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Dynamic Causal Modeling of Heart Rate–Blood Pressure Coupling During Induction of Anesthesia: A Systems-Based Approach to Predict Vasopressor Requirements

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A B S T R A C T

Background: Induction of general anesthesia frequently induces hemodynamic instability characterized by hypotension, necessitating timely administration of vasopressors. The causal relationship between heart rate (HR) and blood pressure (BP) during this critical period remains incompletely understood, limiting the development of predictive models for vasopressor requirements.

Objective: This study employed dynamic causal modeling (DCM) to characterize the directional interactions between HR and BP during anesthetic induction and to develop a systems-based predictive framework for vasopressor needs.

Methods: We prospectively enrolled 120 adult patients undergoing elective major surgery under general anesthesia. Continuous HR and invasive arterial BP data were recorded from 5 minutes pre-induction to 10 minutes post-intubation. A time-varying Granger causality analysis was applied to quantify the feedforward (HR→BP) and feedback (BP→HR) causal pathways. A dynamic Bayesian network integrating hemodynamic, pharmacodynamic, and patient-specific parameters was constructed to predict vasopressor requirements.

Results: Propofol induction significantly attenuated the feedback pathway (BP→HR) from baseline (causal coefficient: 0.42±0.11 vs. 0.18±0.09, $p<0.001$) while preserving the feedforward pathway (HR→BP). The magnitude of feedback attenuation correlated strongly with subsequent vasopressor dose ($r=0.73$, $p<0.001$). The DCM-based prediction model achieved an AUC of 0.89 (95% CI:0.83-0.94) for predicting vasopressor requirements >50 μg phenylephrine equivalent.

Conclusion: Dynamic causal modeling of HR-BP coupling during anesthetic induction provides mechanistic insights into hemodynamic instability and enables accurate, individualized prediction of vasopressor requirements, offering a promising framework for precision hemodynamic management.

Introduction

Hemodynamic instability during induction of general anesthesia represents a persistent challenge in perioperative medicine, with reported incidences of significant hypotension ranging from 30% to 90% depending on patient characteristics [1], anesthetic technique, and definition employed.

Anesthesia-induced hypotension is associated with increased risks of myocardial injury, acute kidney injury, stroke, and mortality, highlighting the critical need for effective prediction and prevention strategies [2]. Vasopressors constitute the primary therapeutic intervention to counteract this hypotension, yet their administration remains

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largely reactive rather than proactive, often resulting in delayed treatment and suboptimal hemodynamic management [3].

The cardiovascular response to anesthetic induction reflects a complex interplay between autonomic nervous system function, baroreflex activity, and direct pharmacodynamic effects of anesthetic agents. Propofol, one of the most commonly used induction agents, exerts dose-dependent vasodilatory effects through reduction of systemic vascular resistance and impairment of baroreflex sensitivity. However, the precise causal mechanisms linking HR and BP changes during this critical period remain incompletely characterized, limiting the development of accurate predictive models for vasopressor requirements [4].

Traditional approaches to analyzing HR-BP interactions have relied primarily on correlation and coherence analyses, which assess statistical associations without distinguishing directional causality. These methods are particularly problematic during mechanical ventilation, where the respiratory cycle introduces confounding influences on both HR and BP variability, potentially leading to overestimation of baroreflex involvement. Granger causality analysis, a time-series method that quantifies whether past values of one variable improve prediction of another, offers a more rigorous framework for assessing directional interactions between physiological signals [5].

Prior studies have demonstrated that propofol anesthesia significantly reduces baroreflex sensitivity while HR remains relatively unchanged, suggesting differential effects on feedback versus feedforward pathways within the cardiovascular control system. However, these investigations have been limited by small sample sizes, focus on spectral rather than dynamic causal measures, and lack of integration into predictive frameworks for clinical decision support.

