OPEN

NARRATIVE REVIEW ARTICLE

Intraoperative Hypotension Prediction: Current Methods, Controversies, and Research Outlook

Ramakrishna Mukkamala, PhD,*† Michael P. Schnetz, MD, PhD,* Ashish K. Khanna, MD, MS,‡§ and Aman Mahajan, MD, PhD, MBA*†

See Article, page 1

Intraoperative hypotension prediction has been increasingly emphasized due to its potential clinical value in reducing organ injury and the broad availability of large-scale patient datasets and powerful machine learning tools. Hypotension prediction methods can mitigate low blood pressure exposure time. However, they have yet to be convincingly demonstrated to improve objective outcomes; furthermore, they have recently become controversial. This review presents the current state of intraoperative hypotension prediction and makes recommendations on future research. We begin by overviewing the current hypotension prediction methods, which generally rely on the prevailing mean arterial pressure as one of the important input variables and typically show good sensitivity and specificity but low positive predictive value in forecasting near-term acute hypotensive events. We make specific suggestions on improving the definition of acute hypotensive events and evaluating hypotension prediction methods, along with general proposals on extending the methods to predict reduced blood flow and treatment effects. We present a start of a risk-benefit analysis of hypotension prediction methods in clinical practice. We conclude by coalescing this analysis with the current evidence to offer an outlook on prediction methods for intraoperative hypotension. A shift in research toward tailoring hypotension prediction methods to individual patients and pursuing methods to predict appropriate treatment in response to hypotension appear most promising to improve outcomes. (Anesth Analg 2025;141:61–73)

Intraoperative hypotension (IOH) is associated with risk of poor outcomes, including cardiac, renal, and central nervous system injuries, and death.[1–8] There is no universal definition for hypotension, but at a population level, the risk of poor outcomes increases as duration and depth below a mean arterial pressure (MAP) of 65 mm Hg increases in adults undergoing noncardiac surgery.[5,8–10] Predicting hypotensive events with early alert systems that signal impending low blood pressure (BP), allowing clinicians to apply therapeutic interventions to limit exposure (duration and depth), has been advocated to mitigate the poor outcome risks associated with hypotension.[11]

Methods for predicting hypotension are attractive as clinical decision support systems, because they can leverage machine learning tools trained with large, multi-variable datasets, including patient's individual characteristics, to maximize performance.[12,13] They offer clinicians new ways to assess the risk of poor outcomes with real-time monitoring[14] and/or identification of individualized hemodynamic targets.[15] These technologies provide the ability to transition from a reactive practice, where hypotension is treated after it occurs, to one where it is preemptively mitigated. Additionally, they could identify drivers of hypotension so precise interventions may be applied.

Several hypotension prediction methods offer not only predictive value, but also recently generated controversy. The objective of this review is to describe the current methods and their performance to date; make specific and general recommendations on future investigations; begin a risk-benefit analysis of these methods in clinical practice; and offer an outlook on IOH prediction in impacting care and informing new research.

2009 PHYSIONET CHALLENGE TO PREDICT ACUTE HYPOTENSIVE EVENTS

Interest in managing IOH has long existed, but the 2009 PhysioNet/Computing in Cardiology

From the *Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; †Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania; ‡Department of Anesthesiology, Section on Critical Care Medicine, Wake Forest University School of Medicine, Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, North Carolina; and §Outcomes Research Consortium, Houston, Texas.

Accepted for publication July 25, 2024.

Conflicts of Interest, Funding: Please see DISCLOSURES at the end of this article.

R. Mukkamala and M. P. Schnetz contributed equally as first authors.

Reprints will not be available from the authors.

Address correspondence to Aman Mahajan, MD, PhD, MBA, Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh, A-1305 Scaife Hall, Pittsburgh, PA 15261. Address e-mail to amahajan@pitt.edu.

DOI: 10.1213/ANE.0000000000007216

Challenge helped popularize hypotension prediction.[16] The motivation for this contest was: "… acute hypotensive episodes (AHEs) require effective, prompt intervention. Left untreated, such episodes may result in irreversible organ damage and death. Timely and appropriate interventions can reduce risks."[16] The goal of the contest was thus to predict AHEs using routine measurements, as shown in Figure 1. The precise problem statement was to predict an AHE defined as MAP <60 mm Hg for at least 27 minutes in a 30-minute period. Data comprising AHEs and nonevents (NEs) were drawn from the popular Medical Information Mart for Intensive Care (MIMIC) database. The winning methods simply leveraged invasive MAP close to the prediction window to successfully forecast the occurrence of events 15 minutes beforehand with around 80% sensitivity and 80% specificity but low positive predictive value.[17,18] Although focused on hypotension occurring in the intensive care unit (ICU), many of the current concepts and results, including in the operating room (OR) setting, stem from, were anticipated by, or are similar to this contest.

CURRENT HYPOTENSION PREDICTION METHODS AND THEIR PERFORMANCE

Various hypotension prediction methods have been proposed. Although hypotension etiology is crucial, most, if not all of the methods, predict hypotension of any cause and are evaluated in terms of all-cause hypotension prediction.

Hypotension Prediction Index Method

Due to its commercial availability, the Acumen Hypotension Prediction Index (HPI) method[14,19] is the most investigated hypotension prediction method. Created by Edwards Lifesciences, this method has helped to develop and promulgate hypotension prediction beyond the PhysioNet Challenge.

Figure 2A shows the HPI method. The current 20-second interval of a BP waveform is analyzed to predict an AHE—defined as consecutive 20-second intervals of MAP <65 mm Hg for at least 1 minute—within 15 minutes in the future. More specifically, a logistic regression model takes 23 proprietary features of an invasive or noninvasive BP waveform as input, then outputs a unit-less value between 0 and 100, where higher numbers indicate heightened risk of impending hypotension. The suggested decision threshold is 85, which means that hypotension is predicted to be imminent when HPI exceeds 85 but not a near-term concern when HPI is <85. Note that, as with any hypotension prediction method, the course of action in response to the early hypotension warning could be increased attention if not a therapeutic intervention, though suggestions for the etiology of hypotension are made by the system. The model was built based on invasive BP waveforms from over 1000 ICU patients and nearly 700 OR patients, with several different hypotension etiologies.

In the initial studies of the HPI method,[14,19,21] an NE was defined as consecutive 20-second intervals of MAP >75 mm Hg for at least 15 minutes, whereas periods of MAP between 65 and 75 mm Hg were considered as a "gray zone" and excluded as events in the evaluation. This gray zone designation makes sense, because MAP values modestly higher than 65 mm Hg could still compromise organ perfusion in select patients. These initial studies assessed the ability of

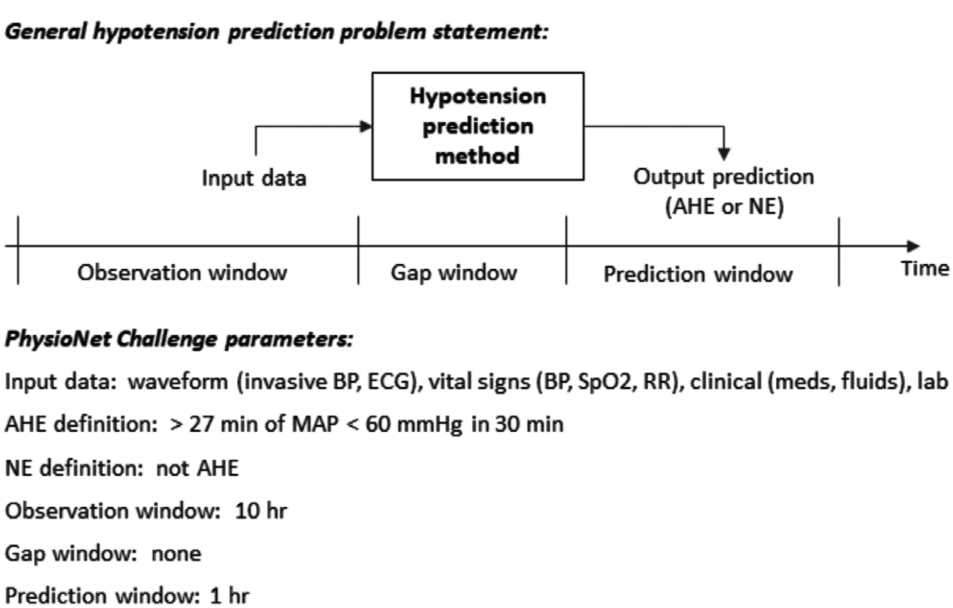

Figure 1. Hypotension prediction problem statement and the PhysioNet Challenge. The general problem is to develop a method that takes input data from a patient over an observation window to predict either an AHE or NE over a subsequent prediction window (upper). The specific PhysioNet Challenge in 2009[16] helped establish and popularize hypotension prediction (lower). AHE indicates acute hypotensive event; BP, blood pressure; ECG, electrocardiography; MAP, mean arterial pressure; NE, nonevent; RR, respiratory rate; Spo_2, arterial oxygen saturation.

