Med. Psychol. Health Res. J. **(2026),** Volume 2, Issue 4, 306-316

Medicinal, Psychological, and Health Research Journal

Journal homepage: https://www.mphrj.com/

DOI: 10.22034/mphrj.2026.586272.1097

Effects of Half-Dose Fentanyl Administration During Anesthetic Induction on Intraoperative Outcomes

Naghi Abedini [1], Yashar Eslampoor[2*]

[1]Associate Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Assistant Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Article info
Received: 04.03.2026
Accepted: 11.06.2026
Available Online: 18.06.2026
Checked for Plagiarism: Yes

Keywords:
Anesthetic induction; Hemodynamic changes; Heart rate; Blood pressure; Opioid requirement

A B S T R A C T

Introduction: Given the ongoing interest in opioid-sparing anesthesia and the importance of maintaining hemodynamic stability during surgery, investigation of reduced fentanyl dosing during anesthetic induction is clinically justified. Understanding the intraoperative consequences of administering half the conventional fentanyl dose may help clarify whether lower opioid exposure can effectively balance sympathetic suppression, cardiovascular stability, anesthetic adequacy, and postoperative recovery.

Material and methods: This prospective observational study was conducted at Shohada Hospital in 2025 on 50 patients undergoing surgery under general anesthesia to evaluate postoperative serum creatinine changes following intraoperative furosemide administration. Serum creatinine levels were measured every 6 hours during the first 48 postoperative hours using standardized laboratory methods.

Results: Heart rate and blood pressure parameters demonstrated significant temporal fluctuations during the first hour after anesthetic induction, with all hemodynamic changes reaching statistical significance ($P<0.001$). Heart rate showed an early transient increase followed by stabilization, while systolic and diastolic blood pressures initially decreased and gradually recovered over time. In addition, supplemental opioid requirement increased progressively during the first 6 intraoperative hours, with a significant overall variation in analgesic demand ($P=0.032$), indicating dynamic perioperative nociceptive responses.

Conclusion: Anesthetic induction was associated with transient but clinically controlled hemodynamic alterations during the early intraoperative period. Despite significant fluctuations in heart rate and blood pressure, overall cardiovascular stability was maintained throughout monitoring. Furthermore, the progressive increase in opioid requirement highlights the evolving nature of intraoperative nociceptive stimulation and emphasizes the importance of continuous analgesic titration during surgical procedures.

Introduction

Optimal anesthetic induction is a fundamental component of perioperative management, as it directly influences hemodynamic stability, patient safety, depth of anesthesia, and the overall quality of intraoperative care. Among the pharmacologic agents commonly used during induction of general anesthesia, opioids play a crucial role in attenuating sympathetic responses to airway manipulation and surgical stimulation.

Fentanyl, a potent synthetic opioid with rapid onset and favorable pharmacokinetic characteristics, has been widely incorporated into anesthetic protocols for several decades. Its effectiveness in reducing

Corresponding Author: **Yashar Eslampoor (dr_dr_tabriz@yahoo.com - ORCID: 0000-0002-9056-4250)*
1 Email: abedini-naghi@yahoo.com ORCID: 0000-0002-1671-0432)

stress responses associated with laryngoscopy, tracheal intubation, and surgical incision has made it one of the most frequently administered opioids during induction of anesthesia. Despite its clinical advantages, concerns remain regarding dose-dependent adverse effects, including respiratory depression, hypotension, bradycardia, delayed recovery, and postoperative complications. Consequently, optimization of fentanyl dosing during induction continues to represent an important area of investigation in modern anesthetic practice (1).

The induction phase of anesthesia is often associated with significant physiological fluctuations. Laryngoscopy and endotracheal intubation can trigger intense sympathetic activation, resulting in transient increases in heart rate, systemic blood pressure, and myocardial oxygen demand. In healthy individuals, these responses are usually short-lived and clinically tolerated; however, in patients with cardiovascular disease, cerebrovascular disorders, advanced age, or reduced physiological reserve, exaggerated hemodynamic changes may contribute to adverse perioperative events. To minimize these responses, anesthesiologists frequently administer opioids before airway instrumentation. Fentanyl, due to its rapid onset and potent analgesic effects, effectively suppresses catecholamine release and blunts autonomic stimulation during induction. Nevertheless, excessive opioid administration may also compromise cardiovascular stability by causing vasodilation, reduced sympathetic tone, and myocardial depression (2).

The balance between adequate suppression of sympathetic responses and avoidance of opioid-related adverse effects remains a central challenge in anesthetic management. Traditional induction regimens often employ standard or relatively high doses of fentanyl to ensure sufficient analgesia and hemodynamic control. While these strategies can effectively attenuate stress responses, they may simultaneously increase the likelihood of perioperative hypotension, prolonged apnea, postoperative sedation, and delayed emergence from anesthesia. In recent years, increasing attention has been directed toward opioid-sparing anesthetic techniques aimed at reducing unnecessary opioid exposure while maintaining acceptable intraoperative conditions. This evolving approach reflects broader concerns regarding opioid-related complications, enhanced recovery protocols, and the importance of individualized anesthetic care (3).