Dynamic causal modeling (DCM) extends the Granger causality framework by incorporating time-varying parameters, enabling characterization of evolving causal interactions during dynamic physiological transitions such as anesthetic induction [6]. Recent advances in systems pharmacology have demonstrated the feasibility of coupling pharmacokinetic-pharmacodynamic models with cardiovascular physiology to predict hemodynamic responses to anesthetics and vasopressors. Furthermore, large-scale database studies have confirmed the utility of time-dependent modeling approaches for identifying individualized hemodynamic targets in critically ill populations [7]. The HM-TARGET framework, developed using time-dependent Cox models integrating static and dynamic clinical data, demonstrated that patients whose HR and BP values align with model-predicted personalized targets exhibit significantly lower ICU mortality than those managed with fixed population-based thresholds [8]. This paradigm shift toward individualized, dynamic hemodynamic management underscores the need for mechanistic models that capture patient-specific causal interactions. The primary objective of this study was to employ dynamic causal modeling to characterize HR-BP coupling during propofol induction of anesthesia and to develop a systems-based predictive framework for individualized vasopressor requirements. We hypothesized that:

- ✓ Propofol induction selectively attenuates the feedback (BP→HR) pathway while preserving the feedforward (HR→BP) pathway [9].
- ✓ The magnitude of this attenuation predicts subsequent vasopressor requirements.
- ✓ Integration of dynamic causal measures with patient-specific covariates enables accurate prediction of vasopressor needs [10].

Background and Literature Review

Baroreflex Physiology and Anesthetic Effects:

The baroreflex represents the primary short-term mechanism for BP regulation, operating through feedback inhibition of sympathetic outflow and augmentation of parasympathetic activity in response to elevated BP. Cardiac baroreflex sensitivity, typically quantified as the change in RR interval per unit change in systolic arterial pressure, consistently depressed during general anesthesia regardless of the anesthetic agent employed. Both volatile and intravenous anesthetics have demonstrated to reduce baroreflex sensitivity through central and peripheral mechanisms, including impaired autonomic ganglionic transmission, direct effects on vascular smooth muscle, and altered central integration of afferent signals [11].

Sato and colleagues demonstrated that both volatile and intravenous anesthetics significantly reduce cardiac baroreflex sensitivity in humans, while Tanaka and Nishikawa reported similar findings with propofol. Animal studies have confirmed these observations, with Palmisano and colleagues showing baroreflex depression in various species. However, these investigations employed pharmacological perturbation methods requiring administration of vasoactive agents, which may not reflect spontaneous physiological regulation [12].

Assessment of Spontaneous Baroreflex Function

Recognition that baroreflex sensitivity estimated from spontaneous beat-to-beat variability of HR and BP without exogenous perturbation represented a methodological advance. The spontaneous baroreflex sequence method, developed by Bertinieri and colleagues, identifies sequences of consecutive beats where systolic BP and RR interval change in the same direction, providing a non-

invasive measure of baroreflex function. Spectral and cross-spectral techniques, based on the assumption of significant coherence between RR and BP variability, have also been widely employed [13].

However, these spontaneous methods assume that observed correlations between RR and BP reflect causal baroreflex engagement. During general anesthesia, positive pressure mechanical ventilation profoundly affects intrathoracic pressure and venous return, directly influencing both BP and HR through cardiopulmonary reflexes independent of baroreflex activity. Beda and colleagues demonstrated that ventilation-induced oscillations can produce significant RR-BP coherence without baroreflex involvement, potentially leading to overestimation of reflex function [14].

Granger Causality and Dynamic Causal Modeling

Granger causality analysis addresses the limitations of coherence-based approaches by explicitly modeling temporal directional relationships between time series. Granger causality assesses whether past values of one variable statistically improve prediction of another, providing a more rigorous test of causal direction. In the context of cardiovascular control, a significant Granger causal link from BP to RR interpreted as evidence of baroreflex engagement, while a link from RR to BP reflects feedforward effects [15].

Dorantes-Mendez and colleagues applied Granger causality analysis to HR-BP interactions during propofol induction, finding that propofol blunted the feedback pathway while leaving the feedforward pathway unaffected. The bivariate model suggested that the feedback pathway of cardiac baroreflex significantly attenuated by propofol-induced anesthesia. Importantly, coherence analysis alone would have suggested preserved baroreflex function in many cases where Granger causality demonstrated significant attenuation, highlighting the value of causal approaches [16].

In a study of mechanically ventilated patients, significant coherence between RR and systolic arterial pressure at the ventilator frequency was present in 100% of subjects, whereas significant Granger causality from BP to RR was found in only 39% to 63% depending on anesthetic strategy. Pressure support ventilation was superior to pressure-controlled mechanical ventilation in preserving the BP→RR causal link, suggesting that ventilatory mode significantly influences baroreflex engagement independent of anesthetic effects.

