniques. When an

MAP measurement existed for both techniques at the same minute in time, the invasive measurement was used. MAPs are not recorded in our Cerner system more frequently than once per minute. The total dataset was divided into 2 sets before analysis. Data from June 2011 to March 2018 were dedicated to model training and selection, and data from April 2018 to August 2020 were dedicated to performance validation. A larger fraction of the data was used for training to maximize the MAPs used to evaluate and compare models. Development and validation data were time-separated to provide a more stringent evaluation of model performance that better mimics real-world testing than randomization.

Primary Outcome

The primary outcome was hypotension risk, defined for each intraoperative MAP value from 65 to 100 mm Hg as the proportion of a value's total measurements followed by at least 1 MAP <65 mm Hg within 5 minutes. MAPs between 65 and 100 mm Hg represent common pressures above an IOH threshold frequently applied in noncardiac surgery (65 mm Hg)[2,5,9] that are difficult to otherwise differentiate in real-world practice. To illustrate the calculation, if 100,000 total 70 mm Hg measurements are evaluated and 15,000 of these were followed by an MAP <65 mm Hg, at any time, in their following 5-minute interval, the hypotension risk for 70 mm Hg would be 15% (15,000/100,000) (Supplemental Digital Content 1, Figure 1, http://links.lww.com/AA/E56). A 5-minute interval was selected because it distinguishes IOH risk following blood pressure measurement better than other (longer) intervals.[10,11]

Statistical Analysis

Descriptive statistics were generated for patient and procedure characteristics for both training and validation datasets. First, second (median), and third quartiles were calculated for continuous variables' patient age and MAP. Proportions were calculated for categorical variables' ASA physical status, emergency surgery, sex, and surgical specialty.

Development of MAP-IOH Risk Model

We sought to develop a model that predicts, before surgery and according to a patient's unique characteristics, the hypotension risk associated with each intraoperative MAP value from 65 to 100 mm Hg. Age, ASA physical status, sex, and emergent surgery are independent predictors of IOH[13] and were incorporated into the model. Each surgery in the training dataset was assigned a unique "subgroup ID" defined by emergency surgery (1-yes and 0-no), ASA physical status (I, II, III, IV, or V), sex (male/female), and age quartile. Age quartiles, defined as Q1 (18–42), Q2 (43–56), Q3 (57–66), and Q4 (>66 years old), were selected as a balance between distinguishing patients according to this risk factor, while maximizing the data available for analysis in each subgroup. Eighty unique subgroups are possible (2 [emergency] × 5 [ASA] × 2 [sex] × 4 [age groups] = 80 subgroups). Hypotension risk was calculated for each MAP value in each subgroup as described in the primary outcome. Only subgroups with at least 21 proportions whose confidence interval (CI) was <0.05 (ie, difference between upper and lower bounds that define the interval is <0.05) were included in model fitting to eliminate the effect of low confidence estimates. This cutoff was selected as a balance between maximizing the number of MAP inputs available for model fitting, while limiting the number of subgroup IDs and total MAP data excluded. Since the true relationship between MAP and IOH risk is unknown, multiple models were generated and compared with the best fitting model selected for validation. Evaluated models are listed below and for each y = Proportion of MAP *m* measurements followed by IOH, and x = MAP *m*, where *m* = single MAP value between 65 and 100 mm Hg.

1. $y = \beta x + alpha$ (linear)
2. $logit(y) = \beta x + alpha$ (logit)
3. $y = \alpha e\text{^}(\beta x)$ (exponential)
4. $y = \alpha x(\beta)$ (power)
5. $y = \alpha e\text{^}(\beta x) + \theta$ (exponential with theta constant)

Using the nls function in the "stats" package, the parameter values that minimized the sum of squared errors (SSE) for each subgroup were identified. The overall SSE for a model was determined by computing the weighted (by each subgroup's total number of MAP measurements) sum of SSEs for the best-fitting parameters for that model for each subgroup. Model fitness was given by this overall SSE; lower values represent better model fit.

Validation of MAP-IOH Risk Model

Performance of the best fitting model was tested using the validation dataset. MAP proportions were calculated, and subgroups selected as described above for training dataset. For each validation subgroup, the SSE was calculated using the fitted curve generated for that subgroup in the training dataset. To compare SSEs between training and validation sets, a subgroup's SSE was divided by its total number of proportions to yield an average squared error (SE) per MAP value.