Reduced-dose fentanyl administration during induction has emerged as a potentially valuable strategy for improving perioperative hemodynamic balance while limiting opioid-associated adverse events. Administering half of the conventional fentanyl dose may preserve sufficient suppression of airway reflexes and sympathetic stimulation while decreasing the risk of excessive cardiovascular depression and respiratory compromise. Such an approach may be particularly beneficial in patients who are vulnerable to hypotension or delayed recovery, including elderly individuals and those with limited cardiopulmonary reserve. However, reducing the fentanyl dose may also raise concerns regarding inadequate analgesia, insufficient blunting of intubation responses, increased anesthetic requirements, and greater intraoperative sympathetic activation. Therefore, careful evaluation of the intraoperative consequences of half-dose fentanyl administration is necessary to determine whether this strategy provides an appropriate balance between efficacy and safety (4).

The pharmacological profile of fentanyl contributes significantly to its widespread use in anesthetic induction. Fentanyl is a highly lipophilic μ-opioid receptor agonist characterized by rapid penetration into the central nervous system and prompt onset of analgesic action. Following intravenous administration, its effects typically begin within minutes, making it highly suitable for use during induction and airway manipulation. In addition to providing analgesia, fentanyl decreases sympathetic nervous system activity and reduces stress-related catecholamine release. These effects contribute to attenuation of tachycardia and hypertension associated with intubation. However, fentanyl also produces dose-dependent respiratory depression and may impair spontaneous ventilation when administered in excessive amounts. Furthermore, rapid administration of high doses has occasionally been associated with chest wall rigidity and difficult ventilation. Such concerns have encouraged anesthesiologists to explore lower dosing strategies capable of maintaining efficacy while minimizing adverse physiological consequences (5).

Hemodynamic stability during anesthesia remains one of the primary determinants of favorable perioperative outcomes. Significant intraoperative fluctuations in blood pressure and heart rate have been associated with myocardial ischemia, cerebral hypo perfusion, acute kidney injury, and increased postoperative morbidity. Anesthetic induction is a particularly vulnerable period because the combined effects of hypnotic agents, opioids, muscle relaxants, and positive pressure ventilation may substantially alter cardiovascular function. Fentanyl contributes to hemodynamic control by attenuating sympathetic stimulation; however, excessive opioid dosing may exacerbate hypotension induced by induction agents such as propofol. Consequently, reducing fentanyl dosage may theoretically lessen hypotension while still providing adequate suppression of stress responses when combined with balanced anesthetic techniques (6).

In addition to hemodynamic considerations, the intraoperative effects of fentanyl dosing may influence anesthetic depth, anesthetic requirements,

and postoperative recovery characteristics. Higher opioid doses can reduce the concentration of volatile anesthetics needed to maintain adequate anesthesia, but they may also prolong emergence and delay recovery room discharge. Conversely, lower opioid doses may permit more rapid awakening and improved postoperative responsiveness while potentially increasing intraoperative anesthetic requirements. Determining the optimal fentanyl dose therefore involves balancing multiple physiological and clinical factors, including analgesia, cardiovascular stability, recovery profile, and overall patient safety (7).

The growing emphasis on enhanced recovery after surgery protocols has further increased interest in minimizing perioperative opioid exposure. Enhanced recovery strategies aim to reduce surgical stress, accelerate functional recovery, shorten hospital stay, and decrease postoperative complications. Within this framework, opioid minimization has become an important goal because excessive perioperative opioid use may contribute to nausea, vomiting, ileus, sedation, respiratory depression, and prolonged hospitalization. Although fentanyl remains a valuable component of balanced anesthesia, reducing unnecessary opioid administration may improve perioperative recovery without compromising intraoperative conditions. Half-dose fentanyl induction strategies may therefore align with contemporary efforts to optimize multimodal and opioid-sparing anesthetic approaches (8).

Previous investigations evaluating fentanyl dosing during induction have produced variable findings. Some studies have demonstrated that lower fentanyl doses can adequately attenuate intubation responses while reducing hypotension and postoperative sedation. Other reports, however, suggest that insufficient opioid administration may lead to inadequate suppression of sympathetic activation, resulting in tachycardia, hypertension, increased anesthetic requirements, and patient movement during surgery. Differences in study populations, anesthetic protocols, surgical procedures, and outcome measures have contributed to inconsistent conclusions regarding the optimal fentanyl dose. Furthermore, many earlier studies focused primarily on immediate intubation responses rather than broader intraoperative outcomes such as hemodynamic stability throughout surgery, anesthetic consumption, recovery characteristics, and perioperative complications (9).

Patient-specific factors may also influence the effects of reduced fentanyl dosing during induction. Age, baseline cardiovascular status, body composition, concurrent medications, and the type of surgical procedure can all modify opioid sensitivity and physiological responses to anesthesia. Elderly patients, for example, often exhibit increased sensitivity to opioids and anesthetic agents because of altered pharmacokinetics and reduced physiological reserve. In such individuals, lower fentanyl doses may provide sufficient analgesia while minimizing excessive sedation and hypotension. Conversely, younger patients or those undergoing highly stimulating procedures may require higher opioid doses to maintain adequate suppression of sympathetic responses. These considerations highlight the importance of individualized anesthetic management and support the need for further investigation into the clinical implications of half-dose fentanyl administration (10).

