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Review

The use of the hypotension prediction index (HPI) software in the operating room: A narrative review

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Abstract

Hypotension is a daily problem in the operating room and a monitoring platform allowing prediction of arterial hypotension and providing assistance to diagnose its mechanisms is clinically needed. The use of HPI (hypotension prediction index) as an alarm system based on a proprietary algorithm derived using machine learning from multiple components of the arterial waveform to predict shortly hypotension has been validated in studies using invasive and non-invasive continuous arterial pressure monitoring in cardiac and non-cardiac surgery. It also has been compared to standard of care in managing intraoperative hypotension with conflicting results. As HPI is very strongly correlated with mean arterial pressure (MAP), it could simply mirror concurrent MAP and have equal predictive performance. Even if HPI and MAP are not interchangeable, the overwhelming influence of MAP in the model could thus lead to a minimal diagnostic advantage of HPI in clinical practice. The additional value of HPI associated with guidance treatment protocols to improve patients' outcomes should probably be further assessed in large-scale well-designed studies to justify its extra-cost before widen the range of patients that might benefit.

Keywords: **Intraoperative hypotension, Hypotension prediction index, Patients' outcomes.**

Introduction

Hypotension is a daily problem that occurs in more than 80% of patients beyond 65 years old in the operating room[1] and a modifiable risk factor for postoperative organ injury. Its incidence depends however on both the definition of intraoperative hypotension (IOH) and the selected thresholds. More than 100 different definitions of IOH have been published over the last 15 years according to age and comorbidities, the use of absolute or relative values of arterial blood pressure, and the type of considered complications. Most importantly and whatever the definition, if the causality between IOH and adverse outcomes is not clearly demonstrated, an independent statistical association is reproducibly reported in the scientific medical literature[2-11]. Besides, we do not know if the correction of IOH with or without an algorithm improves outcomes since the results of available large randomized controlled trials are somewhat conflicting[12-16] (Table I). Thus, avoidance of hypotension rather than correction has been recommended by European guidelines[17]. In this context, it appears that a monitoring platform allowing prediction of arterial hypotension and providing assistance to diagnose its mechanisms is clinically needed.

The hypotension prediction index (HPI) software: clinical validation

One such monitoring platform has been developed using a machine-learning algorithm (namely, the HPI - for hypotension prediction index - technology) based on the features of high-fidelity arterial pressure waveform analysis, and commercialized by Edwards LifeSciences. HPI can be derived from either invasive or non-invasive arterial pressure waveform analysis and more

Table I. — Randomized controlled trials assessing the impact of correction of intraoperative hypotension on patients' outcomes.

RCT and first author	Publication	Number of patients	Impact on outcomes
Futier et al. (INPRESS)	JAMA 2017	298	+ (SIRS/organ dysfunction)
Wu et al.	J Clin Anesth 2017	678	+ (MAKE)
Sessler et al. (Triple-low)	Anesthesiology 2019	7,569	- (90-day Mortality)
Wanner et al.	J Am Coll Cardiol 2021	451	- (MACE/MAKE)
Marcucci et al. (POISE-3)	Ann Intern Med 2023	7,490	- (Mortality/MACCE)

MACE: major adverse cardiac events; MACCE: major adverse cerebral and cardiac events; MAKE: major adverse kidney events; RCT: randomized controlled trial; SIRS: systemic inflammatory response syndrome.