Identification of MAP targets

MAP targets for each subgroup were identified in the training dataset using the best fitting model and according to absolute and historical risk benchmarks. Absolute benchmarks were defined as 5%, 10%, and 15% IOH risk and chosen to highlight subgroup differences. Historical benchmarks were defined for individual subgroups as the IOH risk calculated from all MAPs between 65 and 100 mm Hg, representing the overall risk associated with this blood pressure range. MAP targets were defined as the lowest MAP not to exceed benchmark risks.

Post Hoc Analyses

MAP-Associated IOH Risk According to Differences in Monitoring Frequency, Preceding Blood Pressure Trends, and Prior IOH Exposure. MAP is a standard monitor, but its measurement frequency varies between patients. MAPs followed by more subsequent MAPs are more likely to capture IOH compared to those followed by less. To evaluate this possibility, the number of MAPs recorded in the 5-minute interval used to calculate IOH risk was compared between MAP values 65 to 100 mm Hg in the training dataset. The first, second, and third quartiles were calculated and reported. In addition, the model's ability to capture IOH risk associated with multiple subsequent blood pressures was tested by comparing models generated with 5- and 10- minute intervals.

Factors that occur intraoperatively or whose effect on IOH risk is unclear (eg, surgical procedure, vasoactive medications, etc.) were not included in model development yet may still influence MAP-associated IOH risk. To compare MAP-associated IOH risk in instances where the preceding blood pressure is changing, MAPs in the training dataset were assigned as (1) increasing, (2) decreasing, or (3) unchanged according to the MAP that most immediately preceded it within the prior 10 minutes. For example, an MAP of 75 mm Hg would be assigned as "increasing" if the MAP before it was 72 mm Hg, but "decreasing" if that MAP's value was 78 mm Hg. Models comparing assignment groups were generated.

Finally, prior IOH may predict future IOH, and this may be reflected in the model where MAPs associated with the highest risk are also associated with the greatest prior IOH exposure compared to lower risk MAPs. To evaluate this possibility, MAPs in the training dataset were assigned into quartiles of exposure defined by the number of MAP <65 mm Hg that occurred before their measurement relative to all measurements. Models comparing exposure groups were generated.

IOH Risk Factors as Predictors of MAP-IOH Risk Curve Segments

Alpha, beta, and theta parameters modulate specific portions of the MAP-IOH risk curve as defined by the exponential with theta constant model. Alpha and theta define the y- and x-axis asymptotes, respectively, and beta defines how rapidly IOH risk changes across MAPs (ie, "sharpness" of the curve's elbow). To evaluate patient age, sex, emergent surgery, and ASA physical status as predictors of distinct portions of the curve, factors were analyzed as independent predictors of each parameter using the lm() function in "stats" package.

RESULTS

Training and Validation Datasets

A small fraction of surgeries (<0.3%) lacked intraoperative MAP data within 65 to 100 mm Hg, and these were excluded from the analysis. The patient and procedure factors characterizing the training and validation datasets are shown in the Table. Representing 121,032 surgeries, patients in the training set included majority men (53.9%) with a median age of 56 years old, assigned an ASA physical status III classification, and undergoing a general surgery procedure. Patients in the validation set, composed of 45,059 surgeries, exhibited the same characteristics, but with a median age of 58 years old. Emergent surgery represented 13.5% and 15.7% of all surgeries in each set, respectively. The training set contained 6,987,790 total MAP measurements with a median MAP of 80 mm Hg; 77.9% were between 65 and 100 mm Hg. The validation set contained 2,566,291 total MAP measurements with a median MAP of 81 mm Hg; 77.7% were between 65 and 100 mm Hg.

MAP-IOH Risk Model Development and Validation

Of 80 possible subgroups, 36 were identified in both datasets that contained at least 21 MAP proportions

Table. Patient and Procedure Characteristics in Training and Validation Datasets

Total surgeries N = 166,091		
Clinical demographic	**Training (n = 121,032)**	**Validation (n = 45,059)**
Age, y, median (Q1–Q3)	56 (43–67)	58 (43–68)
ASA physical status I (%)	3.6	3.8
II	29.2	21.5
III	51.2	51.9
IV	15	21.7
V	0.8	0.9
Emergency surgery(%)	13.5	15.7
Male gender (%)	53.9	56.7
Surgical specialty (%)	General (24.3)	General (21.5)
	Neurological (18.7)	Orthopedic (18.7)
	Orthopedic (18.0)	Neurological (17.2)
	Thoracic (9.8)	Thoracic (10.6)
	Otolarynology (9.2)	Otolaryngology (6.5)
MAP, mm Hg, median (Q1–Q3)	80 (72–91)	81 (72–92)
Total MAP measurements	6,987,790	2,566,291
Total MAPs between 65 and 100mm Hg (% of total measurements)	5,449,316 (77.9)	1,994,869 (77.7)