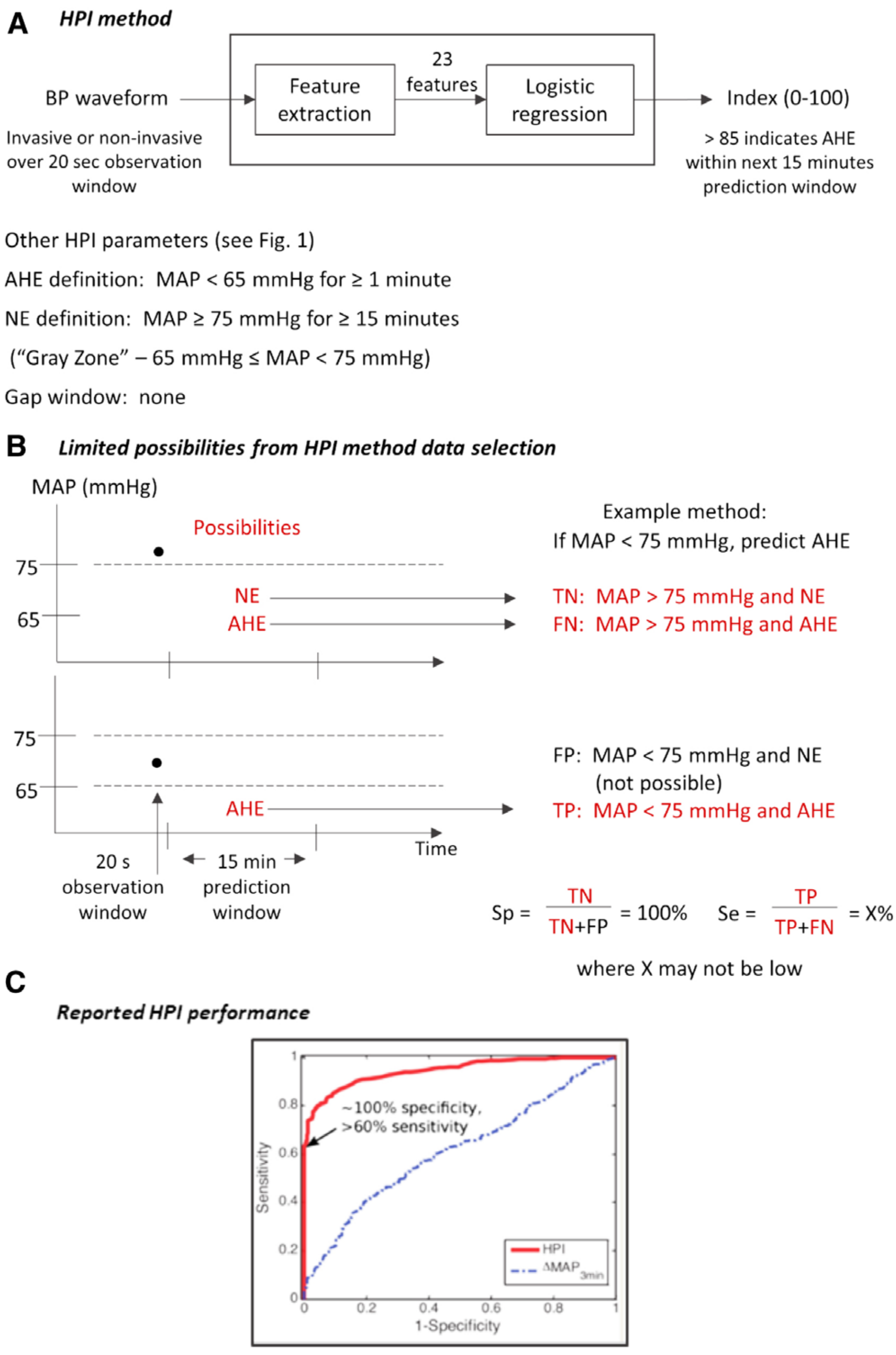

Figure 2. Acumen HPI method. A, Description of the popular commercial method provided by the developers.[14,19] The same 23 proprietary features are used for invasive radial and noninvasive finger BP waveforms. B, Description of the data selection procedure for creating and testing the HPI method provided by the developers.[14,19] The procedure assumes that MAP <75 mm Hg during the observation window can only be followed by an AHE and not an NE during the prediction window (lower panel). These limited possibilities allow the method to appear highly specific. C, Example results of the HPI method reported by the developers.[14,19] These results indeed show high specificity with good sensitivity but may not extend to actual practice wherein MAP <75 mm Hg can be followed by an NE. Reproduced from reference.[20] AHE indicates acute hypotensive event; BP, blood pressure; FN, false negative; FP, false positive; HPI, hypotension prediction index; MAP, mean arterial pressure; NE, nonevent; Se, sensitivity; Sp, specificity; TN is true negative; TP, true positive.

the HPI method to predict AHEs versus NEs from 20-second intervals of the BP waveform occurring 5, 10, or 15 minutes before the start of an event (backward evaluation). However, MAP in the 15-minute observation window before each event was restricted to always be >75 mm Hg for an NE but not for an AHE. This data stratification has generated controversy and confusion, and as shown in Figure 2B, it makes the prediction much easier.[22,20] For example, if the current MAP is <75 mm Hg, then hypotension must necessarily follow in a mathematical sense. The initial evaluation studies, which reported receiver operating characteristic (ROC) curves with exceptional specificity and area under the curves (AUCs) >0.90, as shown in Figure 2C, may have overestimated the ability of the HPI method to predict hypotension in clinical practice. Several subsequent studies did not describe the data selection and stratification or showed very similar ROC curves to the initial studies.[20] Further, many of the studies have not evaluated the method in predicting an AHE within 15 minutes from the current 20-second interval of the BP waveform (forward evaluation). Forward evaluation is vital for assessing real-world performance and determining the all-important positive predictive value of a method. However, just recently, 2 studies on forward analysis of the HPI method were published.[23,24] In a study of 100 patients, Mulder et al reported ROC AUCs near 0.9 and a positive predictive value of 31.9% for 5-minute forward prediction.[23] Davies et al (developers of the HPI method and early clinical trialists) reported in 2022 patients that forward and backward analyses of the HPI method produce similar results with ROC AUCs >0.9 and positive predictive value near the standard 85 decision threshold of <30% for 5-minute ahead prediction (see supplementary information).[24] Consistent with earlier studies,[22,25–27] both of these new studies show that the HPI method produced prediction results that were similar to using standard MAP monitoring. A MAP method in which the current MAP value over the 20-second interval is used to predict a future AHE within the next 15 minutes yields essentially the same ROC AUCs in predicting an AHE as the HPI method. Further, the MAP method at a specific decision threshold of 72 to 73 mm Hg (ie hypotension is predicted to be imminent if MAP falls <72–73 mm Hg but not an immediate concern if MAP is >72–73 mm Hg) affords essentially the same sensitivity and specificity as the HPI method at the standard 85 decision threshold. MAP may thus be the dominant feature, either explicitly or implicitly, behind the 23 features applied by the HPI method. As described above, the data selection approach used in the initial HPI method studies may have foreshadowed MAP as a particularly important feature[22,20] (Figure 2B). The dominance of MAP in the HPI method is also suggested by use of the same 23 features for both invasive radial and noninvasive finger BP waveforms, which have very different intrabeat shapes. In summary, the data indicate that the HPI method is similar to using the current MAP in predicting AHEs with a positive predictive value of ~30%.

