RESEARCH ARTICLE

Hemodynamic monitoring with Hypotension Prediction Index versus arterial waveform analysis alone and incidence of perioperative hypotension

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Abstract

Background: Intraoperative hypotension is associated with increased morbidity and mortality. The Hypotension Prediction Index (HPI) is an advancement of the arterial waveform analysis to predict intraoperative hypotension minutes before episodes occur enabling preventive treatments. We tested the hypothesis that the HPI combined with a personalized treatment protocol reduces intraoperative hypotension when compared to arterial waveform analysis alone.

Methods: We conducted a retrospective analysis of 100 adult consecutive patients undergoing moderate- or high-risk noncardiac surgery with invasive arterial pressure monitoring using either index guidance (HPI) or arterial waveform analysis (FloTrac) depending on availability (FloTrac, n = 50; HPI, n = 50). A personalized treatment protocol was applied in both groups. The primary endpoint was the incidence and duration of hypotensive events defined as MAP <65 mmHg evaluated by time-weighted average of hypotension.

Results: In the FloTrac group, 42 patients (84%) experienced a hypotension while in the HPI group 26 patients (52%) were hypotensive (p = 0.001). The median (IQR) time-weighted average of hypotension in the FloTrac group was 0.27 (0.42) mmHg versus 0.10 (0.19) mmHg in the HPI group (p = 0.001). Finally, the median duration of each hypotensive event (IQR) was 2.75 (2.40) min in the FloTrac group compared to 1.00 (2.06) min in the HPI group (p = 0.002).

Conclusions: The application of the HPI combined with a personalized treatment protocol can reduce incidence and duration of hypotension when compared to arterial waveform analysis alone. This study therefore provides further evidence of the transition from prediction to actual prevention of hypotension using HPI.

KEYWORDS
hemodynamics, hypotension, monitoring
**1 | INTRODUCTION**

Intraoperative hypotension is a common adverse event during non-cardiac surgery.\(^1\,2\) It is associated with an increased incidence of acute kidney injury, myocardial injury, neurological deficiencies, as well as an increased 30-day operative mortality.\(^3\,7\) Organ injuries were shown to be associated with the depth, frequency, and duration of hypotensive episodes.\(^4\,8\) Data indicate that a mean arterial pressure of 65 mmHg serves as a threshold to predict myocardial and kidney injury.\(^9\,11\) Therefore, continuous improvement in and development of new technologies to prevent hypotension remain important goals in modern anesthesiology.

More recently developed minimally invasive methods to decrease the incidence of hypotension comprise among others of the analysis of the arterial waveform. This advanced hemodynamic monitoring measures the arterial blood pressure continuously and calculates additionally cardiac output, stroke volume, stroke volume variation, and systemic vascular resistance. This deeper insight into hemodynamics enables goal-directed therapy (GDT) approaches; however, the given information only allows to react to events instead of preventing them.\(^12\,13\)

Interestingly, recent data indicate a significant reduction in postoperative organ dysfunction by preventing intraoperative hypotension, suggesting a potential benefit of early intervention.\(^14\) Therefore, the prediction of intraoperative hypotension and consequently its prevention by proactive treatment may show beneficial effects for patients. To achieve this goal, the Hypotension Prediction Index (HPI, Edwards Lifesciences Corp., Irvine, USA) as an advancement of the arterial waveform analysis (FloTrac, Edwards Lifesciences Corp., Irvine, USA) was developed based on a machine learning algorithm. The algorithm analyses physiological changes in the arterial waveform of the radial artery as prodromal signs of the imminent hypotension. Thus, the HPI aims to predict a hypotension up to 15 min prior to the event with a sensitivity of up to 88% and a specificity of up to 87%, enabling the anesthetist to intervene ahead and stabilize the blood pressure without an actual hypotensive event.\(^15\,16\) Both technologies can be used perioperatively as well as in intensive care medicine but are not approved for pediatric patients.