Abbreviations: ASA, American Society of Anesthesiologists; MAP, mean arterial pressure; Q, quartile.

with CI <0.05, termed "high-confidence" proportions (Supplemental Digital Content 2, Table 1, http://links.lww.com/AA/E57). Only these subgroups were used for model development and validation. Subgroups represented 76.5% and 88.5% of all high-confidence proportions and 92.2% and 94.0% of total MAP measurements between 65 and 100 mm Hg in training and validation sets, respectively. Figure 1 shows the best fitting model, the exponential with theta, plotted against both training and validation datasets in selected subgroups. IOH risk exponentially decreases as MAP increases from 65 mm Hg before plateauing at higher MAPs. The rate of exponential decrease, the MAP at which risk plateaus, and the risk associated with individual MAP values depends on model parameters (alpha, beta, and theta) that define the fitted curve for each subgroup. The exponential with theta model demonstrated a weighted SSE of 0.0005, the lowest of all models tested, while the linear model demonstrated the poorest fit with a weighted SSE of 0.0998 (Figure 1). Across all subgroups, the average SE per MAP value did not exceed 1.0 × 10E5 in the training set, which the model was fitted, and 1.0 × 10E4 in the validation set (Supplemental Digital Content 3, Table 2, http://links.lww.com/AA/E58).

MAP Targets

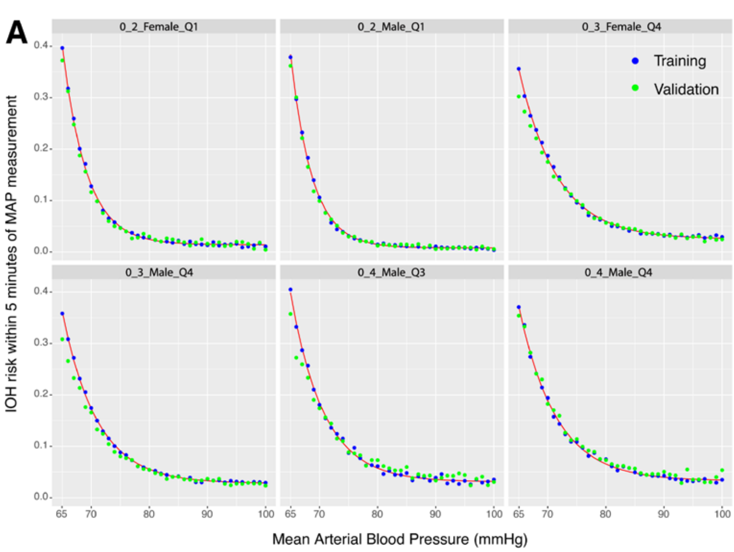
MAP targets, the minimum MAP with lower IOH risk than applied risk benchmarks, are shown in Figure 2 for select subgroups; all targets are reported in Supplemental Digital Content 4, Table 3, http://links.lww.com/AA/E59. Targets vary from 69 to 90 mm Hg depending on subgroup and benchmark. For example, an MAP of 73 mm Hg is required to achieve <5% IOH risk in 0_1_Male_Q1 patients, but 90 mm Hg in 1_4_Male_Q4 patients. Historical risk benchmarks varied between 5.2% and 12.2%, and targets based on these extend from 72 to 77 mm Hg.

Figure 2 compares low-risk MAPs, identified with the 5% risk benchmark, between 0_1_Male_Q1 and 0_3_Male_Q4 patients. A wider range of MAPs are low risk in 0_1_Male_Q1 patients (73–100 mm Hg) compared to 0_3_Male_Q4 patients (82–100 mm Hg). An MAP of 80 mm Hg, well above 65 mm Hg IOH threshold, is considered low risk in the former subgroup (green dot), but high risk in the latter (red dot).