The HPI method has also been tested in prospective, randomized controlled trials comparing hypotension exposure between care with versus without HPI. In nearly 50 patients undergoing total hip arthroplasty, 25 received HPI-directed care and experienced a median of 0 (interquartile range [IQR], 0–1) AHEs compared to a median of 5 (IQR, 2–6) AHEs in patients receiving routine care.[28] Comparing an HPI-directed protocol that included treatment suggestions to standard care, the median time of hypotension per patient was 8.0 minutes (IQR, 1.33–26.00 minutes) in the intervention group versus 32.7 minutes (IQR,11.5–59.7 minutes) in the control group, without more fluids and vasoactive interventions.[29] In contrast, a trial of the HPI method versus standard care failed to demonstrate a difference in hypotension exposure in 214 enrolled patients.[30] However, only about half of all HPI alarms (ie, HPI >85) were intervened on. Additionally, in an observational trial of 702 noncardiac surgery patients under HPI-directed care, the median time with hypotension was only 2 minutes (IQR, 0–9 minutes).[31] These trials collectively indicate that the HPI method can reduce hypotension exposure time.

A key question is if these reductions in hypotension exposure translate to reduced postoperative injury (including acute injury, prolonged ICU stay, or post-hospital injury). Randomized controlled trials of the HPI method have yet to convincingly demonstrate an improvement in these end points. However, prospective single-arm, observational studies are underway with organ failure as an outcome.

Other Published Hypotension Prediction Methods

Hypotension prediction methods other than the HPI method have been proposed. To highlight various approaches and settings, we describe both ICU and OR studies. Despite considerable variation in the studies, including input variables, prediction windows, and evaluation methods, Table 1 aggregates the findings of our literature survey.

Because AHEs are typically defined in terms of MAP, current MAP (MAP over the observation window) can be expected to be a useful feature for predicting future events. A MAP closer to 65 mm Hg is more likely to be followed by an AHE than a MAP further from 65 mm Hg. The body of published studies underscores the importance of current MAP in hypotension prediction. But are there other features that offer significant added value in the prediction?

The HPI method, as described by its developers,[14] suggests that current BP waveform features other than MAP have predictive value. Systolic BP, diastolic BP, and pulse pressure are undoubtedly useful alone, simply due to their correlation with MAP. However, they may offer some value when used together with MAP.[32,33] Two studies suggest that current features reflecting the shape of the BP waveform can provide modest value in predicting hypotension over the individual values of the BP.[34,35] However, only a few studies have examined BP waveform shape features beyond specific BP levels.

The temporal variations in MAP within the observation window could also offer predictive value over the current MAP alone. While a linear extrapolation of MAP over the observation window to the prediction window (LepMAP method) did not predict an

Table 1. Summary of Published Hypotension Prediction Methods and Their Performance

Metpods and performance	Current evidence	Comments
Useful features other than current MAP	BP levels and statistics during observation window Demographics for postinduction hypotension prediction	These features are secondary to MAP BP waveform features and noninvasive vital signs may not be as helpful
Performance of advanced ML	Not substantially better than LR	Includes nonlinear ML and DL
Prediction time	~15 min in advance	Longer times substantially reduce PPV
Hypotension prediction performance	~0.85 ROC AUC | ~0.25 PPV	Rough aggregate of studies

Abbreviations: BP, blood pressure; DL, deep learning; LR, logistic regression; MAP, mean arterial pressure; ML, machine learning; PPV, positive predictive value; ROC AUC, receiver operating characteristics area under the curve.

AHE better than the current MAP,[18,36] 1 study showed that MAP trends (current MAP, recent averages, and variance) increased the ROC AUC by about 10% compared to the current MAP alone.[37]

Capnography, photoplethysmography (PPG), and electrocardiography (ECG) waveforms are also commonly measured in clinical practice, leading investigators to hypothesize that these measurements contain information to predict hypotension. One study reported that analysis of the 3 waveforms can yield an ROC AUC of 0.76 in predicting an AHE: compared to 0.89 for analysis of the invasive BP waveform.[38] While this result may be surprising, the study data were made freely available for future confirmation. However, most have found that oxygen saturation (Spo_2), heart rate, and respiratory rate are not effective in hypotension prediction.[35,39–41]

Many studies have explored available data beyond physiological variables in predicting an AHE, including age, body-mass index, medications, comorbidities, and other features, but none have been shown to be as important as MAP.[33,42–45]

In summary, BP levels and their trends may somewhat improve hypotension prediction over the current MAP alone, whereas there is presently less evidence that beat-to-beat or intrabeat shape features of the BP waveform can enhance prediction. Further, data other than BP do not appear useful, except demographics for postinduction hypotension prediction.

The HPI method is based on a conventional logistic regression model, which employs hand-selected features and combines them via a linear model, to predict an AHE versus NE. Major breakthroughs in machine learning have been made in recent years. So, it is natural to wonder if more sophisticated methods such as those based on support vector machines: to account for nonlinear relationships, or deep learning models: to automatically determine the features, improve the prediction? While 1 study reported that a deep learning method could significantly outperform a logistic regression method,[46] all other identified studies did not reveal a major difference in predictive performance of the tools.[32,33,41–43,47,48] Two of the studies actually reported that basic machine learning outperformed more advanced machine learning.[33,42] These results suggest that nonlinear relationships may not be significant and that the measurements may not include unknown features. However, methods based on random forest models using default parameters could represent a simple way to modestly improve the prediction by allowing for possible nonlinear relationships.[49]

The PhysioNet Challenge and HPI method sought to predict an AHE about 15 minutes before it occurs. Even though 15 minutes of advanced warning may offer enough time for successful intervention, determining an effective treatment often involves trial and error, so further advanced warning could be helpful. So, how far ahead can hypotension be predicted? Several studies have compared hypotension prediction times. One study showed that hypotension can be predicted 1 hour beforehand, with accuracy similar to 15 minutes ahead prediction.[50] Two other studies reported significantly better predictions 10 to 20 minutes in advance than 1 hour beforehand.[46,51] Additional studies aiming to predict hypotension 1 to 2 hours in advance yielded good sensitivity but very low positive predictive value.[39,52,53] Current methods thus seem to be able to predict hypotension around 15 minutes in advance, which would be helpful for resuscitation.

The PhysioNet Challenge also suggested that hypotension can be predicted with a sensitivity and specificity of both around 80%. But what is the performance of current methods? While the studies have used wide ranging methods, we examined the published studies to provide an estimate of current performance. We found that the aggregate of the often-reported ROC AUC is approximately 0.85, whereas the aggregate of the less-reported but important positive predictive value is around 25%. Since the current MAP can yield similar results, the findings suggest that prediction of the direction (increase or decrease) of future MAP movement over time scales of minutes is difficult.

Methods for Preoperative Determination of Individualized MAP Decision Thresholds

Using the current MAP as the hypotension prediction method, with a decision threshold of 72 to 73 mm Hg,