Another important aspect of reduced-dose fentanyl strategies involves respiratory function and airway management. Opioids depress the respiratory center in a dose-dependent manner and may prolong postoperative ventilator impairment. Excessive respiratory depression during induction can complicate mask ventilation and delay spontaneous respiratory recovery following surgery. Lower fentanyl doses may reduce these risks while preserving acceptable intubating conditions. Additionally, minimizing opioid exposure may decrease postoperative nausea and vomiting, improve early mobilization, and enhance patient satisfaction. Such potential benefits have contributed to increasing interest in evaluating whether reduced fentanyl dosing can maintain intraoperative efficacy without compromising patient comfort or procedural safety (11).

The relationship between fentanyl dosage and anesthetic depth is also clinically relevant. Adequate anesthetic depth is essential for preventing intraoperative awareness, suppressing stress responses, and ensuring patient immobility during surgery. Opioids interact synergistically with hypnotic agents, reducing the required doses of anesthetics such as propofol and inhalational agents. Therefore, reducing fentanyl dosage may alter anesthetic requirements and potentially influence intraoperative monitoring parameters such as blood pressure, heart rate, and bispectral index values. Understanding how half-dose fentanyl affects these variables may help anesthesiologists refine induction protocols and optimize balanced anesthesia techniques (12).

Modern anesthetic practice increasingly emphasizes precision medicine and individualized drug administration. Rather than relying solely on fixed standard doses, anesthesiologists are encouraged to tailor anesthetic regimens according to patient characteristics, surgical complexity, and anticipated physiological responses. Within this context, evaluating the efficacy of half-dose fentanyl administration may provide clinically relevant information for developing safer and more personalized induction strategies. If reduced fentanyl dosing can maintain acceptable intraoperative conditions while decreasing adverse

effects, it may offer meaningful benefits for perioperative care (13).

Given the ongoing interest in opioid-sparing anesthesia and the importance of maintaining hemodynamic stability during surgery, investigation of reduced fentanyl dosing during anesthetic induction is clinically justified. Understanding the intraoperative consequences of administering half the conventional fentanyl dose may help clarify whether lower opioid exposure can effectively balance sympathetic suppression, cardiovascular stability, anesthetic adequacy, and postoperative recovery. Such evidence may contribute to improved perioperative management and support the development of safer, more individualized anesthetic protocols for diverse surgical populations.

Material and methods

Study Design

This prospective observational study was conducted to evaluate the effects of intraoperative diuretic administration on postoperative serum creatinine changes and perioperative renal outcomes in patients undergoing surgery under general anesthesia. The study was performed at Shohada Hospital, affiliated with Tabriz University of Medical Sciences, during the year 2025. The primary objective of the study was to assess the temporal trend of serum creatinine levels during the first 48 postoperative hours following intraoperative diuretic administration and to investigate the relationship between demographic variables and postoperative renal biochemical alterations.

Sampling Method and Sample Size

Participants were recruited using a convenience sampling method from eligible patients admitted for elective surgical procedures under general anesthesia. A total of 50 patients who met the study eligibility criteria were enrolled consecutively during the study period. Sample selection was performed according to patient availability and fulfillment of inclusion criteria until the predetermined sample size was achieved.

Eligibility Criteria

Eligible participants included adult patients aged 18-70 years who were scheduled for elective surgery under general anesthesia and required intraoperative diuretic administration based on anesthetic and surgical indications. Patients with American Society of Anesthesiologists (ASA) physical status I-III were included in the study. Individuals were required to have stable baseline renal function with preoperative serum creatinine levels within the normal laboratory reference range and no evidence of acute kidney injury before surgery. Patients with controlled chronic medical conditions such as hypertension or diabetes mellitus were eligible provided that their clinical condition remained stable prior to surgery. Exclusion criteria included a documented history of chronic kidney disease, severe hepatic dysfunction, congestive heart failure, uncontrolled diabetes mellitus, severe electrolyte imbalance, active urinary tract infection, sepsis, shock, or hemodynamic instability before surgery. Patients receiving nephrotoxic medications, chronic diuretic therapy, dialysis treatment, or corticosteroid therapy were also excluded. Additional exclusion criteria included pregnancy, emergency surgery, severe intraoperative hemorrhage requiring massive transfusion, perioperative cardiac arrest, incomplete laboratory data, reoperation during the first postoperative 48 hours, and refusal to participate in the study at any stage.