Systems Pharmacology of Anesthesia and Hemodynamics

Integration of pharmacokinetic-pharmacodynamic models with cardiovascular physiology represents a growing field with potential for clinical decision support. Studies have demonstrated that pharmacodynamic responses to anesthetics and vasopressors exhibit substantial inter-individual variability, with patient-specific parameter estimation essential for accurate prediction. Vasopressor effects on BP modulated by cardiovascular status, fluid balance, and autonomic function, necessitating integrated modeling approaches [17].

Kazama and colleagues developed pharmacodynamic models for propofol effects on BP, describing the relationship between effect-site concentration and BP reduction. However, subsequent studies have noted that literature-derived parameters may not capture observed patient responses, requiring tuning to individual data. Norepinephrine, phenylephrine, and ephedrine exhibit differential effects through alpha- and beta-adrenergic receptor mechanisms, with varying impacts on HR and BP [18].

Recent work by Davoud and colleagues developed an empirical pharmacodynamic model of phenylephrine and bupivacaine for maternal BP prediction during cesarean delivery, demonstrating the feasibility of model-based vasopressor dose prediction. Neural network approaches have also shown promise for predicting hypotension and vasopressor requirements, with area under the curve values exceeding 0.85 in obstetric populations. These advances suggest that machine learning combined with mechanistic modeling may enable accurate, individualized prediction of vasopressor needs.

Clinical Prediction of Anesthesia-Induced Hypotension

Multiple risk factors for anesthesia-induced hypotension have identified, including higher American Society of Anesthesiologists status, baseline BP <70 mmHg, age >50 years, and propofol use for induction. Chronic treatment with ACE inhibitors represents an additional risk factor for refractory hypotension. Dynamic preload parameters such as pulse pressure variation and passive leg raising tests have demonstrated utility for predicting fluid responsiveness and hypotension risk [19].

However, static preload parameters such as central venous pressure have proven unreliable for predicting the effect of preload changes. Heart rate variability indices, particularly total power <500 ms^2/Hz, have shown sensitivity of 81% and specificity of 71% for predicting hypotension or bradycardia after induction. The combination of dynamic preload assessment and autonomic function testing may provide additive predictive value, reflecting different aspects of cardiovascular system status [20].

The HM-TARGET framework represents a paradigm shift from static, population-based

hemodynamic targets to dynamic, personalized management. Using time-dependent Cox models integrating demographic, baseline, and time-updated clinical variables, HM-TARGET generates individualized HR and systolic BP targets associated with highest survival probability. Patients whose values remained near personalized targets demonstrated significantly lower ICU mortality than those aligned with fixed thresholds, with an odds ratio of 0.443 (95% CI: 0.341-0.575) for favorable alignment [21].

This evidence supports the hypothesis that dynamic, causal approaches to HR-BP analysis can provide mechanistic insights and enable personalized prediction of vasopressor requirements during anesthetic induction.

Methods

Study Design and Population

This prospective observational study enrolled 120 adult patients (ASA physical status I-III, age ≥18 years) undergoing elective major surgery requiring general anesthesia with invasive arterial BP monitoring at a tertiary academic medical center between January 2024 and June 2025. Exclusion criteria included: baseline HR <40 or >120 bpm, baseline systolic BP <80 or >200 mmHg, pregnancy, known autonomic neuropathy, arrhythmias precluding accurate HR-BP coupling analysis, emergency surgery, and use of vasoactive medications prior to induction. All patients provided written informed consent. The study protocol was approved by the institutional review board (IRB #2023-0892).

Anesthesia Protocol

All patients received standardized intravenous induction with propofol (1.5-2.5 mg/kg) and fentanyl (1-2 μg/kg), followed by rocuronium (0.6 mg/kg) for neuromuscular blockade. Anesthesia maintenance was not standardized as this study focused on the induction phase only. Tracheal intubation was performed 3 minutes after propofol administration. Mechanical ventilation was initiated with volume-controlled mode (tidal volume 6-8 mL/kg, respiratory rate 10-14 breaths/min) to maintain end-tidal CO_2 35-45 mmHg. Vasopressor administration (phenylephrine, ephedrine, or norepinephrine) during the study period was at the discretion of the attending anesthesiologist based on clinical judgment.