Post Hoc Analyses

The interquartile range for the number of MAPs recorded within the 5-minute interval following MAP measurement is uniform across all MAP values and shown in Supplemental Digital Content 5, Table 4, http://links.lww.com/AA/E60. Most MAPs were followed by 2 subsequent MAPs. All MAP values were associated with a higher IOH risk in a model generated with a 10-minute interval compared to the 5-minute interval model (Figure 3A), demonstrating that the model distinguishes IOH risk of multiple blood pressures following MAP measurement and beyond only those captured in a 5-minute period. The relative risk of a given MAP is similarly distinguished in each model.

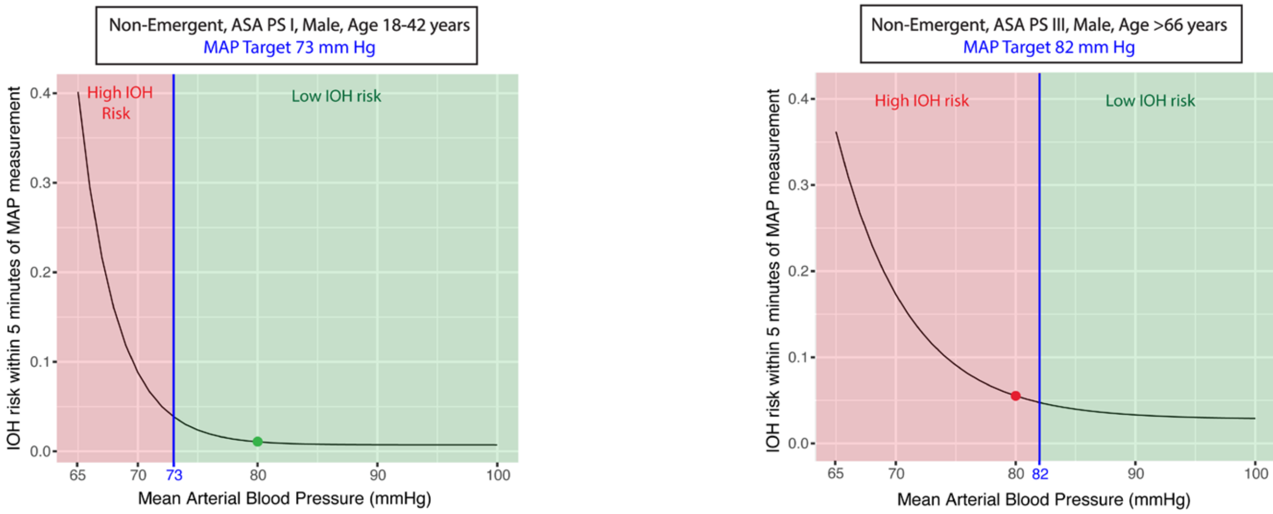
A



B

Model	Weighted SSE
Linear	0.09984
Logit	0.00803
Exponential	0.00550
Power	0.00386
Exponential with theta constant	0.00059

Figure 1. Selection and validation of exponential with theta model for MAP-associated IOH risk. A, Proportion of MAP value measurements followed by IOH within 5 minutes generated from the training dataset (blue dots) compared to that of the validation dataset (green dots) with model superimposed (red line). B, Exponential with theta model demonstrating lowest weighted SSE across 36 subgroups for all models tested. Subgroup definition: column 1 (emergent surgery, yes-1 and no-0), column 2 (ASA PS class I–IV), column 3 (sex male/female), and column 4 (age quartile, Q1–4). ASA indicates American Society of Anesthesiologists; IOH, intraoperative hypotension; MAP, mean arterial pressure; PS, physical status; SSE, sum of squared errors.



ID	IOH risk (5%), mmHg	IOH risk (10%), mmHg	IOH risk (15%), mmHg	Historical IOH risk	Historical target, mmHg
0_1_Male_Q1	73	70	69	5.2%	72
0_3_Male_Q4	82	75	72	8.6%	76
0_3_Female_Q3	81	75	72	8.3%	76
0_4_Female_Q4	86	77	73	10.5%	76
1_4_Male_Q4	90	77	73	12.2%	75

Figure 2. Identification of MAP targets in selected subgroups. High- and low-risk MAPs are distinguished by MAP target (blue line) representing the lowest MAP in each subgroup whose IOH risk is <5% risk benchmark. Low-risk MAPs are 73 to 100 mm Hg in male patients assigned ASA PS I classification between 18 and 42 years of age undergoing nonemergent surgery, while MAPs 82 to 100 mm Hg are low risk in male patients older than 66 years of age assigned ASA PS III classification undergoing nonemergent surgery. MAP of 80 mm Hg is identified as both low (green dot) and high risks (red dot). Targets can be defined according to both absolute and historical risk benchmarks. Subgroup definition: column 1 (emergent surgery, yes-1 and no-0), column 2 (ASA PS, I–IV), column 3 (sex, male/female), and column 4 (age quartile, Q1–4). IOH indicates intraoperative hypotension; MAP, mean arterial pressure; PS, physical status; Q, quartile.