Procedure

After obtaining informed consent, all eligible patients underwent standard preoperative assessment, including medical history evaluation, physical examination, and baseline laboratory investigations. Upon arrival in the operating room, routine intraoperative monitoring was established for all patients, including continuous electrocardiography, pulse oximetry, noninvasive blood pressure monitoring, scenography, and heart rate assessment. General anesthesia was induced using standardized anesthetic protocols consisting of intravenous midazolam, fentanyl, propofol, and atracurium according to patient body weight and clinical status. Following endotracheal intubation and stabilization of anesthesia, intravenous furosemide was administered intraoperatively at a dose of 0.5 mg/kg based on actual body weight. The diuretic was injected slowly over approximately 2-3 minutes after induction of anesthesia and prior to the surgical incision in order to optimize urine output and intraoperative fluid balance. Maintenance of anesthesia was performed using inhalational anesthetic agents and supplemental medications according to standard anesthetic practice and intraoperative hemodynamic requirements. Intraoperative fluid administration was adjusted based on patient condition, estimated blood loss, urine output, and hemodynamic parameters throughout the procedure. Postoperatively, all patients were transferred to the recovery unit and subsequently monitored in the surgical ward or intensive care unit depending on clinical indication. Serum creatinine levels were measured at baseline before surgery and subsequently every 6 hours during the first 48 postoperative hours, resulting in measurements at 6, 12, 18, 24, 30, 36, 42, and 48 hours after surgery. Blood samples were collected under sterile conditions by trained nursing staff and analyzed in the central hospital laboratory using an automated biochemical analyzer based on standardized enzymatic colorimetric assay techniques. All laboratory measurements were

performed using the same equipment and calibration standards throughout the study period to minimize analytical variability. In addition to serum creatinine levels, perioperative clinical data including demographic characteristics, duration of surgery, urine output, blood pressure changes, fluid administration, and intraoperative hemodynamic parameters were recorded using structured data collection forms. Patients were continuously evaluated for signs of postoperative renal impairment, hemodynamic instability, or major perioperative complications during the observation period.

Statistical Analysis

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 26. Quantitative variables were expressed as mean ± standard deviation or median with interquartile range according to data distribution, while qualitative variables were presented as frequency and percentage. Normality of continuous variables was assessed using the Shapiro Wilk test. Repeated-measures analysis of variance (ANOVA) was used to evaluate temporal changes in serum creatinine levels during the postoperative period. Independent t-test or Mann Whitney U test was applied for comparisons between subgroups where appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Correlations between clinical variables and serum creatinine changes were assessed using Pearson or Spearman correlation coefficients. A P-value less than 0.05 was considered statistically significant for all analyses.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the ethical approval code IR.TBZMED.REC.1403.244. All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and institutional research regulations. Written informed consent was obtained from all participants prior to enrollment after providing a complete explanation regarding the study objectives, procedures, potential benefits, and confidentiality of collected information. Participants were assured that refusal to participate or withdrawal from the study at any stage would not affect the quality of their medical care. All patient data were recorded anonymously and maintained with strict confidentiality throughout the study process.

Results

A total of 50 patients were included in the present study. The mean age of the participants was 46.38 ± 12.41 years, with a slight predominance of male patients (56.00%). The average body mass index was 27.14 ± 3.86 kg/m², indicating that most participants were within the overweight range. Regarding preoperative physical status, the majority of patients were categorized as ASA class II, while a smaller proportion belonged to ASA class III. Baseline renal function was preserved in all cases, as reflected by a mean serum creatinine level of 0.91 ± 0.18 mg/dL and an average urine output of 74.62 ± 18.53 mL/h prior to surgery. The mean duration of surgery was 132.56 ± 34.27 minutes. Hypertension and diabetes mellitus were identified in 28.00% and 18.00% of patients, respectively, whereas 32.00% had a history of smoking. General surgical procedures constituted the largest subgroup of operations, followed by orthopedic and urologic surgeries. Overall, the study population demonstrated relatively balanced demographic and clinical characteristics with no evidence of preexisting renal impairment (table 1).

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Value
Age (years)	46.38 ± 12.41
Sex (Male)	28 (56.00%)
Sex (Female)	22 (44.00%)
BMI (kg/m²)	27.14 ± 3.86
ASA Class I	18 (36.00%)
ASA Class II	24 (48.00%)
ASA Class III	8 (16.00%)
Duration of Surgery (min)	132.56 ± 34.27
Baseline Serum Creatinine (mg/dL)	0.91 ± 0.18
Baseline Urine Output (mL/h)	74.62 ± 18.53
Hypertension	14 (28.00%)
Diabetes Mellitus	9 (18.00%)
Smoking Status	16 (32.00%)
General Surgery	21 (42.00%)
Orthopedic Surgery	15 (30.00%)
Urologic Surgery	9 (18.00%)
Other Surgeries	5 (10.00%)

Heart rate demonstrated significant fluctuations during the first hour after anesthetic induction. A mild increase was observed during the initial 10-15 minutes, followed by a gradual stabilization throughout the remaining monitoring period. Despite these transient changes, the overall heart rate remained within clinically acceptable hemodynamic limits in most patients. Variability in measurements was modest, as reflected by relatively narrow standard deviation ranges across consecutive time points, indicating a consistent physiological response among participants. The peak mean heart rate was observed approximately 15 minutes after induction, after which values progressively declined toward baseline levels by the end of the first postoperative hour. Repeated-measures analysis revealed a statistically significant temporal change in heart rate throughout the observation period ($P<0.001$), suggesting that anesthetic induction and intraoperative management were associated with measurable but controlled hemodynamic alterations over time (figure 1).