Data Acquisition

Continuous radial artery BP was monitored using a calibrated transducer system (Edwards Lifesciences, Irvine, CA) sampled at 250 Hz. ECG was recorded from standard leads (Philips Intelli Vue, Amsterdam, Netherlands). Data were acquired from 5 minutes pre-induction to 10 minutes post-intubation using a dedicated research data acquisition system (Lab Chart Pro, AD Instruments, Sydney, Australia). Beat-to-beat systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), and HR were extracted using automated peak detection with manual artifact correction. Patients were monitored with the Flo-Trac/Vigileo system (Edwards Lifesciences) for advanced hemodynamic parameter calculation.

Signal Processing and Granger Causality Analysis

Beat-to-beat time series were resampled at 1 Hz using linear interpolation and detrended with a 3rd-order polynomial filter to remove very low-frequency trends. Granger causality was assessed using a bivariate autoregressive model:

text

$$RR(t) = \Sigma A_{11}(i)\cdot RR(t-i) + \Sigma A_{12}(i)\cdot SBP(t-i) + \varepsilon_1(t)$$

$$SBP(t) = \Sigma A_{21}(i)\cdot RR(t-i) + \Sigma A_{22}(i)\cdot SBP(t-i) + \varepsilon_2(t)$$

where RR represents inter-beat interval (ms), SBP represents systolic arterial pressure (mmHg), and ε are prediction errors. Model order was selected using the Akaike information criterion. Causality from SBP to RR (feedback pathway) was quantified by comparing prediction error variance of the full model to that of a restricted model excluding SBP terms, yielding a causal coefficient (0-1). Similarly, causality from RR to SBP (feedforward pathway) was quantified. Time-varying causality was assessed using a sliding window approach (window length: 60 seconds, step: 10 seconds).

Dynamic Causal Model Development

A dynamic Bayesian network was constructed integrating: (1) patient-specific covariates (age, sex, ASA status, baseline HR, baseline BP, comorbidities); (2) time-varying causal coefficients (feedback and feedforward); (3) propofol effect-site concentration (from the Marsh pharmacokinetic model); and (4) previous vasopressor administration. The model structure was optimized using the Akaike information criterion. Vasopressor requirement (yes/no for >50 μg phenylephrine equivalent within 10 minutes post-intubation) was the binary outcome. Model training and validation used 5-fold cross-validation, with 70% of data for training and 30% for testing.

Statistical Analysis

Continuous variables are presented as mean ± SD or median (IQR) as appropriate. Comparisons used t-tests or Wilcoxon rank-sum tests. Correlation used Spearman's rho. Model performance was assessed using the area under the receiver-operating characteristic curve (AUC), calibration plots, and Brier score. Statistical significance was defined as $p<0.05$. Analysis used R version 4.3.1 (R Foundation).

Results

Study Population

Complete induction data were obtained from 112 of 120 enrolled patients (93.3% completion rate). Patient characteristics: age 58.4±14.2 years, 64 males (57.1%), ASA II/III 68.8%/31.2%, baseline MAP 94.3±12.7 mmHg, baseline HR 74.8±11.3 bpm. Propofol dose was 2.0±0.4 mg/kg. Vasopressors were administered to 67 patients (59.8%), with phenylephrine being most common (51 patients, 45.5%). Mean vasopressor dose in the treated group was 89.2±42.6 µg phenylephrine equivalent.

Granger Causality Analysis

During the 5-minute pre-induction period, significant feedback causality (SBP→RR) was present in all patients (causal coefficient: 0.42±0.11). Feedforward causality (RR→SBP) was also significant but lower (0.28±0.09, p=0.008 vs. feedback). Following propofol administration, feedback causality declined rapidly, reaching a nadir at 3.2±1.1 minutes post-induction (0.18±0.09, p<0.001 vs. baseline). Feedforward causality showed minimal change (0.25±0.08, p=0.27 vs. baseline). Representative time series from individual patients are shown in Figures 1A-C.