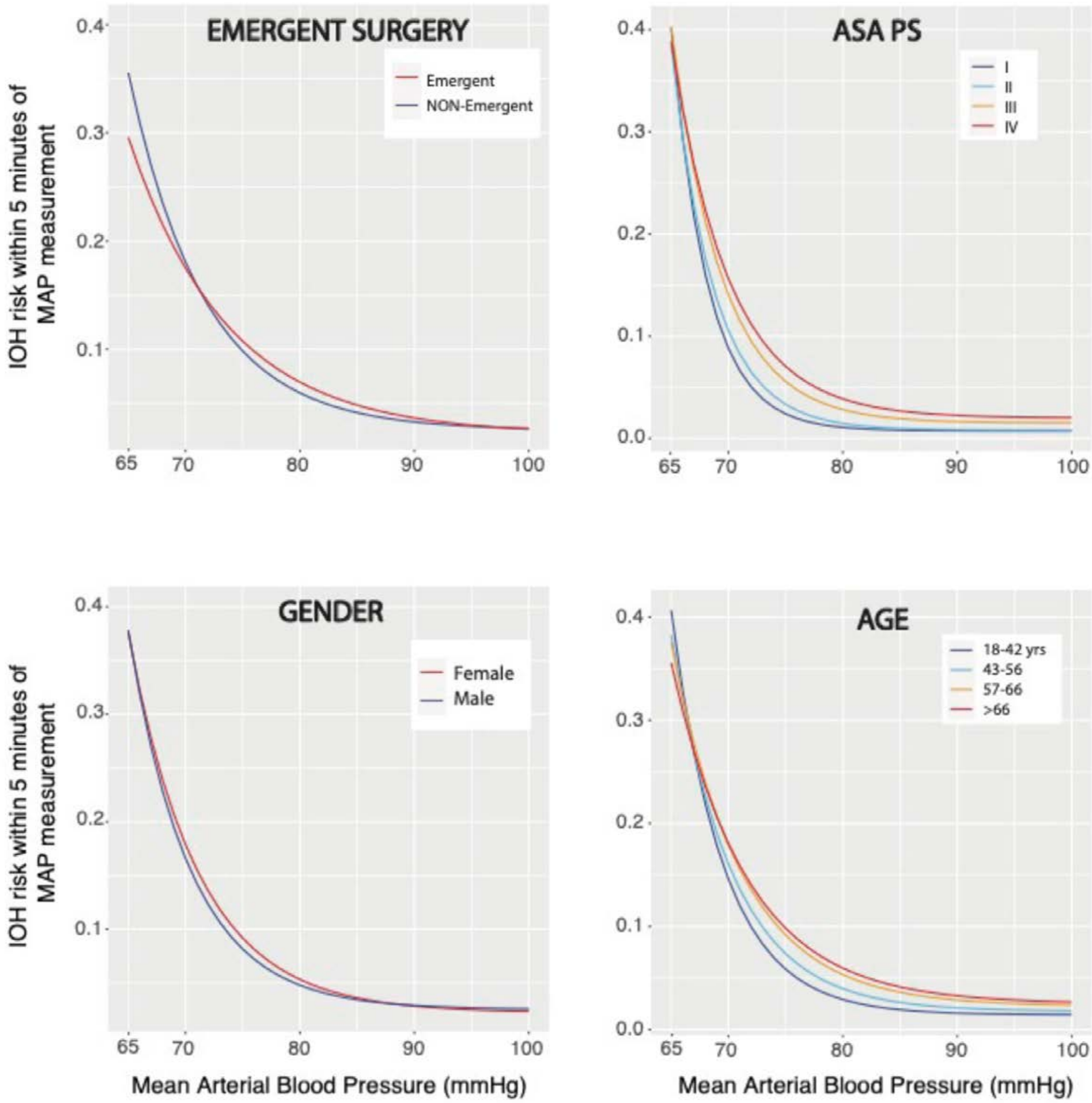

Figure 3. Recent method for preoperative determination of individualized MAP decision thresholds for predicting hypotension. The exponentially decaying curves relate the current MAP (*x*-axis) to the probability of MAP falling <65 mm Hg within 5 min (ie, IOH risk) for different patient characteristics. The curves within each plot are generally different in a statistical sense. As an example, the bottom, right curve indicates that a course of action (increased attention or treatment) is needed for an older patient at a higher MAP than a younger patient to avert a forthcoming AHE. AHE indicates acute hypotensive event; IOH, intraoperative hypotension; MAP, mean arterial pressure; PS, physical status. Reproduced from reference.[15]

can reasonably predict future IOH (MAP <65 mm Hg) in a general population. However, a method recently developed showed that the optimal MAP decision threshold may depend on patient characteristics.[15] In particular, the decision threshold varies according to the patient's age, gender, and preoperative American Society of Anesthesiologists (ASA) physical status score (PSS). As shown in Figure 3, IOH risk (defined as MAP <65 mm Hg within the next 5 minutes) follows an exponential decaying relationship with the current MAP from 65 to 100 mm Hg, and the exponential decay parameters depend significantly on the patient characteristics. In clinical terms, the slower the exponential decay rate, the higher the MAP decision threshold should be. Thus, increased attention or treatment should be given at higher MAP for advanced age and ASA PSS or for males and emergent surgeries to avert an impending AHE.

The risk curves were validated on time-separated data and demonstrated an average error per MAP of <0.1%, indicating highly accurate curves. External validation studies are underway. These risk curves can be applied to determine the MAP decision threshold for a particular patient before surgery to better mitigate their exposure to IOH during the case. However, further research is needed to determine how to couple the risk curves to appropriate action before they can be considered for clinical use.

RECOMMENDATIONS FOR FUTURE INVESTIGATIONS

We make specific recommendations for improving the methodology to establish hypotension prediction methods and general proposals on extending the methods for further predictions. Table 2 provides a summary of these recommendations.

Definition of an Acute Hypotensive Event for Prediction

An AHE for prediction has been defined in various ways. One common way is the PhysioNet Challenge definition of invasive MAP <60 mm Hg for at least 27 minutes in a 30-minute period over a 1-hour prediction window[17,35,39,41,45,48,52,53] (see Figure 1). Another common definition is MAP <65 mm Hg for at least 1 minute[14,36–38,40,47,50] or 5 minutes (see Figure 2A). A recent study of noncardiac surgery patient data indicates that the odds for developing posthospital myocardial or acute kidney injury increases only when the cumulative area under the invasive MAP time series <65 mm Hg, as shown in Figure 4, is greater than around 150 mm Hg-min[7]. The PhysioNet Challenge definition is more consistent with this study but may still be too stringent, since the total area can arise from substantially discontinuous periods of the MAP time series (eg, MAP is 50 mm Hg for 5 minutes and then 50 mm Hg for 5 minutes 1 hour later). On the other hand, MAP <65 mm Hg for 1 to 5 minutes may not be strict enough. MAP <65 mm Hg for 1 to 5 minute periods would contribute to the overall area, but brief AHEs in isolation may typically be harmless: for example, 30 separate 1-minute periods of MAP <65 mm Hg do not increase posthospital risk for acute kidney injury.[7]

An AHE has also been defined using different BP measurement devices, including invasive arterial BP waveforms; an automatic noninvasive arm cuff; and a finger-cuff volume clamp system to measure a noninvasive BP waveforms. Both noninvasive devices are not as accurate as invasively measured BP.[54,55] Yet, several studies of noninvasive methods for hypotension prediction have reported that they are as reliable as hypotension prediction methods that analyze invasive BP waveforms.[19,56,57] This apparent contradiction stems from these studies also using the noninvasive BP measurements to define an AHE for prediction.

Although systolic BP <90 mm Hg is comparably associated with posthospital organ damage as MAP <65 mm Hg,[7] we support the common use of MAP to define an AHE since MAP is more robust to frequent arterial catheter damping than systolic BP. Further research is needed for a precise definition- we propose to define the events in terms of the area under the MAP time series <65 mm Hg. For instance, should a significant AHE be defined as the time integral of MAP <65 mm Hg of at least 75 mm Hg-minute over a 30-minute prediction window? It may also make sense to relax the definition threshold of an AHE in cases of concurrent therapy (eg, from MAP <65 mm Hg to MAP <70 or 75 mm Hg), as hypotension may be more serious when a patient is on a vasopressor or inotrope, than when untreated. In addition, instead of using a blanket MAP of 65 mm Hg to define hypotension in every patient, it may be vital to pursue individualized hypotension definition thresholds based on preoperative patient characteristics. (Note that we have used 2 different MAP thresholds up to now. For instance, if the current MAP falls <72 to 73 mm Hg (MAP decision threshold), a course of action is suggested to try to prevent future MAP from further falling <65 mm Hg (AHE definition threshold).

We further recommend using invasive BP measurement to compute the time integral of MAP below a suitable threshold. The hypotension predictions of a noninvasive method should be evaluated using reference AHEs defined via the invasive BP waveform. Invasive BP and noninvasive BP via automatic arm cuff devices are both often measured, and the MIMIC database and VitalDB database (likely the first perioperative database with waveforms) include this pair of measurements in many patients.[38,58] Scientific studies are needed with invasive BP as reference to understand the capabilities and limitations of hypotension prediction based on noninvasive BP waveform analysis using finger-cuff volume clamp system. As a related point, it is important to continue research to advance noninvasive BP monitoring technology in terms of accuracy[59–61] as well as convenience.[62]

Table 2. Summary of Specific and General Recommendations for Future Investigations

Topic	Recommendation	Type
Definition of AHE	Use area under MAP time series below X mm Hg metric (X = 65 is default)	Specific
	Set X based on preoperative patient characteristics	
Evaluation of hypotension prediction methods	Use invasive BP waveform to compute metric	Specific
	Analyze entire patient record	
	Use PR curve analysis and report PPV	
	Compare method to current MAP in predicting AHEs	
Extension of prediction methods	Pursue methods to predict reduced blood flow	General
	Pursue methods to predict response to therapy	

Abbreviations: AHE, acute hypotensive event; BP, blood pressure; MAP, mean arterial pressure; PPV, positive predictive value; PR, precision-recall.