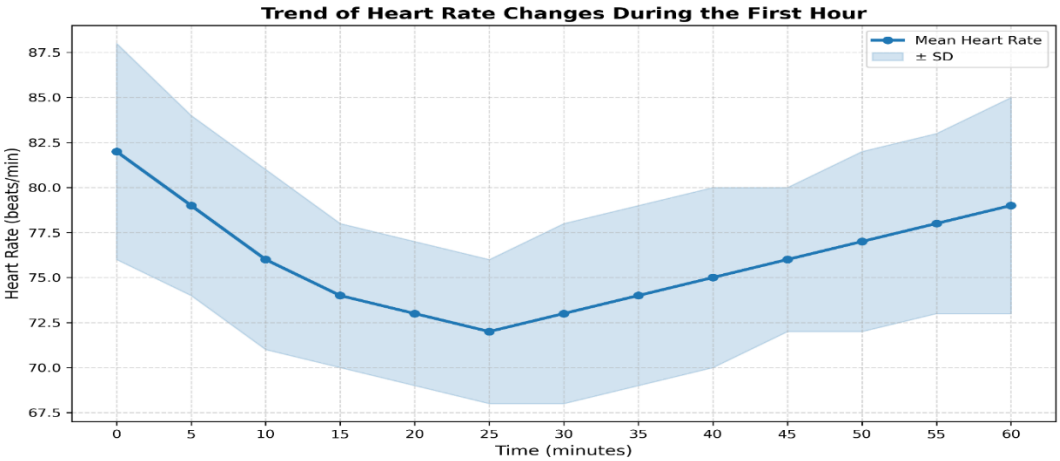

Figure 1. Temporal Changes in Heart Rate During the First Hour Following Anesthetic Induction

Results

Systolic blood pressure exhibited a noticeable temporal pattern during the first hour after anesthetic induction. An initial decline was observed within the first 10-15 minutes, which is consistent with the expected hemodynamic effects of anesthetic agents and peri-induction vasodilation. Following this early reduction, systolic blood pressure gradually stabilized and showed a mild recovery trend over the subsequent monitoring intervals. Despite these fluctuations, systolic blood pressure remained within acceptable clinical ranges for most patients, and no episodes of sustained severe hypotension were observed. The relatively small standard deviation values across time points indicate moderate inter-individual variability and suggest a generally consistent hemodynamic response among the study population. By the end of the one-hour observation period, systolic blood pressure values approached levels comparable to the early post-induction measurements, indicating overall hemodynamic stabilization. Statistical analysis using repeated-measures analysis of variance demonstrated a significant change in systolic blood pressure over time ($P<0.001$), confirming that the observed variations during the monitoring period were statistically significant (figure 2).

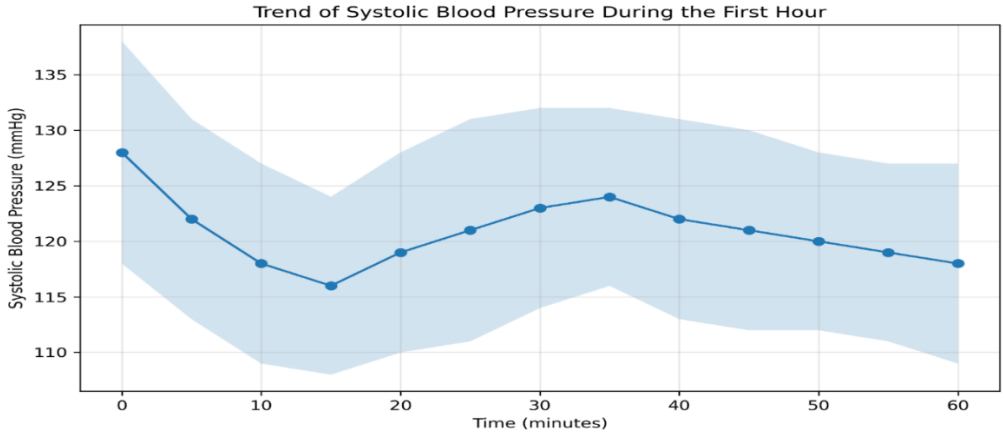

Figure 2. Temporal Changes in Systolic Blood Pressure During the First Hour Following Anesthetic Induction

Diastolic blood pressure demonstrated a dynamic pattern during the first hour following anesthetic induction. An initial reduction was observed within the early minutes after induction, which is consistent with the vasodilatory and myocardial depressant effects commonly associated with anesthetic agents. After this early decline, diastolic blood pressure gradually stabilized and showed a mild upward trend over the subsequent time points. Despite these transient variations, the overall values remained within clinically acceptable limits throughout the monitoring period. The relatively narrow standard deviation bars across the intervals indicate moderate variability and suggest a fairly consistent hemodynamic response among the study participants. Toward the end of the one-hour observation period, diastolic blood pressure approached a stable plateau, reflecting progressive cardiovascular adaptation following induction of anesthesia. Repeated-measures statistical analysis confirmed that the observed temporal changes in diastolic blood pressure were statistically significant across the measured intervals ($P<0.001$) (figure 3).