Models comparing MAP-associated IOH risk between different preceding MAP trends and IOH exposures are shown in Figure 3B, C, respectively. Preceding MAP increases and decreases are associated with higher IOH risks across all MAP values compared to no change. For MAPs 65 to approximately 85 mm Hg, an increasing trending is associated with larger risk than decreasing or no change trends. The maximum difference at any given MAP is <10% and decreases at both ends of the MAP range. The MAP-IOH risk changes little between prior IOH exposure groups. MAPs with the highest prior exposure are associated with no more than 2% greater risk at any MAP value compared to MAPs with other exposures and whose risk curves are poorly distinguished from one another.

Age, sex, and ASA physical status are independent predictors of the beta model parameter, whereas only age and ASA physical status are independent predictors of the theta parameter (Figure 4). Alpha and beta parameters are tightly correlated (>0.99), and alpha shared the same predictors as beta (data not shown). These differences are exemplified in MAP-IOH risk curves between subgroups that vary by a single characteristic.

DISCUSSION

We developed a preoperative prediction model to distinguish intraoperative MAP according to their risk of IOH and identify low-risk pressures before surgery. MAP targets were identified in 36 patient subgroups, each characterized by a unique combination of IOH risk factors. Our major findings are (1) MAP-associated IOH risk exhibits an exponential decay relationship where the rate of risk change increases as values approach 65 mm Hg, (2) MAP targets for reducing risk of IOH range from 69 to 90 mm Hg depending on subgroup and applied risk benchmark, and (3) risk curve segments (plateau and exponential) and their transition are defined by 2 parameters, beta and theta, that are individually predicted by different patient factors.

Our findings have several important implications. First, the model differentiates a wide range of clinically acceptable blood pressures according to individual patient factors before surgery. Clinicians can now identify more patient-specific blood pressures as hemodynamic targets predicted to reduce IOH exposure compared to maintaining MAPs above 65 mm Hg, a common approach in clinical practice. In young, male patients assigned a lower ASA physical