than 20 validation studies have been published yet[18]. Those studies were either retrospective or prospective, observational or randomized, comparative or not comparative, and conducted in both cardiac and non-cardiac surgery patients. They all used the same definition for IOH, i.e. a mean arterial pressure (MAP) less than 65 mmHg for at least 1 minute. The HPI alarm threshold was most often fixed at 85 (on a scale ranging from 0 to 100) and the time from HPI alert to a hypotensive event was 3 minutes on average, theoretically allowing the treatment of impending hypotension before it occurs. The first validation study was published in 2018 in patients undergoing non-cardiac surgery and used a cohort of 1,334 patients and 25,461 episodes of hypotension for internal validation, then 204 patients and 1,923 episodes of hypotension for external validation[19]. In that initial study, hypotension was defined as MAP less than 65 mmHg and normotension was defined as MAP greater than 75 mmHg. The uncertainty zone in between was not analyzed, a common option in clinical care because physiology is not a binary process. HPI was advantageously compared to changes in mean arterial pressure (delta MAP) with very promising results up to 15 min before IOH occurred. More generally, almost all validation studies report a good-to-excellent discrimination of HPI in predicting IOH at 5, 10 and 15 minutes before it occurs, HPI always doing much better than delta MAP and other usual macro-hemodynamic parameters as cardiac output, stroke volume, the absolute value of MAP, pulse pressure, heart rate, stroke volume variation, and shock index[20]. Recently, the multicentre prospective observational registry EU HYPROTECT included 702 patients undergoing major non-cardiac surgery from 12 medical centres and 5 countries, and reported a very low rate of IOH when HPI was systematically used: median time of MAP below 65 mmHg = 2 minutes (interquartile range: 0-9), median number of IOH episodes = 1 (interquartile range: 0-3), median time-weighted average (TWA) of MAP < 65 mmHg = 0.03 mmHg (interquartile range: 0.0-0.2)[21]. This suggests that using HPI software monitoring may help reduce both duration and severity of IOH in non-cardiac surgery.

Overall, what we have learnt from those validation studies is that: i) HPI is accurate and discriminant in predicting IOH up to 15 minutes before it occurs in both cardiac and non-cardiac surgery; ii) initially developed and validated with invasive arterial waveforms, HPI is also valuable with non-invasive estimates of the arterial waveforms. This last point could markedly widen the range of patients who might benefit from HPI in routine clinical practice.

HPI versus standard of care to manage intraoperative hypotension

The use of HPI together with an algorithm to manage IOH has been compared to standard of care in randomized controlled studies with conflicting results. The HYPE randomized clinical trial included 68 adult patients during elective non-cardiac surgery and found a marked decrease in TWA of hypotension as the primary endpoint in the interventional group compared to the control group: 0.10 (0.01-0.43) vs. 0.44 (0.23-0.72) mmHg (P=0.001)[22]. A hemodynamic diagnostic guidance and causal treatment protocol aiming to maintain MAP in a normal range was systematically used in that study. Conversely, a larger study including 213 adult patients undergoing moderate to high-risk non-cardiac surgery and using a very similar population and study design was unable to show any difference between both groups: TWA MAP < 65 mmHg = 0.14 vs. 0.14 mmHg (P=0.757)[23]. The authors explained this negative result mainly because the incidence of hypotension was very low in the control group, and because of a moderate compliance to the protocol treatment. A systematic review of 5 comparative randomized controlled trials including 461 patients scheduled for non-cardiac surgery reported a significant decrease in TWA MAP < 65 mmHg in the HPI group: mean difference of median (95% confidence interval) = -0.27 mmHg (-0.38 to -0.01)[24]. Finally, the HYPE-2 randomized clinical trial showed that

using HPI combined with diagnostic guidance on top of standard care significantly decreased hypotension severity in elective cardiac surgery patients[25]. An example of a proactive strategy avoiding the occurrence of IOH by simultaneous use of HPI and a hemodynamic treatment protocol including fluids, vasopressors, inotropes and depth of anesthesia is depicted on Figure 1.

The HPI software: the concerns

From now, several questions remain before recommending a wider use of HPI in routine clinical practice to decrease IOH and improve patients' outcomes.

Is delta MAP the right comparator for HPI?

Our group recently published a simple and intuitive model of prediction of IOH from the linear extrapolation of MAP (LepMAP)[26]. In a retrospective cohort of 83 adult patients undergoing high-risk non-cardiac surgery in two tertiary university hospitals, LepMAP showed a fair discrimination in predicting IOH up to 2 minutes before it occurs (ROCAUC 0.81 [95%CI: 0.79-0.83]), potentially leaving time for the anesthesiologist to initiate a preventive strategy. The performance of LepMAP was even better after exclusion of segments with MAP between 65 and 75 mmHg (ROCAUC 0.93 [95%CI: 0.92-0.95]), as previously done by Hatib et al[19]. Meanwhile, delta MAP was unable to predict hypotension (ROCAUC 0.61 [95%CI: 0.59-0.64]) and we strongly suggested that HPI should be compared to LepMAP rather than delta MAP in future studies. Similar good results for HPI and LepMAP and bad results for delta MAP have been very recently reported in a prospective observational study including a total of 100 non-cardiac surgery patients[27].