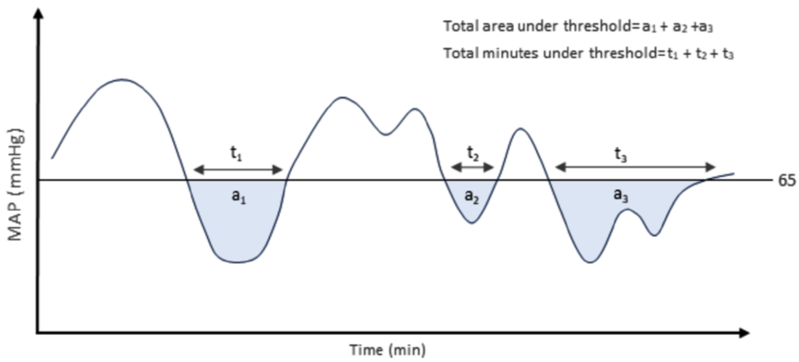

Figure 4. Cumulative area under the invasive MAP time series <65 mm Hg to define an AHE. Since the odds for developing posthospital injury following noncardiac surgery increases with this cumulative area metric in particular,[7] an AHE is recommended to be defined in terms of the metric. AHE indicates acute hypotensive event; MAP, mean arterial pressure. Adapted from reference.[7]

Evaluation of Hypotension Prediction Methods

MAP monitoring represents the current standard of care for managing hypotension. To offer added value, a hypotension prediction method should thus perform significantly better than the current MAP.[20] Yet few studies report comparisons to MAP monitoring.[27,37,40,63]

Hypotension prediction methods are most often evaluated in terms of ROC curve analysis plus sensitivity and specificity. However, the number of AHEs is far fewer than NEs, with ≈ 20% of noncardiac surgery patients exposed to profound hypotension: for example, MAP <65 mm Hg and for >15 minutes.[7] Moreover, in clinically deploying a method, continual predictions of imminent hypotension would be made for a patient throughout a surgical case. For example, consider a patient who is exposed to a MAP of 50 mm Hg for 5 minutes twice during a 3-hour surgery and a method that predicts hypotension every 5 minutes. Because the prevalence of AHEs is only about 5% here, a method that achieves a seemingly good sensitivity and specificity of both 80% would actually be unsatisfactory due to the lower positive predictive value of about 20%. In other words, 4 out of 5 positive predictions outputted by the method would be false, such that the false alarm problem in perioperative care would only be exacerbated.[64] The assessment of the all-important positive predictive value of a method requires the use of all NEs in the patient record, so that the prevalence of AHEs is reflective of the intended continual prediction application. Yet, several studies have selected only a subset of NEs while including all AHEs from each patient record,[14,19,21,38] and the PhysioNet Challenge used just a single event per patient record for prediction.[17]

Consistent with other studies of hypotension prediction methods,[37,50,65] we suggest to analyze entire patient records rather than a subset of the data and to use precision-recall (PR) curve analysis in addition to ROC curve analysis.[66] As shown in Figure 5, a PR curve is a plot of the positive predictive value (precision) versus the corresponding sensitivity (recall) over all decision thresholds. While the ROC AUC must be > 0.5 for a prediction method to offer value over random chance, the PR AUC, which takes on a value between 0 and 1, must be greater than the prevalence of the AHEs (baseline) to offer value. Positive predictive value can be determined by finding all positives produced by the method in the patient record and seeing if they are followed by AHEs. Only the positives during NEs may be considered, as hypotension prediction during an AHE would not be the clinical focus. Sensitivity can be

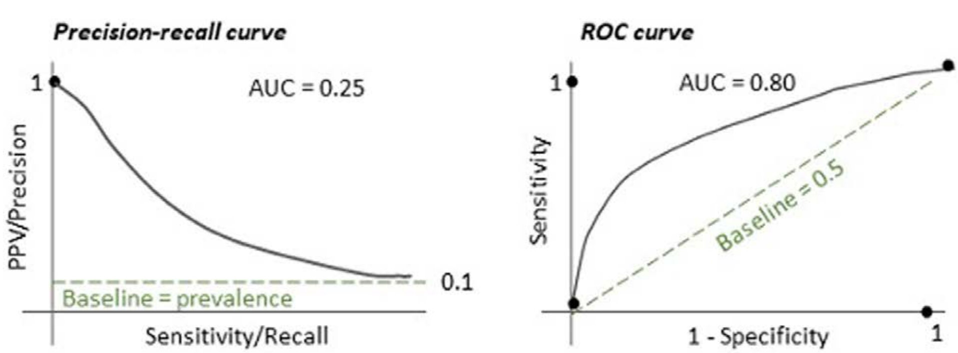

Figure 5. PR curve versus ROC curve for evaluating hypotension prediction methods. ROC curves are commonly used to assess hypotension prediction methods, but PR curves are more appropriate due to the low AHE prevalence.[66] The PR AUC indicates the crucial average PPV across decision thresholds and can be low even when the ROC AUC is high. PR curves are thus recommended to evaluate hypotension prediction methods. AHE indicates acute hypotensive event; AUC, area under the curve; PPV, positive predictive value; PR, precision-recall; ROC, receiver operating characteristics.

ascertained by finding all AHEs in the record and seeing if they are preceded by positives. This process can be repeated for each decision threshold to yield the PR curve.

We also recommend comparing the method to MAP monitoring. The method would ideally yield a significantly higher PR AUC than the MAP monitoring through statistical comparison via bootstrapping.[67] Otherwise, there would be little reason to replace MAP monitoring.

Extension of the Methods for Prediction of Reduced Blood Flow and Treatment Effects

Emerging evidence suggests that therapies used to maintain BP targets may also impact the outcome being measured, potentially confounding the effect of the target itself.[68,69] Large, randomized trials are pending, and a clear answer to an appropriate choice of vasopressors during the intraoperative period is still subject to debate.[70–72] The best solution currently seems to be selecting vasopressors (a) with or without inotropy and (b) with or without fluids, as guided by advanced hemodynamic monitoring. Data suggest that current-day practices are focused on achievement of an MAP target rather than the means to the target.[72]

Adding to the complexity of this issue, keeping a patient's MAP >65 mm Hg may be flawed as a universal approach. Adequate consideration should be given to preoperative BP and individualized intraoperative BP targets based on preprocedure hemodynamics.[73] Finally, tissue injury underlying hypotension-related complications results from a deficit in blood perfusion, not necessarily a deficit in BP.[9,74] Any intervention to optimize BP to avoid hypotension should do so in ways that concurrently optimizes blood flow, lest the intervention may fail to produce its intended effect.

Thus, we recommend to also focus on development of methods to predict hemodynamic instability, which leads to reduced flow states, rather than predicting hypotension alone. We further suggest pursuing methods to predict the effect of therapy, which must implicitly consider the cause of the impending hypotension. For example, what therapy should be given to restore BP while preserving or enhancing blood flow? Should it be phenylephrine at dose x, or a fluid bolus, or this combination with a reduction in inhaled anesthetic? Does the prediction change if the anticipated AHE will occur in the context of acute bleeding versus impaired ventricular contractility?