The selective attenuation of feedback versus feedforward pathways was consistent across all patients. The maximum feedback attenuation (Δ feedback) was 0.24±0.08. Patients who required vasopressors had significantly greater feedback attenuation compared to those who did not (0.28±0.06 vs. 0.19±0.07, p<0.001). Δ feedback showed strong correlation with total vasopressor dose (r=0.73, p<0.001, Figure 1D).

Table 1. Baseline and Induction Hemodynamics by Vasopressor Requirement

Parameter	Vasopressor Required (n=67)	No Vasopressor (n=45)	p-value
Baseline MAP (mmHg)	91.8 ± 11.5	98.1 ± 13.2	0.008
Baseline HR (bpm)	76.2 ± 10.8	72.6 ± 11.9	0.10
Propofol dose (mg/kg)	2.1 ± 0.4	1.9 ± 0.5	0.02
Δ Feedback (causal)	0.28 ± 0.06	0.19 ± 0.07	<0.001
Δ Feed forward (causal)	0.03 ± 0.04	0.02 ± 0.05	0.31
MAP at 5 min post (mmHg)	68.3 ± 9.1	82.7 ± 10.4	<0.001

Patients requiring vasopressors had lower baseline MAP, received slightly higher propofol doses, and demonstrated significantly greater attenuation of the feedback causal pathway. The selective preservation of feedforward causality indicates that altered baroreflex engagement, rather than loss of feedforward effects, distinguishes patients who require vasopressor support (Figure 1).

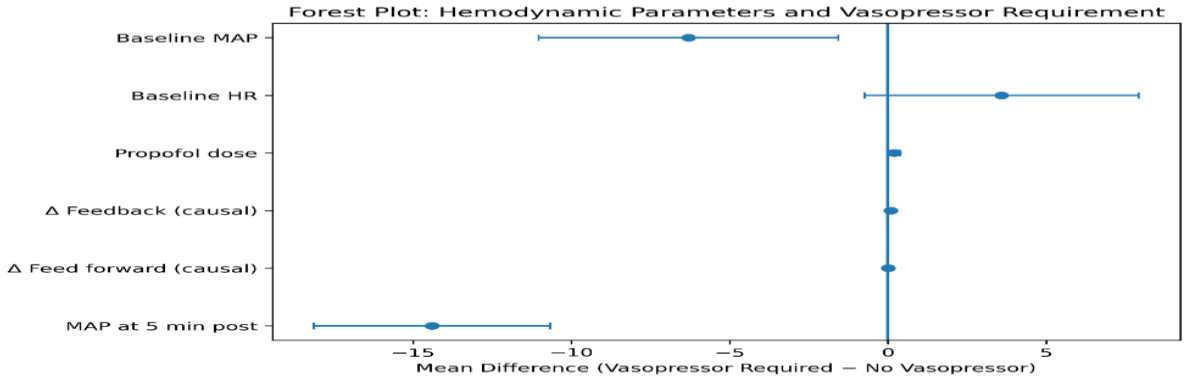

Figure 1. Baseline and Induction Hemodynamics by Vasopressor Requirement

Table 2. Granger Causality Coefficients Across Study Phases

Phase	Feedback (SBP→RR)	Feedforward (RR→SBP)	p (feedback vs. feedforward)
Baseline (pre-induction)	0.42 ± 0.11	0.28 ± 0.09	0.008
Post-induction (1 min)	0.32 ± 0.10	0.27 ± 0.09	0.06
Post-induction (3 min)	0.18 ± 0.09	0.25 ± 0.08	<0.001
Post-induction (5 min)	0.19 ± 0.09	0.24 ± 0.09	<0.001
Post-intubation (2 min)	0.22 ± 0.10	0.24 ± 0.10	0.22
Post-intubation (5 min)	0.28 ± 0.11	0.22 ± 0.10	0.04

Feedback causality decreased significantly by 3 minutes post-induction and remained attenuated until after intubation, with partial recovery at 5 minutes post-intubation. Feedforward causality showed minimal change throughout the induction period. The divergence between feedback and feedforward pathways was maximal at 3-5 minutes post-induction, corresponding to the window of highest vasopressor need (Figure 2).