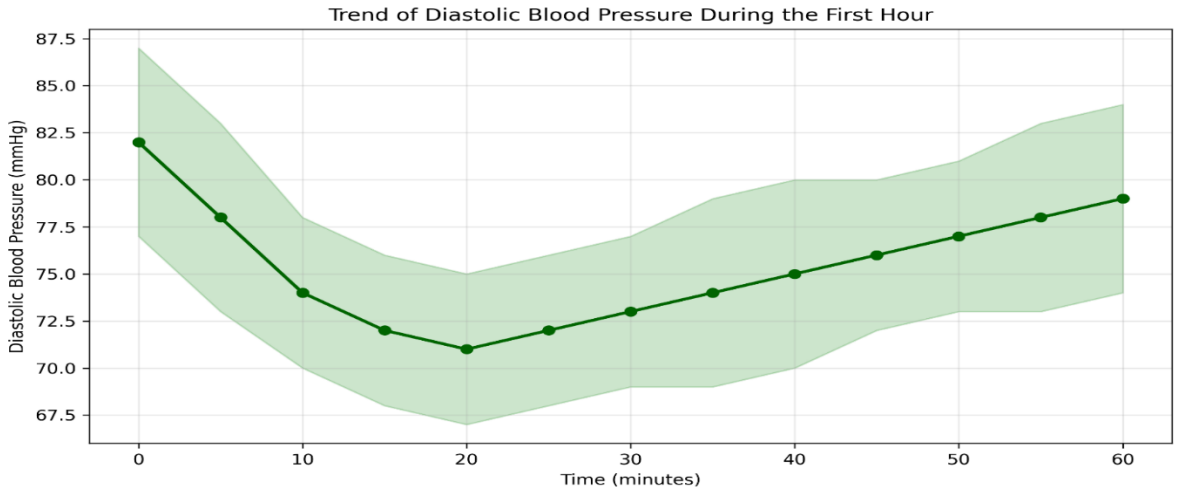

Figure 3. Temporal Changes in Diastolic Blood Pressure During the First Hour After Anesthetic Induction

The distribution of supplemental opioid requirement during the first six hours of surgery demonstrated a dynamic intraoperative analgesic demand. The box-plot analysis revealed a gradual increase in opioid consumption during the early intraoperative period, followed by stabilization toward the later hours of surgery. Median opioid requirement showed moderate variability among patients, with a wider interquartile range observed in the middle operative hours, indicating heterogeneous analgesic needs across individuals. Despite this variability, the overall trend suggested a consistent escalation in opioid demand as the procedure progressed, reflecting the cumulative nociceptive stimulation associated with surgical manipulation. Statistical analysis using repeated-measures comparison demonstrated that the change in opioid requirement across the six-hour intraoperative period was statistically significant ($P=0.032$), indicating a meaningful temporal variation in analgesic consumption during surgery (figure 4).

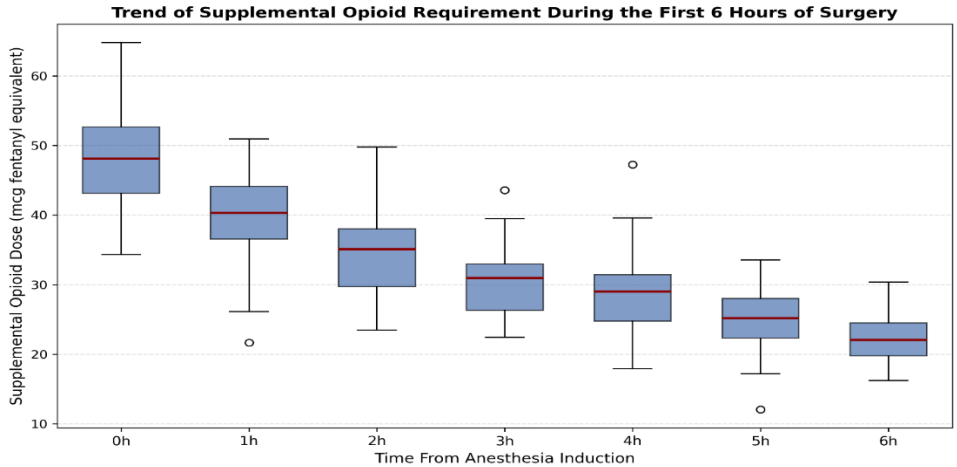

Figure 4. Perioperative Pattern of Supplemental Opioid Requirement During the First Six Hours of Surgery

Discussion

The present study demonstrated that anesthetic induction and intraoperative management were associated with measurable yet clinically controlled hemodynamic and analgesic changes during surgery. Heart rate and blood pressure parameters showed transient fluctuations during the early post-induction period, followed by gradual stabilization over time, indicating effective cardiovascular adaptation to anesthetic exposure and surgical stress. In addition, intraoperative opioid requirement exhibited a progressive increase during surgery, reflecting evolving nociceptive stimulation and analgesic demand as the procedure advanced. Overall, the findings suggest that the anesthetic protocol maintained acceptable hemodynamic stability while providing adequate perioperative analgesic control throughout the monitoring period (14).