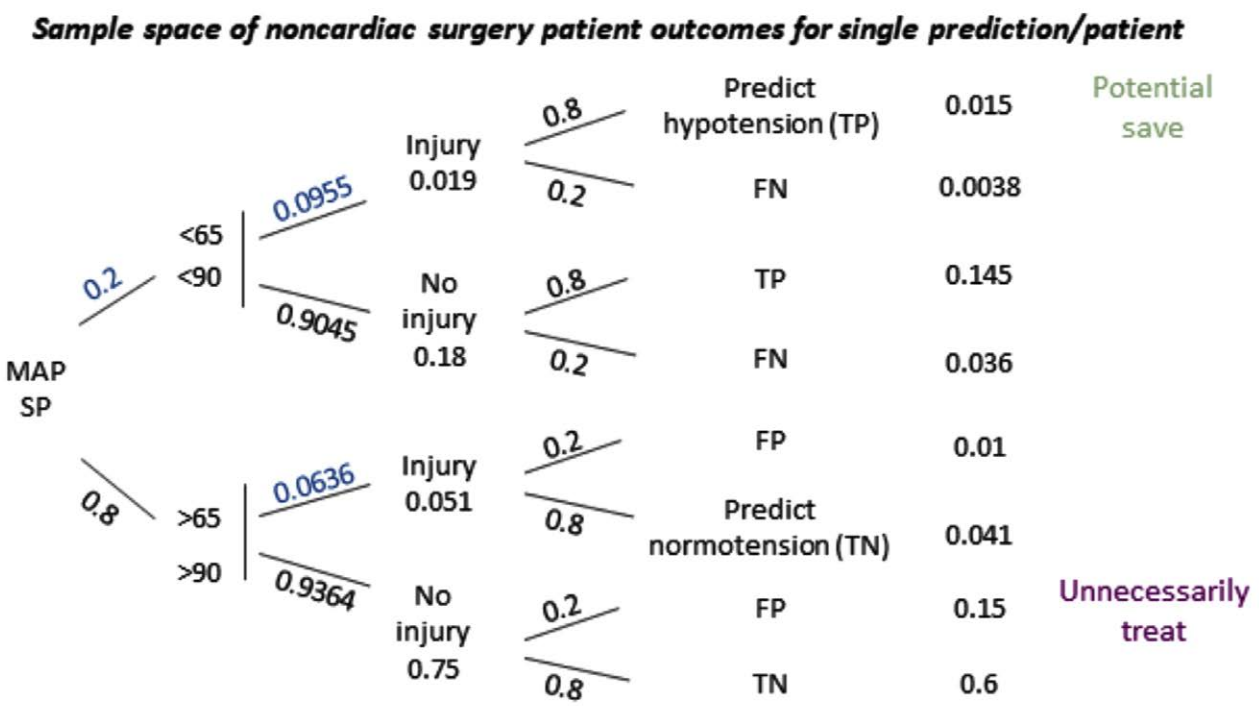

Figure 6. Probabilities of all possible outcomes of noncardiac surgery (ie, sample space). The blue values are from noncardiac surgery patient data.[7] The simplifying assumptions are as follows: (1) a patient is exposed to either 0 or 1 substantial AHE (ie, MAP/systolic BP (SP) well <65/90 mm Hg and sustained for at least 15 min) during a case; (2) a method makes a one-time prediction of the AHE per patient; (3) if the method correctly predicts the hypotension, the subsequent therapy will always be successful in averting posthospital injury; and (4) the method has sensitivity/specificity of 0.8/0.8 in predicting the AHE and thus a PPV of 0.5. The probability of unnecessary treatment is thus severely underestimated but still 10 times higher than the probability of saving a patient from posthospital injury. Interpretation of the other possibilities is more difficult. AHE indicates acute hypotensive event; BP, blood pressure; MAP, mean arterial pressure; PPV, positive predictive value; SP, systolic pressure.

START OF A RISK-BENEFIT ANALYSIS OF HYPOTENSION PREDICTION

While prompt treatment of IOH can potentially mitigate postoperative organ injury, IOH appears to be significantly inferior to baseline patient characteristics as an injury predictor.[7] Hypotension prediction may also lead to unnecessary treatment and increase hypertensive-related risks.[75] We attempt here to assign numbers to these qualitative statements to better understand the risks and benefits of hypotension prediction.

In this analysis, we make the following simplifying assumptions: (1) a patient is exposed to either zero or 1 substantial AHE: MAP well <65 mm Hg or systolic BP well <90 mm Hg, and sustained for at least 15 minutes during a case; (2) a method makes a 1-time prediction of the AHE per patient; and (3) if the method correctly predicts the hypotension, the subsequent course of action will always be successful in averting posthospital injury. We also used the following noncardiac surgery patient data: (1) the probability of posthospital injury for the standard of care is 0.07; (2) the probability of a substantial AHE in a patient is 0.2; and (3) the probability of injury for a patient given the occurrence of hypotension is 0.0955, while the probability of injury for a patient given the absence of hypotension is 0.0636.[7] The latter 2 conditional probabilities were adjusted for baseline confounders and indicate that hypotension increases the odds of posthospital injury by a factor of 1.5.[7] We lastly assume that the method has a sensitivity and specificity both of 0.8 (80%) in predicting hypotension. Based on this sensitivity and specificity and the 0.2 probability for an AHE, the positive predictive value is thus 0.5 (50%).

Figure 6 shows the resulting probabilities of all possible outcomes of noncardiac surgery (sample space). First, consider the case in which hypotension is perfectly predicted in 1000 patients. Of the 70 patients who would have suffered from posthospital injury with standard care, only 19 can be rescued. Furthermore, compared to the standard care, 181 of the patients who became hypotensive but did not later suffer from injury will now be treated for their hypotension. These outcomes might be similar to prompt and successful treatment of severe hypotension after it is detected. Now, consider the case of inevitable hypotension prediction error. Posthospital injury will be averted in around the same number of patients (≈ 20). However, 150 patients who will not develop hypotension or posthospital injury will now be treated. In summary, compared to standard care, about 20 of 1000 patients will benefit by avoiding posthospital injury at the risk of unnecessarily treating 150 patients who did not even develop hypotension.

These numbers represent lower bounds on how many unnecessary treatments may be given, since a method would not make only 1 prediction of hypotension during a case but rather make continual predictions throughout the surgery. While basic lockout techniques (eg, a method does not make a prediction for 30 minutes after an AHE is predicted) can be used to reduce the number of false positives,[50,65] there will undoubtedly be more mis-predictions. For example, a patient who has successfully been treated for an AHE due to a correct prediction could be given unnecessary fluids and/or vasopressors after 1 hour due to an incorrect prediction. So, well >150 unnecessary treatments would be given to 1000 patients.

This initial study is not a formal risk- or cost-benefit analysis, which would also assign a value (eg, disability-adjusted life years lost) for preventing an injury and another value for unnecessary treatment. However, the results here may still enhance our quantitative understanding of the potential of hypotension prediction.

OUTLOOK ON INTRAOPERATIVE HYPOTENSION PREDICTION

The premise of hypotension prediction is to allow more time to identify and to administer appropriate therapy and thereby to avert subsequent injury. While rational, the risk-benefit analysis and the current evidence described above present 2 considerations. First, only a small fraction of patients can benefit due to the low odds ratio of developing posthospital injury with an AHE vs NE[7]—at the risk of numerous unnecessary treatments due to inevitable false positives in the prediction. Furthermore, each time treatment is given, it can be incorrect. Thus, avoiding unnecessary treatment is crucial to minimize iatrogenic effects. Secondly, the current MAP has proven to be a most important feature in the various hypotension prediction methods. Deployment of these methods may thus be similar to targeting a higher MAP (eg, 72–73 mm Hg) for treatment. Though based on the body of randomized controlled trials conducted up to now, blanket targeting of higher MAP does not appear to reduce morbidity and mortality in noncardiac and cardiac surgery patients: meta-analysis of 10 randomized controlled trials totaling 9000+ patients[76] as well as septic patients: Surviving Sepsis Campaign.[77] One reason may be that hypotension does not cause, but merely associates with posthospital injury. Another reason is that for every would-be hypotensive patient who benefits from the higher MAP, these effects are overshadowed by those harmed by the unnecessary treatments. In support of the latter, effects of profound and sustained hypotension may be far reaching and extend into the postoperative period.[78] For example, strong associations suggest an increased risk of persistent acute kidney disease,[6] while other data implicate perioperative hypotension with several health resource utilization burdens.[79] It should also be mentioned that the currently completed trials[76] are early and have several limitations, especially in terms of treatment methods.

The area of hypotension prediction may thus be at a crossroad. Tailoring hypotension prediction methods to the hemodynamic goals of the individual patient may be crucial. Proving that such methods are significantly better than standard MAP monitoring is then needed to promote their clinical use. Developing prediction methods for prompt identification of the cause of impending hypotension and thus the appropriate therapy for resuscitation[80] appears even more vital to improve relevant patient outcomes. All new prediction methods must be tested through robust trials with patient-centric outcomes and a fully-defined standard of care such as increased vigilance when MAP falls <72 to 73 mm Hg. With such research redirection, the outlook on prediction methods for IOH may in fact be promising.

ACKNOWLEDGMENTS

The authors thank Ms Deanne Krugh for helping to draft the figures.

DISCLOSURES

Conflicts of Interest: R. Mukkamala is co-founder of, and holds equity interests in, Retia Medical Systems. M. P. Schnetz leads a co-development project with Directed Systems Inc to incorporate blood pressure-associated risk scores with intraoperative monitoring systems. A. K. Khanna currently consults for or has consulted for Medtronic, Edwards Life Sciences, Philips Research North America, Baxter, GE Healthcare, Potrero Medical, Fifth Eye Inc, Retia Medical, Caretaker Medical, Renibus Therapeutics, Trevena Pharmaceuticals, and Pharmazz Inc. He is on the research committee of the surviving sepsis campaign and co-chairs a joint task force for norepinephrine dosing and formulations for the SCCM. He is a founding partner for the BrainX group with interests in advancements of AI based technology. The Department of Anesthesiology at Wake Forest University School of Medicine is supported by Edwards Lifesciences under a master clinical trial agreement. A. Mahajan is co-founder of Sensydia Inc, and chief medical officer for Pip Care. **Funding:** This work was supported in part by NIH Grant HL163691 to A.M. and R.M. **This manuscript was handled by:** Thomas R. Vetter, MD, MPH.