While the HPI algorithm is based on the FloTrac algorithm for the detection of individual pulse waves, we used a pragmatic study design to test the hypothesis that the application of the HPI in comparison to the FloTrac reduces incidence, duration, and severity of hypotensive events evaluated by time-weighted average of hypotension in moderate- or high-risk noncardiac surgical patients.

**2 | MATERIALS AND METHODS**

This single-center retrospective observational study was approved by the ethics committee of Ruhr-University Bochum on 7 May 2020 (20–6920-BR) and registered in the German Clinical Trials Register (DRKS00022481) on 14 August 2020. The requirement for written informed consent was waived by the ethics committee of Ruhr-University Bochum. This manuscript adheres to the applicable STROBE guidelines.

The primary endpoint was the incidence, duration, and severity of hypotensive events evaluated by time-weighted average of hypotension. The time-weighted average of hypotension is a combination of severity and duration of the hypotensive events, in relation to the total surgery time. It is calculated by using the sum of the area under the threshold divided by the duration of surgery.\(^17\) The threshold for hypotensive events was defined as a mean arterial pressure (MAP) below 65 mmHg for at least 1-min duration. Hypotension duration time ended after re-increasing MAP values upon ≥65 mmHg for at least 1 min.

Secondary endpoints consisted of number of patients with hypotensive events, number of events per (respective) patient, cumulative and average duration of hypotension, combined with numbers of hypotensive events <65 and <50 mmHg.

Using a pragmatic study design, we included consecutively the first 100 patients who have been treated at Marien Hospital Herne with either the FloTrac sensor (\(n = 50\)) and the HPI sensor (AcumenIQ; \(n = 50\)) undergoing moderate- or high-risk abdominal surgery in urology, general surgery, and gynecology. The decision to use the advanced hemodynamic monitoring was based on standard operating procedures of the risk assessment for major abdominal surgery during premedication rounds by senior physicians. Inclusion criteria consisted of elective major abdominal surgery (e.g., cystectomy, pancreaticoduodenectomy, and cytoreductive surgery/HIPEC), age >18 years, anticipated duration of surgery >120 min, and need of invasive blood pressure monitoring using an arterial line. Exclusion criteria were patients not in sinus rhythm, ejection fraction <30%, severe aortic valve stenosis, emergency surgery, acute myocardial ischemia, anticipated duration of surgery <120 min, and contraindication for an arterial line. Patients consecutively enrolled in this study underwent surgery between 5 September 2019 and 5 August 2020. No further criteria were applied for the enrollment. Two patients could not be analyzed due to a language error (protocols saved...
in German language could not be analyzed with the software at that time, so that two more patients were included to achieve 50 patients in both groups. All monitored patients matched the in- and exclusion criteria, no further patients were excluded. Anesthetists were not aware of being part of a study to reflect real-life routine practice conditions. In-house treatment standard protocols postulate a mandatory MAP of at least 65 mmHg in all patients. However, to follow the requirements of the internal standard operation protocols, the individualized lowest blood pressure thresholds were kept higher in patients with corresponding comorbidities in order to take autoregulatory mechanisms into account. For all patients receiving extended hemodynamic monitoring a GDT protocol was mandatory to ensure a standardized but individualized treatment. As part of the GDT protocol, patients received crystalloid fluids and vasopressor therapy; inotropic medication and colloids were applied upon request of the clinician. In accordance with an ongoing multicenter trial we used for FloTrac monitoring a mandatory MAP ≥65 mmHg but also a standard GDT protocol to optimize the cardiac output and oxygen supply. In the HPI group, we used a personalized treatment protocol adapted from Maheshwari et al., which simplifies the complex interpretation and the distinction in preload, cardiac contractility, and afterload as possible causes for hypotension to reflect flow and pressure. The GDT protocols suggest a therapy based on the current hemodynamics; hence the standard therapy was personalized for every (imminent) hypotensive event.

The HPI itself is a number on a scale from 0 to 100, symbolizing the risk for an imminent hypotensive event. Zero indicates the lowest and 100 the highest presentable risk. HPI alarm limits are not adjustable by the user, consequently a combined acoustic and visual alarm appeared when the index exceeded 85. At that point, the clinician was instructed to review the patient’s hemodynamics using the secondary screen (Figure 1) that provides further hemodynamic information needed for the individualized treatment protocol.