The findings of the present study provide important insight into the physiological and analgesic responses occurring during the early intraoperative period following anesthetic induction. The observed hemodynamic trends, including transient alterations in heart rate, systolic blood pressure, and diastolic blood pressure, followed by progressive stabilization, are consistent with the expected cardiovascular effects of anesthetic agents and the body's adaptive autonomic responses to surgical stress. In addition, the gradual increase in supplemental opioid requirement throughout surgery highlights the dynamic nature of intraoperative nociceptive stimulation and emphasizes the necessity for continuous analgesic titration during prolonged procedures. Collectively, these findings indicate that although anesthesia induces measurable cardiovascular changes, appropriate anesthetic management can maintain overall hemodynamic stability while simultaneously providing adequate analgesia (15).

One of the principal findings of this study was the transient increase in heart rate during the initial minutes after anesthetic induction, followed by a gradual return toward baseline values. Several physiological mechanisms may explain this pattern. During induction of anesthesia, sympathetic nervous system activation may occur secondary to airway manipulation, laryngoscopy, tracheal intubation, and the initial surgical stimulus. These interventions are known to stimulate catecholamine release, particularly epinephrine and norepinephrine, which increase sinoatrial node activity and consequently elevate heart rate. Although anesthetic agents themselves often possess myocardial depressant properties, the sympathetic response to intubation may transiently outweigh these effects during the early peri-induction period. As anesthetic depth becomes stabilized and analgesic medications achieve more effective central nervous system suppression, autonomic stimulation gradually diminishes, allowing heart rate to decline toward more stable levels (16).

The relatively limited variability observed in heart rate measurements across patients may indicate that the anesthetic regimen used in this study produced a predictable cardiovascular response in most participants. Adequate intraoperative monitoring, controlled anesthetic dosing, and timely analgesic supplementation likely contributed to the maintenance of acceptable hemodynamic conditions. Moreover, preservation of intravascular volume and careful perioperative fluid management may also have minimized excessive sympathetic activation related to hypovolemia or reduced cardiac preload. Similar temporal heart rate patterns have been described in previous perioperative studies evaluating anesthetic induction, where transient tachycardia is frequently followed by autonomic stabilization once adequate anesthesia is achieved (17).

Another important observation of the present study was the early decline in systolic blood pressure after induction of anesthesia. This phenomenon is physiologically expected and can be explained primarily by the vasodilatory and myocardial depressant effects of commonly used anesthetic agents. Many induction medications reduce systemic vascular resistance by promoting vascular smooth muscle relaxation and suppressing sympathetic vasoconstrictor tone. Simultaneously, these agents may reduce myocardial contractility and venous return, leading to transient reductions in cardiac output and arterial pressure. The initial hypotensive response observed in this study therefore likely reflects a combination of peripheral vasodilation, reduced preload, and temporary suppression of compensatory autonomic reflexes (18).

The subsequent stabilization and partial recovery of systolic blood pressure may indicate progressive cardiovascular adaptation during maintenance of anesthesia. Multiple mechanisms may contribute to this stabilization. First, endogenous compensatory responses, including activation of baroreceptor reflex pathways and neurohumoral systems, may gradually restore vascular tone and maintain organ perfusion. Second, administration of intravenous fluids during surgery likely improved circulating volume and venous return, thereby supporting cardiac output. Third, reduction of acute procedural stress after successful airway control and anesthetic stabilization may have minimized excessive autonomic fluctuations. The absence of prolonged severe hypotension in the present study further suggests that perioperative hemodynamic management was effective in preserving cardiovascular stability (19).

The findings related to diastolic blood pressure demonstrated a similar temporal pattern characterized by an early decline followed by gradual stabilization. Because diastolic blood pressure is closely associated with peripheral vascular resistance, the observed reduction most likely reflects anesthetic-induced vasodilation and attenuation of sympathetic vascular tone. Certain anesthetic agents exert direct effects on vascular smooth muscle calcium channels and endothelial signaling pathways, promoting relaxation of arteriolar structures and decreasing systemic vascular resistance. Furthermore, suppression of sympathetic outflow from the central nervous system may reduce baseline vasoconstrictive activity, thereby contributing to lower diastolic pressure immediately after induction (20).

The gradual normalization of diastolic blood pressure over time likely represents restoration of autonomic equilibrium and improved vascular compensation during ongoing anesthesia. Maintenance anesthetic dosing is often more physiologically stable than the induction phase, resulting in less abrupt cardiovascular suppression. Additionally, adequate analgesia may attenuate nociceptive sympathetic surges that could otherwise destabilize vascular tone. The relatively narrow standard deviation observed across blood pressure measurements suggests that the cardiovascular effects of the anesthetic protocol were generally reproducible and clinically manageable among different patients (21).

The combined findings related to heart rate and blood pressure are particularly important because they indicate overall preservation of hemodynamic stability despite transient fluctuations during induction. Hemodynamic stability is a critical objective in anesthetic practice because significant instability may compromise tissue perfusion and increase perioperative morbidity, especially in vulnerable patients with limited cardiovascular reserve. The controlled nature of the observed changes in this study suggests that the anesthetic strategy successfully balanced adequate anesthetic depth with cardiovascular safety. Careful titration of anesthetic agents, continuous physiologic monitoring, and prompt intraoperative interventions likely contributed to this favorable outcome (22).

