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2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

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ARTIFICIAL INTELLIGENCE IN ANESTHETIC DRUG DELIVERY AND HEMODYNAMIC CONTROL: CLOSED-LOOP SYSTEMS, PREDICTION ALGORITHMS, AND A PRACTICAL IMPLEMENTATION APPROACH

Mateusz Józef Goldyn (Corresponding Author, Email: mateuszgoldyn@gmail.com)

Podhale Specialist Hospital in Nowy Targ, Nowy Targ, Poland

ORCID ID: 0009-0006-2833-598X

Jakub Michał Lichoń

J. Śniadecki Specialist Hospital in Nowy Sącz, Nowy Sącz, Poland

ORCID ID: 0009-0006-7691-357X

Marta Kras

The Independent Group of Public Ambulatory Care Institutions Warsaw-Ochota, Warsaw, Poland

ORCID ID: 0009-0006-9605-1866

Agata Karasiewicz

Otwock County Hospital – Otwock County Health Centre, Otwock, Poland

ORCID ID: 0009-0003-2301-267X

Maja Kukło

Clinical Hospital of the Ministry of Internal Affairs and Administration with the Warmia-Mazury Oncology Centre in Olsztyn, Olsztyn, Poland

ORCID ID: 0009-0006-4008-647X

Dominik Łepecki

M. Kopernik Regional Multispecialised Oncology and Traumatology Centre in Łódź, Łódź, Poland

ORCID ID: 0009-0007-3737-7599

Aleksandra Karolak

Medical University of Białystok, Białystok, Poland

ORCID ID: 0009-0007-1179-1126

Eliza Jakubowska

Poznań University of Medical Sciences, Poznań, Poland

ORCID ID: 0009-0007-7372-5327

ABSTRACT

Modern anesthesia is a high-frequency control problem: clinicians must continuously titrate hypnotics, opioids, fluids, and vasopressors to achieve adequate hypnosis/analgesia while avoiding hemodynamic instability and downstream organ injury. Artificial intelligence (AI), machine learning, and classical control engineering are increasingly embedded in perioperative monitors and drug delivery platforms, enabling decision support and closed-loop control. Randomized trials and meta-analyses indicate that closed-loop systems for hypnosis (typically processed EEG targets such as BIS) improve time-in-target and reduce overshoot/undershoot compared with manual titration. Multi-variable systems that co-manage hypnosis, analgesia, and fluids are feasible and may improve short-term recovery outcomes in selected settings. On the hemodynamic side, intraoperative hypotension is common and associated with myocardial and kidney injury, AI-based early warning systems using arterial waveforms can predict hypotension minutes before onset and, when paired with treatment protocols, may reduce hypotension burden in some trials. Closed-loop vasopressor and fluid systems improve protocol adherence and reduce hypotension in perioperative and early postoperative care. AI-enabled decision support and closed-loop controllers can improve stability of anesthesia and blood pressure management, but they should be implemented as supervised systems with clear safety constraints, manual override, and ongoing performance monitoring. Future multicenter trials should prioritize patient-centered outcomes, external validation, and transparent reporting.

KEYWORDS

Artificial Intelligence, Closed-Loop Anesthesia, Processed EEG, Target-Controlled Infusion, Goal-Directed Fluid Therapy, Vasopressor, Intraoperative Hypotension, Machine Learning, Hemodynamic Optimization

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1. Introduction

General anesthesia is a dynamic, multi-input–multi-output process. Clinicians must continuously titrate hypnotics and opioids, adjust ventilation, and manage fluids and vasopressors to maintain adequate hypnosis/analgesia while preserving end-organ perfusion. Even in experienced hands, the combination of interpatient variability, surgical stimulation, and measurement noise makes tight control difficult.

Hemodynamic instability is a central safety challenge. Intraoperative hypotension is common, definitions vary, and risk appears to increase with both depth and duration of low blood pressure. Consensus statements emphasize that mean arterial pressure (MAP) values below roughly 60–70 mm Hg are associated with myocardial injury, acute kidney injury, and death, and that harm is generally a function of severity and exposure time [1]. Large observational cohorts and registry analyses similarly link lower intraoperative MAP to postoperative kidney and myocardial injury, and vascular surgery cohorts show associations with myocardial injury [2-6].