REFERENCES

1. Wesselink EM, Kappen TH, Torn HM, Slooter AJC, van Klei WA. Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. *Br J Anaesth*. 2018;121:706–721.
2. Wijnberge M, Schenk J, Bulle E, et al. Association of intraoperative hypotension with postoperative morbidity and mortality: systematic review and meta-analysis. *BJS Open*. 2021;5:zraa018.
3. Gregory A, Stapelfeldt WH, Khanna AK, et al. Intraoperative hypotension is associated with adverse clinical outcomes after noncardiac surgery. *Anesth Analg*. 2021;132:1654–1665.
4. Walsh M, Devereaux PJ, Garg AX, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology*. 2013;119:507–515.
5. Mascha EJ, Yang D, Weiss S, Sessler DI. Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. *Anesthesiology*. 2015;123:79–91.
6. Shaw AD, Khanna AK, Smischney NJ, et al. Intraoperative hypotension is associated with persistent acute kidney disease after noncardiac surgery: a multicentre cohort study. *Br J Anaesth*. 2022;129:13–21.
7. Ahuja S, Mascha EJ, Yang D, et al. Associations of intraoperative radial arterial systolic, diastolic, mean, and pulse pressures with myocardial and acute kidney injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology*. 2020;132:291–306.
8. Salmasi V, Maheshwari K, Yang D, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology*. 2017;126:47–65.
9. Karamchandani K, Dave S, Hoffmann U, Khanna AK, Saugel B. Intraoperative arterial pressure management: knowns and unknowns. *Br J Anaesth*. 2023;131:445–451.
10. Weinberg L, Li SY, Louis M, et al. Reported definitions of intraoperative hypotension in adults undergoing non-cardiac surgery under general anaesthesia: a review. *BMC Anesthesiol*. 2022;22:69.
11. van der Ven WH, Veelo DP, Wijnberge M, van der Ster BJP, Vlaar APJ, Geerts BF. One of the first validations of an artificial intelligence algorithm for clinical use: The impact on intraoperative hypotension prediction and clinical decision-making. *Surgery*. 2021;169:1300–1303.
12. Beam AL, Kohane IS. Big data and machine learning in health care. *JAMA*. 2018;319:1317–1318.
13. Bellini V, Valente M, Bertorelli G, et al. Machine learning in perioperative medicine: a systematic review. *J Anesth Analg Crit Care*. 2022;2:2.
14. Hatib F, Jian Z, Buddi S, et al. Machine-learning algorithm to predict hypotension based on high-fidelity arterial pressure waveform analysis. *Anesthesiology*. 2018;129:663–674.
15. Schnetz MP, Danks DJ, Mahajan A. Preoperative identification of patient-dependent blood pressure targets associated with low risk of intraoperative hypotension during noncardiac surgery. *Anesth Analg*. 2023;136:194–203.
16. Moody G, Lehman L. Predicting acute hypotensive episodes: The 10th Annual PhysioNet/Computers in Cardiology Challenge. *Comput Cardiol*. 2009;36:541–544.
17. Rocha T, Paredes S, de Carvalho P, Henriques J. Prediction of acute hypotensive episodes by means of neural network multi-models. *Comput Biol Med*. 2011;41:881–890.
18. Chen X, Xu D, Zhang G, Mukkamala R. Forecasting acute hypotensive episodes in intensive care patients based on a peripheral arterial blood pressure waveform. In: 2009 36th Annual Computers in Cardiology Conference (CinC), Park City, UT, USA, 2009:545–548.
19. Maheshwari K, Buddi S, Jian Z, et al. Performance of the Hypotension Prediction Index with non-invasive arterial pressure waveforms in non-cardiac surgical patients. *J Clin Monit Comput*. 2021;35:71–78.
20. Enevoldsen J, Vistisen ST. Performance of the hypotension prediction index may be overestimated due to selection bias. *Anesthesiology*. 2022;137:283–289.

21. Davies SJ, Vistisen ST, Jian Z, Hatib F, Scheeren TWL. Ability of an arterial waveform analysis-derived hypotension prediction index to predict future hypotensive events in surgical patients. *Anesth Analg*. 2020;130:352–359.
22. Enevoldsen J, Hovgaard HL, Vistisen ST. Selection bias in the hypotension prediction index: Reply. *Anesthesiology*. 2023;138:450–452.
23. Mulder MP, Harmannij-Markusse M, Fresiello L, Donker DW, Potters JW. The Hypotension Prediction Index is equally effective in predicting intraoperative hypotension during non-cardiac surgery compared to a mean arterial pressure threshold: a prospective observational study. *Anesthesiology*. 2024;141:453–462.
24. Davies SJ, Sessler DI, Jian Z, et al. Comparison of differences in cohort (forwards) and case control (backwards) methodological approaches for validation of the Hypotension Prediction Index. *Anesthesiology*. 2024;141:443–452.
25. Ability of an arterial waveform analysis-derived hypotension prediction index to predict future hypotensive events in surgical patients: erratum. *Anesth Analg*. 2023;137:e33.
26. Michard F, Biais M, Futier E, Romagnoli S. Mirror, mirror on the wall, who is going to become hypotensive? *Eur J Anaesthesiol*. 2023;40:72–74.
27. Mulder MP, Harmannij-Markusse M, Donker DW, Fresiello L, Potters JW. Is continuous intraoperative monitoring of mean arterial pressure as good as the hypotension prediction index algorithm?: Research letter. *Anesthesiology*. 2023;138:657–658.
28. Schneck E, Schulte D, Habig L, et al. Hypotension Prediction Index based protocolized haemodynamic management reduces the incidence and duration of intraoperative hypotension in primary total hip arthroplasty: a single centre feasibility randomised blinded prospective interventional trial. *J Clin Monit Comput*. 2020;34:1149–1158.
29. Wijnberge M, Geerts BF, Hol L, et al. Effect of a machine learning-derived early warning system for intraoperative hypotension vs standard care on depth and duration of intraoperative hypotension during elective noncardiac surgery: the HYPE randomized clinical trial. *JAMA*. 2020;323:1052–1060.
30. Maheshwari K, Shimada T, Yang D, et al. Hypotension prediction index for prevention of hypotension during moderate- to high-risk noncardiac surgery. *Anesthesiology*. 2020;133:1214–1222.
31. Kouz K, Monge Garcia MI, Cerutti E, et al. Intraoperative hypotension when using hypotension prediction index software during major noncardiac surgery: a European multicentre prospective observational registry (EU HYPROTECT). *BJA Open*. 2023;6:100140.
32. Kang MW, Kim S, Kim YC, et al. Machine learning model to predict hypotension after starting continuous renal replacement therapy. *Sci Rep*. 2021;11:17169.
33. Lee J, Woo J, Kang AR, et al. Comparative analysis on machine learning and deep learning to predict post-induction hypotension. *Sensors (Basel)*. 2020;20:4575.
34. Lee S, Lee M, Kim SH, Woo J. Intraoperative hypotension prediction model based on systematic feature engineering and machine learning. *Sensors (Basel)*. 2022;22:3108.
35. Moghadam MC, Masoumi E, Kendale S, Bagherzadeh N. Predicting hypotension in the ICU using noninvasive physiological signals. *Comput Biol Med*. 2021;129:104120.
36. Jacquet-Lagreze M, Larue A, Guilherme E, et al. Prediction of intraoperative hypotension from the linear extrapolation of mean arterial pressure. *Eur J Anaesthesiol*. 2022;39:574–581.
37. Feld SI, Hippe DS, Miljacic L, et al. A machine learning approach for predicting real-time risk of intraoperative hypotension in traumatic brain injury. *J Neurosurg Anesthesiol*. 2023;35:215–223.
38. Lee S, Lee HC, Chu YS, et al. Deep learning models for the prediction of intraoperative hypotension. *Br J Anaesth*. 2021;126:808–817.
39. Bhattacharya S, Huddar V, Rajan V, Reddy CK. A dual boundary classifier for predicting acute hypotensive episodes in critical care. *PLoS One*. 2018;13:e0193259.
40. Cherifa M, Blet A, Chambaz A, Gayat E, Resche-Rigon M, Pirracchio R. prediction of an acute hypotensive episode during an ICU hospitalization with a super learner machine-learning algorithm. *Anesth Analg*. 2020;130:1157–1166.
41. Sun Y, Rashedi N, Vaze V, et al. Predicting future occurrence of acute hypotensive episodes using noninvasive and invasive features. *Mil Med*. 2021;186(suppl 1):445–451.
42. Kang AR, Lee J, Jung W, et al. Development of a prediction model for hypotension after induction of anesthesia using machine learning. *PLoS One*. 2020;15:e0231172.
43. Kendale S, Kulkarni P, Rosenberg AD, Wang J. Supervised machine-learning predictive analytics for prediction of postinduction hypotension. *Anesthesiology*. 2018;129:675–688.
44. Li XF, Huang YZ, Tang JY, Li RC, Wang XQ. Development of a random forest model for hypotension prediction after anesthesia induction for cardiac surgery. *World J Clin Cases*. 2021;9:8729–8739.
45. Moghadam MC, Masoumi E, Kendale S, Bagherzadeh N. The value of short-term physiological history and contextual data in predicting hypotension in the ICU settings. *Comp Meth Prog Biomed Update*. 2023;3:100100.
46. Chan B, Chen B, Sedghi A, Laird P, Maslove D, Mousavi P. Generalizable deep temporal models for predicting episodes of sudden hypotension in critically ill patients: a personalized approach. *Sci Rep*. 2020;10:11480.
47. Choe S, Park E, Shin W, et al. Short-term event prediction in the operating room (STEP-OP) of five-minute intraoperative hypotension using hybrid deep learning: retrospective observational study and model development. *JMIR Med Inform*. 2021;9:e31311.
48. Zhang G, Yuan J, Yu M, Wu T, Luo X, Chen F. A machine learning method for acute hypotensive episodes prediction using only non-invasive parameters. *Comput Methods Programs Biomed*. 2021;200:105845.
49. Couronne R, Probst P, Boulesteix AL. Random forest versus logistic regression: a large-scale benchmark experiment. *BMC Bioinf*. 2018;19:270.
50. Yoon JH, Jeanselme V, Dubrawski A, Hravnak M, Pinsky MR, Clermont G. Prediction of hypotension events with physiologic vital sign signatures in the intensive care unit. *Crit Care*. 2020;24:661.
51. Cherifa M, Interian Y, Blet A, Resche-Rigon M, Pirracchio R. The physiological deep learner: first application of multitask deep learning to predict hypotension in critically ill patients. *Artif Intell Med*. 2021;118:102118.
52. Ghosh S, Feng M, Nguyen H, Li J. Hypotension risk prediction via sequential contrast patterns of ICU blood pressure. *IEEE J Biomed Health Inform*. 2016;20:1416–1426.
53. Lee J, Mark RG. An investigation of patterns in hemodynamic data indicative of impending hypotension in intensive care. *Biomed Eng Online*. 2010;9:62.
54. Lehman LW, Saeed M, Talmor D, Mark R, Malhotra A. Methods of blood pressure measurement in the ICU. *Crit Care Med*. 2013;41:34–40.