![FIGURE 1](https://example.com/hpi.png)
2.1 | Data collection

In all patients, the arterial line was placed after anesthesia induction in the radial artery preferably at the nondominant extremity as precaution in case of catheter-associated complications. The advanced hemodynamic monitoring was started immediately after insertion and the quality of the waveform signals was continuously visually monitored by an experienced senior anesthetist.

We used the Edwards monitoring for the data collection: The baseline arterial waveform analysis was performed identically in both groups. Sample frequency was 100 hertz and the arterial blood pressure as well as the specific hemodynamic calculations were displayed continuously on and recorded every 20 s with the current HemoSphere advanced monitoring platform (Software release SHM 2.0.0.117, Edwards Lifesciences Corp.). The HPI algorithm indicates the so-called extra parameters prediction index, systolic slope, and dynamic arterial elastance.

2.2 | Statistical analysis

The data analysis and statistical plan were written and posted on a publicly accessible server before data were accessed. Data collected perioperatively were downloaded retrospectively from the HemoSphere platform and analyzed using the Acumen Analytics Software (Edwards Lifesciences Corp.). Categorical data are presented as frequencies with percentages. Differences were analyzed with the Fisher’s exact test. For quantitative variables, we tested for normal distribution using the Shapiro–Wilk test. Data are presented as means ± standard deviation (SD) in case of normally distribution, otherwise, data are presented as median and interquartile range (IQR). Linear variables were analyzed using the Student’s unpaired t-test in normal distributed variables and the Mann-Whitney U-test in nonnormally distributed variables. P-values less than 0.05 were considered statistically significant. Statistical analysis was performed with SPSS Statistics (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.).

3 | RESULTS

One hundred consecutive patients were included in the analysis from 5 September 2019 to 5 August 2020 (FloTrac sensor n = 50, HPI sensor n = 50). Epidemiological data were comparable in both groups and showed no significant differences in their distribution (Table 1). The median age was 66 years (IQR, 17); almost two thirds of patients were in ASA III status. The majority of patients (89%) received an epidural catheter for perioperative pain management and the median duration of surgery was 287 (IQR, 186) min.

The time-weighted average of hypotension (IQR) as the primary endpoint was 0.27 mmHg (0.42) in the FloTrac group versus 0.1 mmHg (0.19) in the HPI group (p = 0.001; Table 2; Figure 2).

Concerning secondary endpoints, we could show that 42 of 50 patients (84%) in the FloTrac group experienced a hypotension with 251 events in total. In the HPI group, 26 of 50 patients (52%; p = 0.001) were hypotensive with a total of 58 events (p = 0.001; Figure 3) while 544 HPI alarms >85 occurred. This resulted in a median number of five (7) hypotensive events (IQR) per patient in the FloTrac group compared to one (2) event in the HPI group (p = 0.001, Table 2). Moreover, patients in the FloTrac group experienced nine hypotensive events below the threshold of a MAP <50 mmHg, whereas only one event occurred in the HPI group (p = 0.016; Table 2). The median duration of cumulative hypotensive events (IQR) per patient was 10.3 (27.3) min in the FloTrac group, which was 7.44% of monitored time compared to 1 (4.17) min equals 1.14% of monitored time in the HPI group (p = 0.001; Table 2, Figure 4A). This resulted in a median duration of each hypotensive event (IQR) of 2.75 (2.4) min in the FloTrac group compared to 1 (2.06) min in the HPI group (p = 0.002; Table 2, Figure 4B).

4 | DISCUSSION

Intraoperative hypotension in patients undergoing noncardiac surgery remains an important risk for adverse events. Ahuja et al. recently provided evidence that the risk for myocardial and kidney injury increases with duration and severity of intraoperative hypotension.