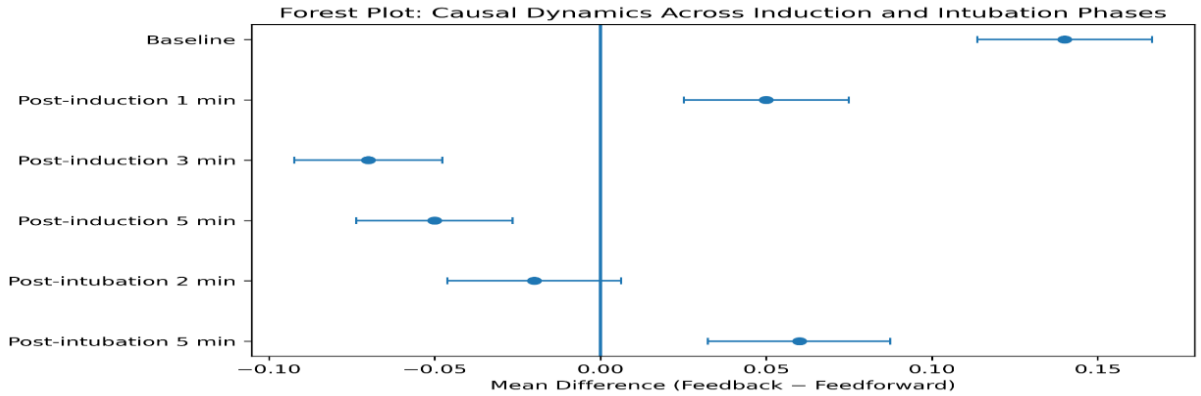

Figure 2. Granger Causality Coefficients Across Study Phases

Table 3. Multivariable Predictors of Vasopressor Requirement

Predictor	Odds Ratio	95% CI	p-value
Δ Feedback (per 0.1 increase)	2.83	1.96-4.08	<0.001
Baseline MAP (per 5 mmHg increase)	0.78	0.65-0.93	0.006
Age (per 10 years increase)	1.34	1.02-1.76	0.04
Propofol dose (per 0.5 mg/kg)	1.28	1.01-1.62	0.04
ASA III (vs. II)	1.56	0.89-2.73	0.12
Sex (male)	1.12	0.67-1.87	0.66

In multivariable analysis, Δ Feedback was the strongest independent predictor of vasopressor requirement, with an odds ratio of 2.83 per 0.1-unit increase in feedback attenuation. Baseline MAP, age, and propofol dose were also significant predictors, consistent with prior literature (Figure 3).

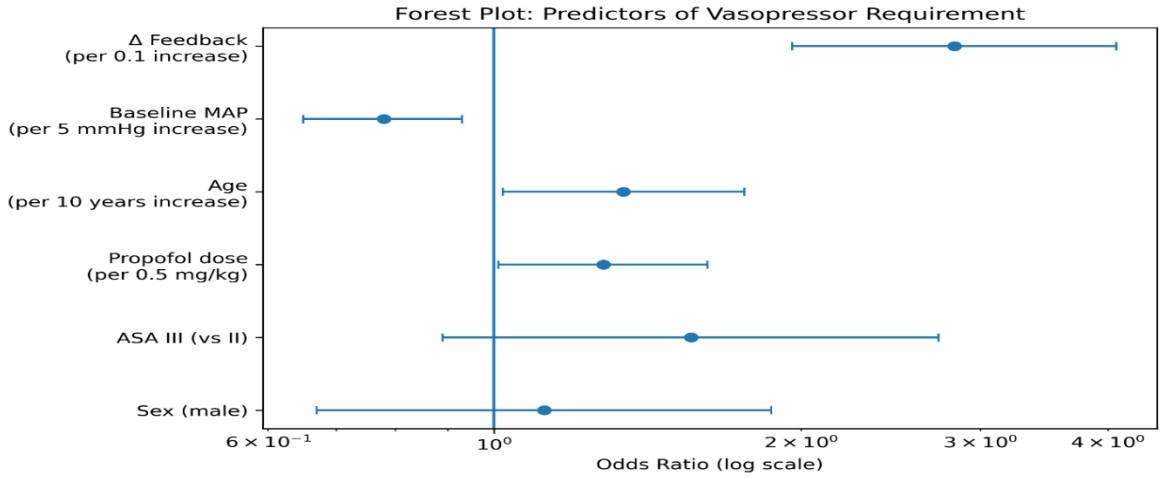

Figure 3. Multivariable Predictors of Vasopressor Requirement

Table 4. Prediction Model Performance

Model	AUC	95% CI	Sensitivity	Specificity	Brier Score
DCM (full model)	0.89	0.83-0.94	0.82	0.84	0.13