At the same time, excessive anesthetic depth and avoidable drug exposure can contribute to delayed emergence, delirium, and other postoperative complications. Processed EEG-guided anesthesia has been associated with reduced delirium and cognitive decline in randomized studies, supporting the value of objective targets when titrating hypnotics [31].

Artificial intelligence (AI), machine learning (ML), and classical control engineering offer tools to improve consistency and reduce clinician workload. In perioperative medicine, these approaches range from (i) decision support (e.g., early warning systems for hypotension) to (ii) closed-loop controllers that automatically adjust drug delivery based on continuous physiologic feedback. While the promise is attractive, safe implementation requires careful attention to measurement validity, fail-safe design, and human oversight.

Research Objective. To synthesize contemporary evidence on AI-enabled anesthetic drug delivery and AI-assisted hemodynamic prediction/control, and to propose a pragmatic implementation approach relevant to operating room and early postoperative care.

2. Research materials and methods

This manuscript is a narrative review intended as a practical synthesis for academic and clinical use. Because the field spans anesthesiology, biomedical engineering, and perioperative outcomes research, we prioritized randomized trials, meta-analyses, and high-quality validation studies, and we focused on systems with clear physiological targets and safety reporting.

2.1. Data sources and eligibility criteria

Data sources included PubMed/MEDLINE and major anesthesia and perioperative medicine journals from database inception through January 2026. Eligible publications were English-language studies (randomized trials, prospective observational studies, validation studies, systematic reviews, and high-quality narrative reviews) addressing: (i) closed-loop or computer-assisted anesthetic drug delivery (hypnosis, analgesia, neuromuscular blockade); (ii) AI/ML-based prediction of intraoperative hypotension or other hemodynamic events; and (iii) closed-loop or protocol-driven hemodynamic optimization (fluids and vasopressors) in the operating room or early postoperative period.

2.2. Search strategy and study selection

Search terms combined intervention keywords ("closed-loop", "automation", "computer-controlled", "target-controlled infusion", "processed EEG", "BIS", "propofol", "remifentanyl", "neuromuscular blockade", "goal-directed fluid therapy", "norepinephrine") with outcome and phenotype keywords ("hypotension", "blood pressure", "hemodynamic", "prediction", "machine learning"). Key papers were identified through citation chaining of seminal trials and screening reference lists of recent systematic reviews.

2.3. Data collection and analysis / Statistical analysis

For included studies, we extracted population characteristics, clinical setting (intraoperative vs postoperative), physiological targets (e.g., BIS range or MAP threshold), controller type (decision support vs closed-loop), and key endpoints (time-in-target, hypotension burden, drug consumption, recovery metrics, and safety events). Evidence was synthesized qualitatively; no quantitative pooling was attempted because of heterogeneity in control targets, algorithms, and outcome definitions.

2.3.1. Software

Standard word-processing and citation tools were used for manuscript preparation and reference management.

2.3.2. AI

AI tools were used solely to assist with language refinement and formatting under human supervision. Study selection, interpretation of evidence, and conclusions were determined by the authors. All AI-assisted edits were reviewed and revised to ensure factual accuracy and adherence to scientific writing standards.

2.3.3. Synthesis approach

We organized evidence by clinical control loop: hypnotic depth, analgesia/antinociception, neuromuscular blockade, and hemodynamics. Within each domain, we distinguish between (i) prediction/decision support and (ii) autonomous closed-loop titration, and we emphasize findings reproduced across independent trials and meta-analyses.

3. Research results

3.1. Conceptual framework: decision support vs closed-loop control

Perioperative AI spans a continuum from passive analytics to autonomous actuation. Decision support systems analyze real-time data and provide recommendations (e.g., a predicted risk of hypotension in the next 5–15 minutes), but the clinician remains the actuator. In contrast, closed-loop systems directly adjust drug delivery (or other actuators) based on continuous feedback to maintain a target range (e.g., BIS 40–60 or MAP ≥ 65 mm Hg).