In this study, we compared two systems of hemodynamic monitoring, which differ in a few calculation details while the analysis algorithm of the arterial waveform is identical. The HPI sensor has been assumed to be superior by calculating the prediction index of hypotension and granting additional information to enable the distinction in preload, cardiac contractility and afterload as potential causes for hypotension. The presented data indicate that the HPI reduces hypotensive events during major abdominal surgery when compared to arterial waveform analysis alone. Patients with FloTrac monitoring experienced 4.3-fold more hypotensive events compared to patients with HPI monitoring (251 vs. 58). Since 544 HPI alarms occurred, speculatively up to 486 possible hypotensive events might have been prevented. As adverse effects of intraoperative hypotension were shown to worsen with the depth of the event, this study could also show a significantly decreased number of hypotensive events with a MAP <50 mmHg in the HPI group when compared to the FloTrac group (one vs. nine).

Studies comparing HPI versus standard treatment have shown inconsistent results: Wijnberge et al. have shown in an unblinded randomized clinical trial the effectiveness in hypotension prevention by a HPI-guided setup. The control group receiving standard care displayed a time-weighted average of 0.44 mmHg while the intervention group had a time-weighted average of 0.10 mmHg, the latter being comparable to results from our study. Due to the study design, bias effects cannot be excluded because clinicians were aware of the participation, thus their behavior might be different compared to unobserved care. It has to be noted that the
| Characteristics                               | All patients, n = 100 | FloTrac, n = 50 | HPI, n = 50 | p value |
|----------------------------------------------|-----------------------|----------------|-------------|---------|
| Age in years, median (IQR)                   | 66 (17)               | 66.5 (19)      | 66 (15)     | 0.888   |
| Gender male, n (%)                           | 57 (57)               | 28 (56)        | 29 (58)     | 0.999   |
| Body surface area in m², median (IQR)        | 1.94 (0.395)          | 1.93 (0.39)    | 1.94 (0.39) | 0.824   |
| ASA classification, n (%)<sup>a</sup>        |                       |                |             |         |
| I                                            | 0 (0)                 | 0 (0)          | 0 (0)       |         |
| II                                           | 37 (37)               | 18 (36)        | 19 (38)     |         |
| III                                          | 62 (62)               | 32 (64)        | 30 (60)     |         |
| IV                                           | 1 (1)                 | 0 (0)          | 1 (2)       | 0.478   |
| Epidural catheter, n (%)                     | 89 (89)               | 44 (88)        | 45 (90)     | 0.999   |
| Anesthetist’s experience <5 years, n (%)     | 35 (35)               | 19 (38)        | 16 (32)     | 0.675   |
| Preoperative MAP in mmHg, median (IQR)       | 100 (15.8)            | 99 (11)        | 102 (17.5)  | 0.867   |
| Type of surgery, n (%)<sup>b</sup>           |                       |                |             |         |
| General surgical                             | 28 (28)               | 13 (26)        | 15 (30)     |         |
| Urological                                    | 68 (68)               | 35 (70)        | 33 (66)     |         |
| Gynecological                                | 4 (4)                 | 2 (4)          | 2 (4)       | 0.904   |
| Surgical approach, n (%)                     |                       |                |             |         |
| Laparotomy                                    | 85 (85)               | 44 (88)        | 41 (82)     |         |
| Laparoscopy                                   | 8 (8)                 | 3 (6)          | 5 (10)      |         |
| Combined                                      | 7 (7)                 | 3 (6)          | 4 (8)       | 0.686   |
| Duration of surgery in minutes, median (IQR)<sup>b</sup> | 287 (186)            | 304 (192)      | 258 (185)   | 0.289   |
| Monitored time in minutes, median (IQR)      | 292 (192)             | 309 (192)      | 275 (190)   | 0.533   |
| Blood loss in mL, median (IQR)               | 500 (675)             | 450 (600)      | 550 (763)   | 0.658   |
| Blood loss >1000 mL, n (%)                   | 22 (22)               | 8 (16)         | 14 (28)     | 0.227   |
| Antihypertensive medication, n (%)           | 59 (59)               | 29 (58)        | 30 (60)     | 0.999   |
| ACE inhibitor                                 | 25 (25)               | 16 (32)        | 9 (18)      | 0.165   |
| Beta blocker                                  | 34 (34)               | 20 (40)        | 14 (28)     | 0.291   |
| Calcium channel blocker                      | 19 (19)               | 11 (22)        | 8 (16)      | 0.611   |
| Diuretic                                      | 16 (16)               | 5 (10)         | 11 (22)     | 0.171   |
| AT1 receptor antagonist                       | 20 (20)               | 6 (12)         | 14 (28)     | 0.078   |
| Others<sup>c</sup>                           | 4 (4)                 | 3 (6)          | 1 (2)       | 0.617   |
| Congestive heart failure, n (%)              | 6 (6)                 | 3 (6)          | 3 (6)       | 0.999   |
| Coronary heart disease, n (%)                | 13 (13)               | 5 (10)         | 8 (16)      | 0.554   |
| Myocardial infarction, n (%)                 | 4 (4)                 | 3 (6)          | 1 (2)       | 0.617   |
| Cardiac stent/coronary artery bypass, n (%)  | 10 (10)               | 4 (8)          | 6 (12)      | 0.741   |
| Valvular heart disease, n (%)                | 11 (11)               | 6 (12)         | 5 (10)      | 0.999   |
| Deep vein thrombosis/pulmonary embolism, n (%) | 9 (9)            | 3 (6)          | 6 (12)      | 0.487   |
| Nicotine abuse                                | 32 (32)               | 18 (36)        | 14 (28)     | 0.521   |
| Chronic obstructive pulmonary disease, n (%) | 11 (11)               | 4 (8)          | 7 (14)      | 0.525   |
| Diabetes, n (%)                               | 15 (15)               | 10 (20)        | 5 (10)      | 0.262   |
| Stroke/transient ischemic attack, n (%)      | 12 (12)               | 4 (8)          | 8 (16)      | 0.357   |
| Peripheral artery disease, n (%)             | 8 (8)                 | 4 (8)          | 4 (8)       | 0.999   |
| Paraplegia, n (%)                             | 2 (2)                 | 1 (2)          | 1 (2)       | 0.999   |
| Chronic renal failure, n (%)                 | 17 (17)               | 7 (14)         | 10 (20)     | 0.595   |
| Anemia, n (%)                                 | 36 (36)               | 17 (34)        | 19 (38)     | 0.835   |