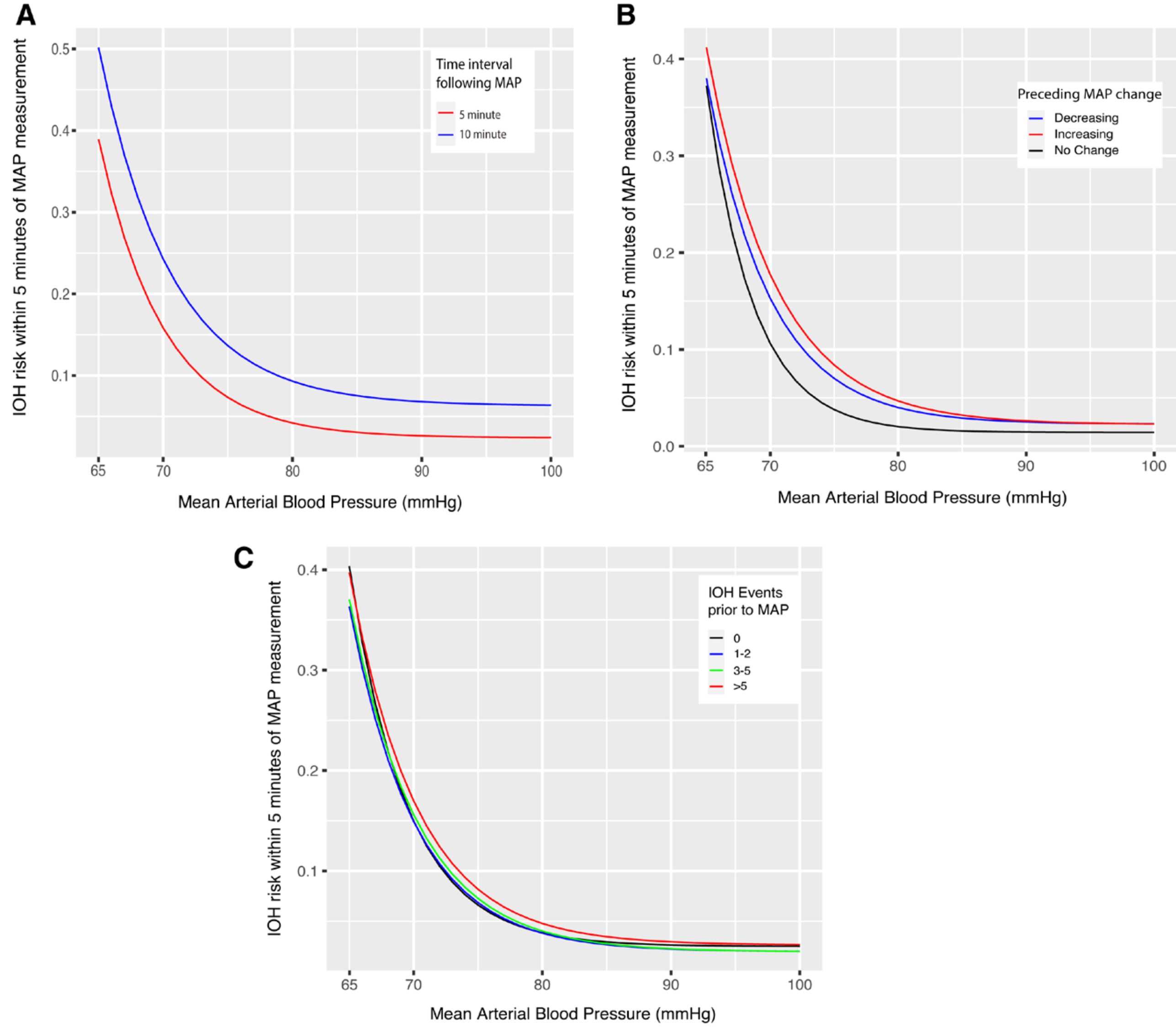


Figure 3. Models showing IOH risk associated with MAP values between 65 and 100 mmHg. Models compare time interval following MAP measurement (A), and MAP change (B) and IOH exposure preceding measurement (C). IOH, intraoperative hypotension; MAP, mean arterial pressure; Q, quartile.

status, IOH risk remains low until MAP nears 65 mm Hg, at which point it rapidly increases. In patients with higher risks, the exponential increase begins earlier, at a higher MAP and from a higher plateau, suggesting these patients require greater clinical vigilance to anticipate/treat IOH events even when MAPs are well above 65 mm Hg. This is particularly notable considering patients with elevated preoperative risks appear to be the most susceptible to IOH-induced end-organ injury and those likely to benefit most from strategies that reduce exposure.[16]

Declining autonomic nervous system function may help explain differences between subgroups. Women exhibit less sympathetic tone than men,[17,18] and heart rate variability, an established surrogate for autonomic function, declines with increasing age[19] and disease burden.[20,21] Deficits in autoregulation secondary to chronic hypertension and peripheral vascular disease may require higher MAPs to maintain adequate perfusion to avoid risks associated with IOH, consistent with our findings. Emergency surgery, perhaps more indicative of clinical decision-making than patient physiology, was not identified as an independent predictor of model parameters.

Second, we note that small differences in blood pressure translate to large differences in IOH risk, particularly at MAP nearest 65 mm Hg. An MAP of 70 mm Hg was associated with nearly a 4-fold greater risk, on average across all subgroups studied, than 80 mm Hg (16.1 vs 4.6%, data not shown), despite both being within acceptable limits recommended by current perioperative guidelines.[9] Prospective, randomized trials evaluating the effect of blood pressure interventions on IOH or its associated