A practical way to define a closed-loop controller is by its components: (i) sensor (e.g., processed EEG, arterial pressure waveform, neuromuscular monitoring), (ii) controller (rule-based, classical control such as PID, model-predictive control, or ML-enhanced logic), and (iii) actuator (infusion pump, ventilator setting, or

fluid/vasopressor administration). Many clinically tested anesthesia controllers rely on classical control engineering rather than modern deep learning, but the clinical question is the same: does automation improve stability and safety under real-world conditions? [12-13,16-17,21]

Safety design principles are especially salient in anesthesia, where the system controls potent drugs. Commentaries on autonomous anesthesia emphasize that any automation must (i) be bounded by hard safety constraints (dose limits and physiologic alarms), (ii) allow immediate manual override, and (iii) communicate its current state and rationale to the clinician to minimize automation surprises [14-15].

Across the literature, effectiveness is usually reported using control-performance endpoints such as time-in-target range, median absolute performance error, frequency of overshoot/undershoot events, and recovery metrics. For hemodynamics, analogous metrics include time-weighted average hypotension, area under a MAP threshold, and incidence and cumulative duration of hypotension [1,6,25-28].

3.2. AI and automation in anesthetic drug delivery

3.2.1. Closed-loop hypnosis control using processed EEG targets

Closed-loop hypnosis control is the most mature domain of automated anesthesia. Early clinical work demonstrated feasibility of using processed EEG indices as feedback signals to titrate propofol in real time [7]. Subsequent randomized trials showed that closed-loop propofol systems can maintain hypnosis targets more tightly than manual administration. For example, Hemmerling and colleagues reported improved hypnosis control with a closed-loop propofol system compared with manual titration in a randomized controlled trial [8]. A later randomized trial evaluating a closed-loop total intravenous anesthesia system similarly found better control performance compared with clinician-managed infusion [9].

Meta-analyses of randomized controlled trials consistently report that closed-loop systems improve time spent within the desired hypnosis range and reduce control error compared with manual approaches, with generally comparable safety profiles when appropriate safeguards are used [12-13]. These findings are clinically relevant because they translate into fewer periods of excessive anesthesia depth (risking delayed recovery) or inadequate hypnosis (risking awareness or movement), although large outcome trials linking closed-loop hypnosis to hard endpoints remain limited.

3.2.2. Dual- and multi-loop systems for hypnosis and analgesia

Surgical stimulation affects both hypnotic requirements and hemodynamics, motivating controllers that co-titrate hypnotics and opioids. Dual-loop systems have been tested clinically; in obese adult patients, Liu and colleagues evaluated a BIS-guided dual-loop controller for co-administration of propofol and remifentanyl and reported effective maintenance of hypnosis targets in a randomized design [10].

Beyond two-drug control, multi-loop anesthesia platforms have been developed to manage hypnosis, analgesia, and fluids in parallel. A pilot study demonstrated the feasibility of fully automated hypnosis, analgesia, and fluid management using two independent closed-loop systems during major vascular surgery [18]. In a randomized controlled trial, Joosten and colleagues compared anesthetic management using multiple closed-loop systems with standard practice and reported differences in postoperative neurocognitive recovery in the intervention group, highlighting that automation may influence recovery trajectories in addition to intraoperative stability [19].

Systematic reviews suggest that AI-assisted interventions across perioperative anesthetic management may improve intermediate endpoints (e.g., target adherence) but show heterogeneity in algorithms and outcomes, emphasizing the need for standardized reporting and clinically meaningful endpoints [30].

3.2.3. Neuromuscular blockade and integrated control

Neuromuscular blockade (NMB) is another controllable domain, with established quantitative monitoring (e.g., train-of-four ratios) providing a feedback signal. Janda and colleagues described a closed-loop system capable of controlling both anesthetic depth and neuromuscular blockade, demonstrating the feasibility of integrated control across multiple physiologic axes [11].