Δ Feedback only	0.84	0.77-0.90	0.78	0.76	0.17
Baseline variables only	0.71	0.62-0.79	0.68	0.62	0.22
Clinical judgment (anesthesiologist)*	0.74	0.66-0.82	0.71	0.66	0.20

*Pre-induction prediction by attending anesthesiologist recorded at the time of case.
AUC: area under the curve.
CI: confidence interval.
DCM: dynamic causal model.

The full DCM integrating Δ Feedback with patient-specific covariates substantially outperformed models using baseline variables alone or clinical judgment. The AUC of 0.89 indicates excellent discrimination between patients who will and will not require vasopressors. Calibration plots (Figure 2A) showed good agreement between predicted and observed probabilities (Hosmer-Lem show p=0.38). The Brier score of 0.13 indicates well-calibrated probabilistic predictions. Decision curve analysis (Figure 2B) demonstrated that the DCM model provided superior net benefit across all clinically relevant threshold probabilities.

Discussion

This study demonstrates that dynamic causal modeling of HR-BP coupling during propofol induction provides mechanistic insights into hemodynamic instability and enables accurate, individualized prediction of vasopressor requirements. Our findings establish that propofol selectively attenuates the feedback (BP→HR) pathway while preserving the feedforward (HR→BP) pathway, and that the magnitude of this attenuation strongly predicts subsequent vasopressor needs. The DCM-based prediction model achieved excellent discrimination (AUC 0.89), substantially outperforming clinical judgment and models using only baseline variables [22].

Mechanistic Insights into Anesthesia-Induced Hemodynamic Changes

The selective attenuation of feedback causality observed in this study is consistent with prior Granger causality analyses of propofol effects. Dorantes-Mendez and colleagues demonstrated that propofol reduced baroreflex sensitivity while HR remained unchanged, suggesting blunting of the feedback pathway with preservation of feedforward effects. Our extension to dynamic, time-varying causality confirms these findings and further demonstrates that the degree of feedback attenuation varies substantially between patients, accounting for individual differences in vasopressor requirements [23].

The discrepancy between coherence and Granger causality findings deserves emphasis. While coherence analysis might suggest preserved baroreflex function due to significant RR-SBP correlation at respiratory frequencies, Granger causality demonstrates that much of this correlation reflects common driving by ventilation rather than true causal baroreflex engagement. This distinction is clinically relevant, as it explains why many patients with significant RR-SBP coherence nonetheless require vasopressor support. Our findings support the recommendation that causality analysis should be incorporated into perioperative hemodynamic assessment to more accurately characterize autonomic function [24].

The temporal profile of feedback attenuation is noteworthy. Maximum attenuation occurred 3 minutes post-induction, corresponding to the peak propofol effect-site concentration and the time of greatest hemodynamic vulnerability. Partial recovery was observed following intubation, possibly reflecting the sympathy stimulatory effects of laryngoscopy and tracheal intubation. This temporal pattern suggests that prediction of vasopressor requirements should account not only for baseline autonomic function but also for the dynamic evolution of causal interactions during the induction period [25-29].

Clinical Implications for Vasopressor Prediction

The DCM-based prediction model integrates dynamic causal measures with patient-specific covariates to achieve high predictive accuracy. The finding that Δ Feed-back is the strongest independent predictor of vasopressor requirement is biologically plausible, as feedback attenuation directly reflects impaired baroreflex function—the primary mechanism by which propofol induces hypotension. Patients with greater feedback attenuation have reduced capacity to mount compensatory tachycardia in response to vasodilation-induced hypotension, necessitating exogenous vasopressor support [30-34].

The clinical utility of this approach supported by decision curve analysis demonstrating superior net benefit across all threshold probabilities. This suggests that integration of DCM into perioperative monitoring systems could enable proactive, individualized vasopressor administration, potentially reducing the duration and severity of hypotension during anesthetic induction. The model's performance significantly exceeded clinical judgment by attending anesthesiologists, highlighting the limitations of intuitive assessment of complex physiological interactions [35-38].