Does HPI > 85 work better than MAP < 70-75 mmHg?

That specific point is crucial. Indeed, as HPI is very strongly correlated with MAP (R2 = 0.875 before logarithmic transformation and 0.951 after logarithmic transformation)[28], and despite it is derived from many other complex variables related to the features of the arterial waveform[19] which rely on the physiological robust changes in the cardiopulmonary and arterial baroreflexes[29], several authors suggested that HPI simply mirrored concurrent MAP and that HPI and the single value of MAP had equal predictive performance[26,30]. Thus, the HPI greater than 85 alarm could be substituted with a MAP threshold around 70 to 75 mmHg with essentially identical predictive abilities[31]. Recently, a prospective observational study including 100 patients undergoing non-cardiac surgery reported that a MAP threshold < 73 mmHg had a proportionate agreement of 0.97 with HPI > 85, and a similar discrimination in predicting IOH 5 minutes before it occurred[27]. As well, a retrospective analysis including 2,022 patients and yielding 4,152,124 measurements of invasive and non-invasive MAP reported AUCs in the range of 0.9 for both MAP and HPI[32]. Reanalyzing an entire dataset including 14,053 cases of HPI ≤ 85 and 6,033 cases of HPI > 85, we

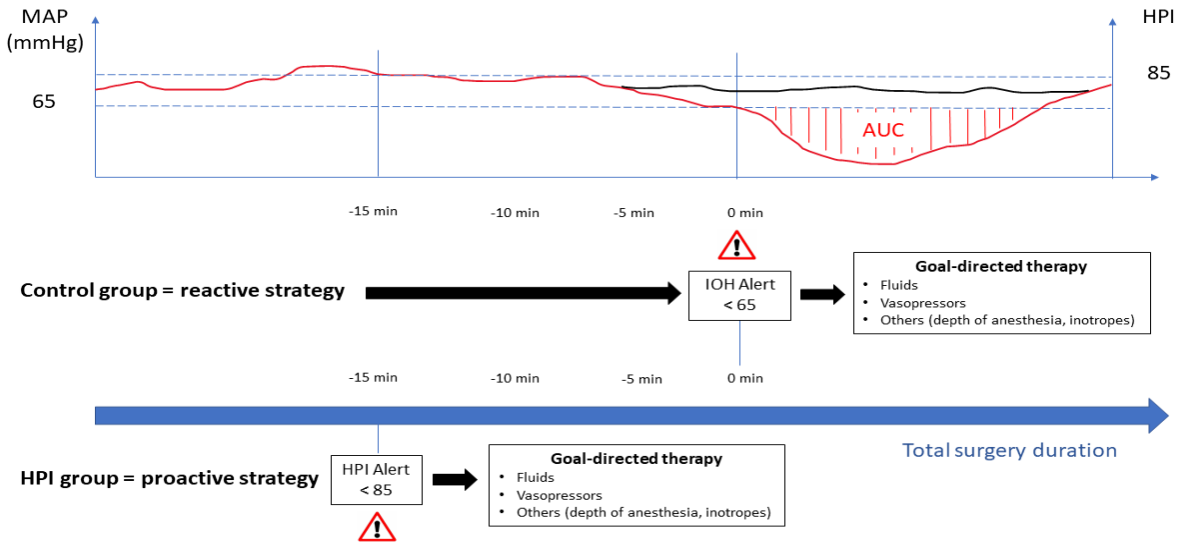

Fig. 1 — Example of a proactive strategy associating HPI and hemodynamic treatment protocol in order to prevent intraoperative hypotension before it occurs.
AUC: area under curve (red hatched area); HPI: hypotension prediction index; IOH intraoperative hypotension; MAP: mean arterial pressure.
In the HPI group, the proactive strategy of hemodynamic optimization when HPI reaches 85 allows to keep MAP constantly above 65 mmHg (black line), whereas the reactive strategy when MAP decreases below 65 mmHg leads to a given duration of intraoperative hypotension in the control group (red line). The time-weighted analysis (TWA) is equal to AUC/total surgery duration.

found the best threshold of MAP to diagnose HPI > 85 was 72.5 mmHg, with a sensitivity of 96% (95% CI: 95-96) and a specificity of 95% (95% CI: 95-96)[28]. Quantifying further the dependence between MAP and HPI, we determined that MAP accounts for 95% of the HPI variance, leaving 5% attributable to other factors[28].