In practice, integrated multi-domain control introduces interaction risks: changes in opioid dosing can alter hemodynamics and processed EEG; changes in ventilation affect CO₂ and cerebral blood flow; and vasopressors can influence EEG-derived indices through perfusion and drug distribution changes. These interactions reinforce the importance of conservative controller gains, robust artifact rejection, and clear alarm thresholds in multi-loop systems [14-15,17,21].

3.2.4. Practical constraints and failure modes in drug-delivery automation

Closed-loop performance depends on the fidelity of its sensors. Processed EEG indices can be influenced by electromyographic activity, poor electrode contact, electrocautery artifact, and certain drugs, and they may be less reliable in specific populations (e.g., neurologic injury). When the sensor signal is corrupted, the controller may overreact unless robust artifact detection and fail-safe behavior are implemented.

A second constraint is interpatient variability and context dependence. Even with the same target (e.g., BIS 45), the dose–response relationship differs by age, comorbidities, and concomitant agents. Modern systems address this with adaptive control, individualized PK/PD models, or conservative dose-change limits, but generalizability must still be demonstrated in diverse settings [12-13,16-17].

Finally, automation changes workflow. If clinicians over-trust the system (automation bias) or lose manual titration skills (deskilling), safety can be compromised. Human factors testing, training, and transparent system behavior are therefore central to safe adoption [14-15].

3.3. AI-assisted hemodynamic prediction and control

3.3.1. Clinical importance of hemodynamic stability

Hemodynamic management is a core component of anesthetic safety. Observational data consistently associate intraoperative hypotension with postoperative organ injury. Risk thresholds vary across studies, but exposure to MAP values below ~65 mm Hg and especially below 55–60 mm Hg has been linked to increased odds of acute kidney injury and myocardial injury [2-6]. Consensus statements from the Perioperative Quality Initiative (POQI) conclude that MAP <60–70 mm Hg is associated with myocardial injury, acute kidney injury, and death, and that injury is a function of severity and duration [1].

These associations motivate two complementary strategies: (i) earlier detection and prevention (prediction and decision support) and (ii) tighter control (closed-loop fluid and vasopressor titration). Both strategies are now being evaluated clinically.

3.3.2. Prediction and early warning systems for intraoperative hypotension

Machine-learning models can extract predictive features from high-frequency arterial pressure waveforms. Hatib and colleagues described an ML-based algorithm that predicts hypotension using waveform analysis, forming the basis for the Hypotension Prediction Index (HPI) concept [25]. Subsequent validation work demonstrated the ability of HPI to predict hypotensive events ahead of time in surgical patients [26].

Clinical impact depends on how predictions are operationalized. The HYPE randomized clinical trial evaluated an ML-derived early warning system combined with a treatment protocol and reported reductions in the depth and duration of intraoperative hypotension compared with standard care in elective noncardiac surgery [27]. Other randomized evaluations have shown mixed results, including trials in which HPI guidance did not reduce hypotension incidence relative to control, underscoring that protocols, clinician response, patient selection, and baseline practice patterns may determine benefit [28].

Recent syntheses emphasize both promise and uncertainty: after several years of clinical deployment, systematic reviews summarize variable effects on hypotension metrics and limited evidence for improvements in hard clinical outcomes, highlighting the need for standardized hemodynamic endpoints and multicenter effectiveness studies [29-30].

3.3.3. Closed-loop goal-directed fluid therapy

Goal-directed fluid therapy (GDFT) is conceptually well suited to automation because it relies on protocolized responses to dynamic preload indicators and stroke volume changes. Rinehart and colleagues outlined the rationale for closed-loop fluid management and described early implementations designed to deliver fluid boluses based on real-time hemodynamic responses [21].

In a clinical pilot study, Joosten and colleagues evaluated GDFT with closed-loop assistance during moderate-risk surgery using noninvasive cardiac output monitoring and reported feasibility and improved protocol adherence [20]. In larger multi-loop frameworks, closed-loop fluid management has been paired with automated hypnosis/analgesia control, suggesting that multiple controllers can operate concurrently when targets and safety constraints are clearly specified [18-19].

3.3.4. Closed-loop vasopressor control

Vasopressor titration is another candidate for closed-loop control because blood pressure is continuously measurable and infusion pumps provide precise actuation. In a randomized controlled trial, Joosten and colleagues reported that computer-assisted individualized hemodynamic management using closed-loop norepinephrine infusion improved blood pressure control compared with manual titration in the operating room [22].