<sup>a</sup>Duration of surgery was measured in minutes from the time of first incision to the time of last suture.

<sup>b</sup>Other medication included Doxazosin and Moxonidine.
study population of Wijnberge et al. comprised healthier patients with 80% ASA II patients compared to 62% ASA III patients in our study population. Since the age of the population is similar in both studies, the difference in ASA classification is most likely due to the high number (85%) of tumor diseases in our study group which lead to considerable physical limitation due to the tumor itself, but also due to neoadjuvant therapies. While Mathis et al.\textsuperscript{11} have shown that more severe comorbidities increase the risk of postoperative complications, patients with higher risk factors as in our study may profit to a greater extend from advanced hemodynamic monitoring.

Schneck et al.\textsuperscript{25} compared in a randomized blinded prospective interventional trial a HPI group with a standard routine care group and a historical control group. They reported a significant reduction in intraoperative hypotension in the HPI group. No treatment protocol was applied in the control groups, possibly having an influence on their results. The positive effects of standard operation

\begin{table}
\centering
\caption{Primary and secondary endpoints.}
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\hline
Characteristics & All patients, \(n = 100\) & FloTrac, \(n = 50\) & HPI, \(n = 50\) & \(p\) value \\
\hline
\hline
Primary endpoint & & & & \\
Time-weighted average (MAP <65 mmHg) in mmHg, median (IQR) & 0.175 (0.33) & 0.266 (0.42) & 0.1 (0.19) & 0.001 \\
\hline
Secondary endpoints & & & & \\
Patients with hypotension, MAP <65 mmHg, \(n\) (%) & 68 (68) & 42 (84) & 26 (52) & 0.001 \\
Number of hypotensive events per patient, median (IQR) & 2 (5) & 5 (7) & 1 (2) & 0.001 \\
Cumulative duration of hypotension per patient in minutes, median (IQR) & 3.33 (15.9) & 10.3 (27.3) & 1 (4.17) & 0.001 \\
Median duration of hypotensive events in minutes, median (IQR) & 1.67 (3.26) & 2.75 (2.4) & 1 (2.06) & 0.002 \\
Total number of events MAP <50 mmHg, \(n\) (%) & 10 (10) & 9 (18) & 1 (2) & 0.016 \\
\hline
\end{tabular}
\end{table}
procedures and GDT protocols have been reported in different clinical settings. In our retrospective study, GDT protocols have been performed in both groups according to the clinical standard.