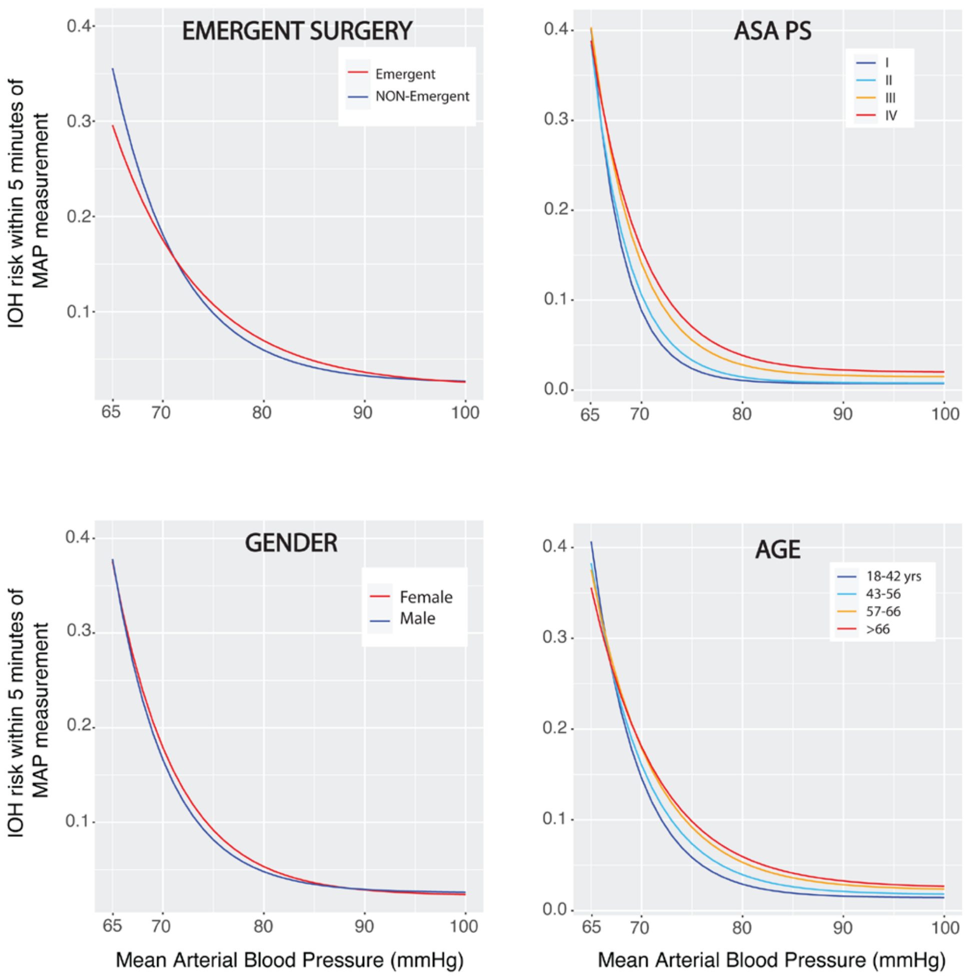


Figure 4. Patient and procedure predictors of model parameters. Models for select subgroups that vary by single patient/procedure characteristic: Emergent surgery: emergent and non-emergent surgery in patients who were female, ASA PS III, and >66-y old. ASA physical status: ASA PS I–IV in patients who were male, between the age of 18 and 42 y old, and undergoing nonemergent surgery. Sex: male and female patients who were ASA PS III, between the age of 57 and 66 y old, and undergoing nonemergent surgery. Age: age quartiles in patients who were female, ASA PS III, and undergoing nonemergent surgery. Table displays linear regression analysis of age, sex, ASA PS, and emergent surgery on beta and theta parameters. ASA indicates American Society of Anesthesiologists; IOH, intraoperative hypotension; MAP, mean arterial pressure; PS, physical status; SSE, sum of squared error.

Parameter	Predictor	Coefficient	SE	p-value	p<0.05
BETA	**Emergent**	0.018028	0.010392	9.00E-02	
	ASA PS	0.029669	0.005382	1.86E-06	*
	Male	-0.028225	0.009967	7.02E-03	*
	Age	0.021573	0.004606	2.83E-05	*
THETA	**Emergent**	0.000928	0.001383	5.06E-01	
	ASA PS	0.002965	0.000716	1.59E-04	*
	Male	0.002574	0.001327	5.89E-02	
	Age	0.003939	0.000613	8.74E-08	*

complications support our findings. The difference in MAP between the individualized versus standard management groups in the INPRESS (Intraoperative Norepinephrine to Control Arterial Pressure) trial was only 6 mm Hg (81 vs 75 mm Hg), yet patients with the slightly higher MAPs experienced 13.6% and 17.1% less postoperative organ dysfunction at 7 and 30 days, respectively.[22] Higher dose infusions of norepinephrine administered prophylactically to women undergoing cesarean delivery increased systolic blood pressure no more than 10 mm Hg, yet these patients experienced ~15% less IOH.[23] Prospective, randomized studies comparing outcomes of different blood pressure targets are limited, and our work provides well-motivated, testable targets for future studies that will provide much-needed evidence to support, or refute, early findings from the INPRESS trial and others.