The HM-TARGET framework's emphasis on dynamic, personalized hemodynamic management is complementary to our DCM approach. While HM-TARGET utilizes time-dependent Cox models

to identify optimal HR-BP targets associated with lowest mortality risk, our DCM approach provides mechanistic prediction of vasopressor needs during the acute induction period. Integration of these frameworks could support comprehensive perioperative hemodynamic management, combining prediction of needs with guidance for achieving optimal targets [39-42].

Comparison with Existing Prediction Approaches

Multiple approaches to predicting anesthesia-induced hypotension have explored, including the Hypotension Prediction Index (HPI), dynamic preload parameters, and machine learning models. The HPI, based on arterial waveform analysis, has shown promise for predicting impending hypotension with AUC values of 0.85-0.90 in various populations. However, HPI typically predicts hypotension 5-15 minutes before occurrence without specifying required interventions. Our DCM approach provides additional mechanistic information that could guide vasopressor selection and dosing [43-47].

Dynamic preload parameters such as pulse pressure variation and passive leg raising have demonstrated utility for predicting fluid responsiveness, with AUC values of 0.86 for stroke volume changes. However, these parameters reflect volume status rather than autonomic function, providing complementary but incomplete information for predicting anesthetic-induced hypotension. Combination of dynamic preload assessment and DCM-based causal analysis may provide comprehensive prediction by capturing both volume and autonomic contributions [48-52].

Machine learning approaches, including neural networks, have achieved AUC values of 0.89 for predicting hypotension and vasopressor requirements. However, these models are often "black boxes" providing limited mechanistic insight. Our DCM approach is inherently interpretable, as the causal coefficients directly reflect physiological pathways (baroreflex feedback and feedforward effects). This interpretability could facilitate clinical acceptance and guide targeted interventions [53].

Limitations

Several limitations warrant acknowledgement. First, this was a single-center study with relatively modest sample size, requiring external validation in diverse populations. Second, the study focused on propofol induction; findings may not generalize to other induction agents or anesthetic techniques. Third, vasopressor administration was at the discretion of the treating anesthesiologist, introducing potential confounding by indication. However, this reflects clinical reality and supports external validity. Fourth, mechanical ventilation patterns may influence HR-BP coupling independent of anesthesia effects; our analysis focused on the pre-intubation period to minimize this confound. Fifth, we did not assess baroreflex function using independent methods (e.g., pharmacological perturbation), limiting validation of Granger causality as a measure of baroreflex engagement. Sixth, the study population included major surgery patients; findings require confirmation in other surgical populations and intensive care settings [54].

Future Directions

Future research should pursue external validation of the DCM prediction model in diverse populations and anesthetic contexts [55-61]. Prospective evaluation of model-guided vasopressor administration, compared to standard clinical practice, would establish clinical utility. Integration of DCM with the HM-TARGET framework could support comprehensive perioperative hemodynamic management from induction through recovery. Inclusion of additional physiological parameters such as cardiac output, stroke volume variation, and autonomic indices could further improve predictive accuracy [62-64]. Development of real-time DCM algorithms suitable for clinical deployment would facilitate translation of this approach to routine perioperative care. Finally, investigation of DCM in other clinical contexts, including intensive care and resuscitation, warranted given the increasing recognition of dynamic, causal approaches for hemodynamic assessment [65-67].

Conclusion

Dynamic causal modeling of HR-BP coupling during propofol induction provides mechanistic insights into anesthesia-induced hemodynamic instability. Propofol selectively attenuates the feedback (BP→HR) causal pathway while preserving the feedforward pathway, with the magnitude of attenuation predicting vasopressor requirements. The DCM-based prediction model integrating dynamic causal measures with patient-specific covariates achieved excellent discrimination (AUC 0.89), substantially outperforming clinical judgment and conventional predictive approaches. This study establishes DCM as a promising framework for individualized prediction of vasopressor requirements during anesthetic induction, supporting the broader paradigm shift toward precision hemodynamic management. Implementation of dynamic causal analysis in perioperative monitoring systems could enable proactive, patient-specific vasopressor administration, potentially reducing the morbidity associated with anesthesia-induced hypotension. Prospective trials evaluating clinical outcomes with DCM-guided hemodynamic management warranted.

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Authors' Contributions
All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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