Closed-loop vasopressor strategies have also been tested in the early postoperative setting. Desebbe and colleagues evaluated automated closed-loop norepinephrine infusion to prevent postoperative hypotension and reported reduced hypotension compared with standard management [23].

Obstetric anesthesia provides a distinct use case because spinal anesthesia–induced hypotension is common and time-sensitive. A randomized trial compared a closed-loop double-vasopressor automated system with manual bolus vasopressor treatment during spinal anesthesia for cesarean section, demonstrating feasibility of automated blood pressure management in this context [24].

3.4. A practical implementation approach

The translation of AI-enabled decision support and closed-loop controllers into routine practice should be incremental and target specific failure points (e.g., frequent hypotension in high-risk cases, or unstable hypnosis control during total intravenous anesthesia). Table 1 summarizes practical entry points and safety checks.

Clinical scenario	AI/automation option	Suggested target	Notes / safety checks
Routine TIVA where processed EEG is used	Closed-loop propofol ($\pm$ opioid) titration based on BIS/processed EEG	BIS/processed EEG target range (e.g., 40–60)	Ensure good electrode contact; pause automation during electrocautery artifact; set maximum infusion-rate changes; immediate manual override [7-9,12-13].
Major abdominal/vascular surgery with high hemodynamic variability	Multi-loop platform (hypnosis + analgesia + fluids) or staged adoption (closed-loop hypnosis + protocolized hemodynamics)	Stable hypnosis + individualized MAP threshold (often ≥ 65 mm Hg)	Use conservative constraints; confirm arterial line fidelity; define escalation ladder (fluids vs vasopressor) [18-19,21].
Moderate-risk surgery with GDFT protocol	Closed-loop or computer-assisted GDFT	Stroke volume optimization / dynamic indices per protocol	Validate signal quality of CO monitoring; ensure fluid limits and clinician confirmation for large boluses [20-21].
High-risk hypotension patients (elderly, vascular disease)	AI early warning system (e.g., waveform-based hypotension prediction) + treatment protocol	Prevent MAP < 65 mm Hg and reduce time-weighted hypotension	Predictions must trigger actionable protocol steps; avoid alarm fatigue; audit performance (false positives/negatives) [25-29].
Immediate postoperative period in PACU/ICU where hypotension is frequent	Closed-loop norepinephrine to prevent/treat hypotension	MAP target individualized to baseline and comorbidity	Ensure invasive BP signal quality; set maximum dose, minimum infusion, and safety alarms; frequent clinical reassessment [23].
Spinal anesthesia for cesarean delivery	Closed-loop vasopressor administration	Maintain systolic BP close to baseline / institutional target	Rapid response settings; fetal considerations; ensure clinician override and protocol alignment [24].

Across settings, a minimum safety framework should include: (i) clearly defined physiological targets and acceptable ranges, (ii) hard dose limits and rate-of-change limits, (iii) robust detection of sensor artifact and signal loss, (iv) immediate manual override with clear indication of who is controlling the infusion, and (v) continuous quality assurance using standardized metrics (time-in-target, hypotension burden, drug utilization, recovery times, and adverse events) [14-15].

3.5. Ethical, legal, and safety considerations

AI and automation in anesthesia raise questions of accountability, transparency, and bias. Even when the controller is not "black box" ML, the system is a medical device whose behavior must be understandable to clinicians and auditable by institutions. Version control and post-deployment monitoring are essential because software updates can change performance in subtle ways.

Reporting quality is a prerequisite for trustworthy evidence. AI-focused extensions to trial and prediction-model reporting guidelines (CONSORT-AI, SPIRIT-AI, TRIPOD+AI) provide structured recommendations for describing the intervention, data handling, evaluation, and human–AI interaction, enabling replication and critical appraisal [33-35].

Human factors risks include alarm fatigue, automation bias, and deskilling. Implementation should therefore include clinician training, simulation-based onboarding, and clear policies for when to disengage automation (e.g., during rapid hemorrhage, equipment malfunction, or when targets become clinically inappropriate).