Is there a risk of overtreatment related to the low positive predictive value of HPI?

For the clinician, the most important metric is not the AUC, but a metric estimating how often an alert correctly predicts IOH, namely the positive predictive value. It is notable that the previous reported positive predictive values for HPI are low, around 30%[27,32]. In other words, seven of 10 hypotension alerts are false and could lead to overtreatment[33]. This point is of paramount importance and has been assessed at least in two randomized studies comparing a treatment protocol based on HPI to a standard of care during moderate and high-risk surgery[34,35]. If less significant hypotension was observed in the HPI group (TWA hypotension median difference with the control group = -0.28 mmHg [95%CI: -0.48 to -0.09], P<0.001), a higher incidence of hypertension was also reported (TWA hypertension median difference with the control group = 0.40 mmHg [95%CI: 0.10 to 0.83], P=0.003), probably as a result of overtreatment related to false alerts[34]. A significant higher dosing of vasopressors and inotropes was also observed[35]. Even if it was not associated with a significant increase in clinical adverse events (but none of those studies had been powered for a patient-centred outcome analysis), this issue should probably be highlighted in future studies.

Does HPI improve postoperative outcomes?

If the ability of HPI to decrease both the incidence and duration of hypotension has repeatedly been reported in randomized clinical trials during noncardiac and cardiac surgery, we do not know yet if it could be associated with a significant decrease in postoperative organ dysfunction and an improvement in patients' outcomes. Further well-conducted studies will need to assess that crucial point in the next future before recommending a wider use of HPI in routine clinical practice. In this context, the hemodynamic guidance protocol used together with HPI for the pre-emptive management of impending IOH is probably a cornerstone of its clinical impact on postoperative outcomes.

Other methodological concerns

Several authors suggested the predictive ability of HPI could have been overestimated due to a selection bias in previous validation studies[26,30]. Indeed, the original validation used a case control (backward) analysis with a gray zone that could have been biased[19]. The use of a cohort (forward) methodology may be a more clinically appropriate validation method. Using a cohort pooled from nine previous studies involving intraoperative and critical care patients, Davies et al.[32] compared a backward approach with a gray zone and a forward approach without a gray zone and found very high and similar ROC curves, but a high positive predictive value in the backward analysis and a low positive predictive value in the forward analysis for both HPI and the concurrent MAP. In addition, as the relation between HPI and MAP is sigmoidal and not linear, the high R2 value (0.77 to 0.95) could even underestimate the overwhelming agreement between both parameters[33]. Subsequently, although HPI incorporates numerous combinatorial variables derived from 2,600,000 features of the arterial pulse wave analysis, it could have a minimal impact on its overall clinical value to predict IOH and finally decrease end-organ dysfunction and improve patients' outcomes. Lastly, it is notable that HPI can only be used to predict hypotension defined as MAP < 65 mmHg and could not be suitable for patient-specific blood pressure targets, especially patients with chronic hypertension. Conversely, MAP thresholds can easily be adjusted to predict any desired blood pressure in a timely manner.

Conclusions

It remains uneasy to define an intraoperative hypotensive threshold that could be associated with a worse prognosis for a given patient, and an improvement in outcomes by correcting IOH when it occurs is far from certain. The use of HPI as an alarm system based on a proprietary algorithm derived using machine learning from components of the arterial waveform to predict shortly hypotension has been validated in studies using invasive and non-invasive continuous arterial pressure monitoring. Nevertheless, and even if HPI and MAP are not interchangeable, the overwhelming influence of MAP in the model could lead to a minimal diagnostic advantage of HPI in clinical practice. The additional value of HPI associated with guidance treatment protocols to improve patients' outcomes should probably be further assessed in large-scale well-designed studies to justify its extra-cost before widen the range of patients that might benefit.

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