55. Raggi EP, Sakai T. Update on finger-application-type non-invasive continuous hemodynamic monitors (CNAP and ccNexfin): physical principles, validation, and clinical use. *Semin Cardiothorac Vasc Anesth*. 2017;21:321–329.
56. Frassanito L, Giuri PP, Vassalli F, et al. Hypotension Prediction Index with non-invasive continuous arterial pressure waveforms (ClearSight): clinical performance in Gynaecologic Oncologic Surgery. *J Clin Monit Comput*. 2022;36:1325–1332.
57. Wijnberge M, van der Ster BJP, Geerts BF, et al. Clinical performance of a machine-learning algorithm to predict intraoperative hypotension with noninvasive arterial pressure waveforms: a cohort study. *Eur J Anaesthesiol*. 2021;38:609–615.
58. Vistisen ST, Pollard TJ, Enevoldsen J, Scheeren TWL. VitalDB: fostering collaboration in anaesthesia research. *Br J Anaesth*. 2021;127:184–187.
59. Argha A, Celler BG, Lovell NH. Artificial intelligence based blood pressure estimation from auscultatory and oscillometric waveforms: a methodological review. *IEEE Rev Biomed Eng*. 2022;15:152–168.
60. Babbs CF. Oscillometric measurement of systolic and diastolic blood pressures validated in a physiologic mathematical model. *Biomed Eng Online*. 2012;11:56.
61. Liu J, Cheng HM, Chen CH, Sung SH, Hahn JO, Mukkamala R. Patient-specific oscillometric blood pressure measurement: validation for accuracy and repeatability. *IEEE J Transl Eng Health Med*. 2017;5:1900110.
62. Mukkamala R, Stergiou GS, Avolio AP. Cuffless blood pressure measurement. *Annu Rev Biomed Eng*. 2022;24:203–230.
63. Yang SM, Cho HY, Lee HC, Kim HS. Performance of the hypotension prediction index in living donor liver transplant recipients. *Minerva Anestesiol*. 2023;89:387–395.
64. Clifford GD, Silva I, Moody B, et al. The PhysioNet/Computing in cardiology challenge 2015: reducing false arrhythmia alarms in the ICU.In: 2015 Computing in Cardiology Conference (CinC), Nice, France, 2015:273–276, doi: 10.1109/CIC.2015.7408639
65. Hyland SL, Faltys M, Huser M, et al. Early prediction of circulatory failure in the intensive care unit using machine learning. *Nat Med*. 2020;26:364–373.
66. Saito T, Rehmsmeier M. The precision-recall plot is more informative than the ROC plot when evaluating binary classifiers on imbalanced datasets. *PLoS One*. 2015;10:e0118432.
67. https://www.medcalc.org/manual/precision-recall-comparison.php Accessed September 28, 2024
68. Khanna AK, Saha AK, Segal S. Association of the exclusive use of intraoperative phenylephrine for treatment of hypotension with the risk of acute kidney injury after noncardiac surgery. *Anaesth Crit Care Pain Med*. 2023;42:101224.
69. Khanna AK, Zarbock A, Legrand M. All intraoperative hypotension is not created equal - A call for an individualized approach. *J Clin Anesth*. 2023;87:111076.
70. Legrand M, Kothari R, Fong N, et al; VEGA-1 trial investigators. Norepinephrine versus phenylephrine for treating hypotension during general anaesthesia in adult patients undergoing major noncardiac surgery: a multicentre, open-label, cluster-randomised, crossover, feasibility, and pilot trial. *Br J Anaesth*. 2023;130:519–527.
71. Farag E, Makarova N, Argalious M, et al. Vasopressor infusion during prone spine surgery and acute renal injury: a retrospective cohort analysis. *Anesth Analg*. 2019;129:896–904.
72. Chiu C, Fong N, Lazzareschi D, et al. Fluids, vasopressors, and acute kidney injury after major abdominal surgery between 2015 and 2019: a multicentre retrospective analysis. *Br J Anaesth*. 2022;129:317–326.
73. Saugel B, Reese PC, Sessler DI, et al. Automated ambulatory blood pressure measurements and intraoperative hypotension in patients having noncardiac surgery with general anesthesia: a prospective observational study. *Anesthesiology*. 2019;131:74–83.
74. Awad H, Alcodray G, Raza A, et al. Intraoperative hypotension-physiologic basis and future directions. *J Cardiothorac Vasc Anesth*. 2022;36:2154–2163.
75. Tsoumpa M, Kyttari A, Matiatou S, et al. The use of the hypotension prediction index integrated in an algorithm of goal directed hemodynamic treatment during moderate and high-risk surgery. *J Clin Med*. 2021;10:5884.
76. D'Amico F, Fominskiy EV, Turi S, et al. Intraoperative hypotension and postoperative outcomes: a meta-analysis of randomised trials. *Br J Anaesth*. 2023;131:823–831.
77. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med*. 2017;43:304–377.
78. Sessler DI, Khanna AK. Perioperative myocardial injury and the contribution of hypotension. *Intensive Care Med*. 2018;44:811–822.
79. Stapelfeldt WH, Khanna AK, Shaw AD, et al. Association of perioperative hypotension with subsequent greater healthcare resource utilization. *J Clin Anesth*. 2021;75:110516.
80. Kappen T, Beattie WS. Perioperative hypotension 2021: a contrarian view. *Br J Anaesth*. 2021;127:167–170.