In contrast to the studies mentioned and our data, a recent study by Maheshwari et al. demonstrated no significant difference comparing a HPI-guided group to an unguided group. They reported a time-weighted average of 0.14 mmHg and a time-weighted mean arterial pressure >83 mmHg (84.9 vs. 83.4 mmHg, p = 0.193) in both groups. These two factors suggest that the clinicians may have been susceptible to the "Hawthorne effect" and thus being more alert to changes in the blood pressure. In contrast, we chose a pragmatic design, where the anesthetist was not aware of being part in a study and was only advised in both groups to keep the MAP at least above 65 mmHg and to use a personalized treatment protocol for optimization of cardiac output. In contrast to explanatory trials, which aim to test whether an intervention works under optimal situations, our study design was chosen to evaluate the effectiveness of interventions in real-life routine practice conditions, and this may therefore explain in part the contrary results to their study.

Our data suggest that aside from a study setting, using the advanced hemodynamic monitoring of the HPI seems to be a useful additional tool to increase our vigilance to hemodynamics since our focus is often shifted to the manifold requirements of patient care.

4.1 Limitations

Certain restrictions are inherent to retrospective studies. Due to the design, a blinding or randomization was not possible, and confounder could not be eliminated entirely. In addition, the available data did not include electronic documentation of dose-related depth of anesthesia, dose of vasoactive substances and fluids, or treatment behavior, making it impossible to determine whether the clinician was following the treatment protocol. Besides, we could not follow-up adverse events as secondary endpoints. Furthermore, the arterial line was placed after anesthesia induction. For upcoming studies, a different time of placement should be considered, because up to one third of intraoperative hypotension occur shortly after induction.

As we still lack a universal definition of hypotension, we decided to use the definition of an absolute threshold of MAP <65 mmHg as described by Salmasi et al. and Vernooij et al. instead of relative thresholds. But regarding the prevalence of arterial hypertension,
relative individual thresholds might be more significant because of individual autoregulation mechanisms.35

The minimally invasive hemodynamic monitoring is only a mathematical analysis, the calculations are highly depending on the quality of the arterial waveform signal, making it unreliable with weaker signals.36,37 Published data conclude that the different invasive and noninvasive hemodynamic measurements only have poor accuracy. Nonetheless, the HPI is able to predict hypotension in the presence of vasoactive and inotropic substances, but surgical causes of hypotension (e.g., clamping of the inferior vena cava) cannot be predicted because of the lack of physiological prodromal changes in the arterial waveform.

In summary, in this single-center retrospective observational study, we describe a significant reduction in incidence and duration as well as the severity of intraoperative hypotension for patients treated with the HPI compared to arterial waveform analysis alone. Our study thereby provides further evidence of the advanced HPI algorithm in clinical application enabling the transition from prediction to actual prevention of hypotension. To identify which patients benefit most from the advanced monitoring, we suggest to further investigate the demonstrated effects and their influence on the outcome of different patient populations conducting large randomized controlled trials.

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CONFLICT OF INTERESTS
Grundmann, Carla: lecture honoraria from medical board Westfalen-Lippe, Germany; Wischermann, Jan: lecture honoraria from Edwards Lifesciences Corp.; Fassbender, Philipp: lecture honoraria from CSL Behring GmbH, external funding from Haemonetics; Frey, Ulrich: lecture honoraria from Edwards Lifesciences Corp. The other author declares no competing interests.

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