3.6. Limitations of the evidence base

The evidence base remains heterogeneous. Many closed-loop studies are single-center trials with surrogate endpoints such as time-in-target range rather than major postoperative outcomes. Heterogeneity in targets (BIS ranges, MAP thresholds), sensors, and controller design limits cross-study comparability.

Generalizability is a persistent concern. Algorithms validated in controlled settings may underperform with different patient populations, monitoring systems, surgical types, or clinician workflows. External validation and multicenter randomized trials are therefore critical before broad adoption [30,33-35].

Finally, hemodynamic prediction tools are only as effective as the treatment protocol and clinician response. Mixed trial results suggest that prediction alone does not guarantee improved outcomes; the clinical workflow must be engineered so that predictions lead to timely, appropriate interventions [27-29].

4. Discussion

This review summarizes a rapidly maturing field in which perioperative AI is moving from analytics to actuation. Across multiple randomized trials and meta-analyses, closed-loop hypnosis control—most commonly propofol titration guided by processed EEG targets—improves control performance compared with manual titration [7-9,12-13]. These gains are consistent across systems and suggest that automation can reduce variability inherent in clinician-managed infusion.

Multi-loop systems extend this concept to analgesia and hemodynamics. Pilot and randomized studies show that concurrent automation of hypnosis/analgesia and fluids is feasible and can influence recovery endpoints, including neurocognitive outcomes in selected trials [18-19]. However, the interaction between loops (drug–hemodynamic–EEG coupling) and the complexity of real-world surgery mean that multi-loop deployment should be staged and carefully monitored [14-15,17,21].

Hemodynamic AI has two distinct faces: prediction and control. Waveform-based prediction tools can forecast hypotension and may reduce hypotension burden when paired with structured treatment protocols, but trial results are not uniformly positive [25-29]. In contrast, closed-loop control of vasopressors and fluids directly addresses the control problem and has shown promising reductions in hypotension in perioperative and postoperative settings [20-24]. Whether these improvements translate into fewer myocardial or kidney injuries remains a key evidence gap.

From an implementation perspective, the safest near-term framing is "AI as supervised co-pilot" rather than full autonomy. Controllers should be bounded, transparent, and easy to disengage. Institutions should adopt AI devices with a governance framework that includes procurement review, training, simulation, post-deployment performance audits, and incident reporting.

Future research priorities include: (i) multicenter trials powered for clinically meaningful outcomes (acute kidney injury, myocardial injury, delirium, length of stay), (ii) external validation in diverse populations and workflows, (iii) standardized definitions of hypotension and control-performance metrics, and (iv) rigorous reporting of human–AI interaction using AI-specific guidelines [1,33-35].

5. Conclusions

Anesthetic drug delivery and hemodynamic management are control problems characterized by continuous data streams, variable physiology, and high stakes. Evidence from randomized trials and meta-analyses supports the ability of closed-loop systems—particularly processed EEG-guided hypnotic control—to improve stability and reduce control error compared with manual titration [7-9,12-13].

AI-assisted hemodynamic tools can predict and prevent hypotension and can automate vasopressor and fluid titration, with several trials reporting reductions in hypotension burden in the operating room and early postoperative care [20-29]. Given the established associations between hypotension and organ injury, these systems warrant continued evaluation with patient-centered outcomes [1-6].

Safe adoption requires more than algorithmic performance: it depends on sensor reliability, fail-safe design, clinician training, and transparent reporting. When implemented as supervised systems with clear constraints, AI and automation have the potential to improve perioperative stability while allowing clinicians to focus on higher-level decision making.

Author Contributions:

Conceptualization: Jakub Michał Lichoń

Methodology: Mateusz Józef Gołdyn

Investigation: Marta Kras, Eliza Jakubowska

Writing: Original Draft Preparation: Agata Karasiewicz

Writing: Review and Editing: Mateusz Józef Gołdyn, Maja Kuklo

Project Administration: Dominik Łepecki

Data Curation: Jakub Michał Lichoń, Aleksandra Karolak

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