Third, MAP targets represent relative, population-based risk metrics specific to IOH exposure. These characteristics must be considered to interpret our findings fairly and assess their clinical impact. Target MAPs do not indicate the "ideal" intraoperative blood pressures for individual patients. Baseline blood pressure and organ system autoregulation are not accounted for, but, certainly, play a role in any approach defining optimal pressures.[24,25] Targets are relative to the benchmarks used to generate them, and without a universal benchmark, strong clinical motives should support any benchmark applied.

Historical benchmarks, for example, may be leveraged to identify which MAPs are lower risk compared to past surgeries' overall risk. Interestingly, an MAP of 77 mm Hg was associated with less risk than each subgroup's calculated historical benchmark, which ranged between 5.2% and 12.2%, and reflects not only the specific subgroups analyzed but also our institution. A different target may exist for different patients cared for at other hospitals. MAP targets offer clinicians the unqualified advantage of identifying which MAPs, within a broadly acceptable range, are low risk for subsequent IOH, thus providing valuable information for hemodynamic management.

Our study offers several strengths. Both training and validation datasets were sufficiently large to allow generalizability of our findings and assess model performance across many distinct patient types. Multiple models (including both linear and nonlinear) were evaluated to identify a high-quality model with excellent fitness. The average SE per MAP value was less than 1 × 10E4 for all subgroups even in validation testing, which used time-separated data from those for model development, a more stringent approach to test performance than simple randomization. The exponential with theta model provides a necessary structure to examine effects of future factors that may be of interest, like heart failure or medication administration, on MAP-IOH risk by accounting for known risk factors and providing 3 model parameters that uniquely modulate risk but can be influenced separately. Our model may be applied to alternate IOH definitions (eg, MAP < 55 mm Hg), which is critical considering a universal definition may not exist across all patients and different organ system injuries. By distinguishing IOH risk of multiple blood pressures, up to 10 minutes following MAP measurement, our model predicts IOH exposure defined by more than single depressions below 65 mm Hg, a feature with clinical impact as IOH-associated complications are dose-dependent. The IOH threshold of 65 mm Hg and 5- or 10-minute interval to assess IOH risk following MAP measurement are aspects of our approach coming from strong experimental precedent involving multiple, high-impact studies.[1,9–11,26]

The present study has the following limitations. Of the 80 subgroup IDs that were possible, we generated and validated models for 36 due to challenges in estimating IOH risk with sufficient confidence for enough MAP values in the others. Twenty-one, high-confidence proportions were required for a subgroup to be included in the analysis, limiting our conclusions on certain types of patients who may be better represented in different clinical settings or present infrequently for surgery (ASA physical status V). It is unlikely these criteria, however, impacted our broader findings given (1) 21 represents the majority of possible proportions and only 2 subgroups had this minimal number, (2) models depicting the relationship between MAP and IOH risk were compared using the same subgroups and proportions, and (3) excluding less-confident risk estimates allows only stronger conclusions to be made on the models that were generated. Only known preoperative IOH risk factors were incorporated into the model, others whose influence on risk is not well-established were not included. MAP-associated IOH risk changes with ASA physical status, presumably because it captures differences in patient comorbidities that impact risk. Classifications are, in part, subjective, and we did not attempt to verify these data, which can be challenging in large, retrospective studies. Charlson Comorbidity Index is more objective, but incompatible with a subgroup approach because 2 patients with the same index can have very different underlying comorbid conditions, making any resulting model less precise. Furthermore, patients undergoing gynecological and urological surgeries were not part of the dataset and are a limitation of the data analysis. We did not incorporate procedure type into our model because it is unclear how to group individual procedures according to their potential impact on IOH risk, despite recognizing differences in blood loss, fluid shifts, and time to complete a likely impact. Taken together, models for different, or more specific, patient groups are possible with sufficient data, but given the high performance of our general models across the 36 diverse patient subgroups tested, these are unlikely to change our main findings that IOH risk decreases exponentially as MAP increases from 65 to 100 mm Hg, and low-risk targets can be identified by capitalizing on these differences.

In summary, MAPs commonly seen during noncardiac surgery have uniquely associated IOH risks that are predictable before surgery and across widely different patient groups. Differences can be used to identify MAPs that may be favored as hemodynamic targets since they are less likely to produce IOH, and therefore, favored over others that simply meet traditional threshold criteria but have a higher risk of IOH.

DISCLOSURES

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