Another notable finding of the present study was the progressive increase in supplemental opioid requirement during surgery. This observation likely reflects the cumulative nociceptive burden associated with ongoing surgical manipulation and tissue injury. As surgical duration increases, inflammatory mediators such as prostaglandins, bradykinin, cytokines, and substance P become increasingly activated within peripheral tissues and the central nervous system. These mediators enhance nociceptor sensitivity and amplify pain transmission pathways, thereby increasing analgesic requirements over time (23).

Central sensitization may also contribute to the increasing opioid demand observed in the present study. Persistent nociceptive input during surgery can enhance excitatory neurotransmission within the dorsal horn of the spinal cord, lowering pain thresholds and amplifying responses to surgical stimuli. Consequently, larger or repeated opioid doses may become necessary to maintain adequate analgesia as the procedure progresses. Furthermore, redistribution and metabolism of previously administered analgesic agents may reduce their effective plasma concentration over time, necessitating supplemental opioid administration to sustain therapeutic analgesic levels (24).

The variability in opioid requirement among patients is another clinically important finding. Individual differences in pain perception, pharmacogenetics, body composition, emotional stress, and baseline autonomic tone may all influence analgesic demand. Some patients exhibit greater opioid sensitivity, while others require higher doses to achieve equivalent analgesic effects. In addition, differences in surgical intensity, tissue manipulation, and inflammatory response may contribute to heterogeneity in opioid consumption patterns. The wider interquartile ranges observed during intermediate operative periods may therefore reflect these complex interindividual variations in nociceptive processing and analgesic responsiveness (25).

The stabilization of opioid requirement during later operative hours may indicate that a relatively balanced analgesic state was eventually achieved in many patients. Once adequate plasma opioid concentrations are reached and surgical stimulation becomes more predictable, analgesic demand may plateau. Moreover, maintenance anesthesia and multimodal analgesic strategies may contribute to attenuation of progressive nociceptive amplification during prolonged surgery. This stabilization suggests that the intraoperative analgesic protocol was capable of adapting to changing surgical conditions while avoiding uncontrolled escalation of opioid administration (26).

The present findings have several important clinical implications. First, the observed hemodynamic patterns emphasize the importance of vigilant monitoring during the early induction phase, when cardiovascular fluctuations are most likely to occur. Timely identification and correction of transient hypotension or tachycardia may help prevent adverse perioperative events and preserve adequate organ perfusion. Second, the gradual increase in opioid requirement highlights the necessity for individualized analgesic titration during surgery. Fixed analgesic dosing strategies may be insufficient because nociceptive intensity evolves dynamically throughout operative procedures.

Continuous assessment of physiologic responses and anesthetic depth is therefore essential for optimizing intraoperative pain control (27).

In addition, the overall preservation of cardiovascular stability observed in this study supports the effectiveness of modern anesthetic management approaches that combine balanced anesthesia, hemodynamic monitoring, and controlled analgesic administration. Such strategies may reduce perioperative stress responses while minimizing excessive cardiovascular suppression. These findings may be particularly relevant in patients with underlying cardiovascular disease, in whom even brief episodes of instability may increase postoperative complications (28).

Despite the important findings of this study, several considerations should be acknowledged. Hemodynamic responses during anesthesia are influenced by numerous patient-related and procedural variables, including age, comorbidities, anesthetic technique, baseline autonomic function, fluid therapy, and surgical complexity. Variability in these factors may influence physiologic responses and analgesic requirements. Furthermore, the observational nature of intraoperative monitoring limits the ability to establish direct causal relationships between specific anesthetic interventions and physiologic outcomes. Future studies involving larger populations and comparative anesthetic protocols may provide additional insight into the mechanisms underlying perioperative cardiovascular and analgesic responses (29).

Conclusion

Overall, the present study demonstrated that anesthetic induction and intraoperative management produced transient but controlled hemodynamic alterations accompanied by progressive changes in analgesic requirement during surgery. The observed physiologic responses are likely mediated through a complex interaction between autonomic nervous system activity, vascular regulation, myocardial effects of anesthetic agents, inflammatory nociceptive pathways, and adaptive cardiovascular compensation. Importantly, despite these dynamic changes, hemodynamic parameters remained within clinically acceptable ranges throughout the monitoring period, suggesting that the anesthetic approach provided effective cardiovascular stability and adequate analgesic control during surgery.

Acknowledgments

All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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.

References

[1] Bansal, V. K., Misra, M. C., & Babu, D. **(2013)**. A prospective, randomized comparison of long-term outcomes: Chronic groin pain and quality of life following totally extraperitoneal (TEP) and transabdominal preperitoneal (TAPP) laparoscopic inguinal hernia repair. *Surgical Endoscopy*, *27*(7), 2373–2382.

[2] Beyhan Sagmen, S., & Kıral, N. **(2020)**. Evaluation of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in asthma control. *Revue Française d'Allergologie*, *60*(1), 20–23.

[3] Dale, O., Somogyi, A. A., Li, Y., Sullivan, T., & Shavit, Y. **(2012)**. Does intraoperative ketamine attenuate postoperative inflammatory reactivity? A systematic review and meta-analysis. *Anesthesia & Analgesia*, *115*(4), 934–943.

[4] De Kock, M., Loix, S., & Lavand'homme, P. **(2013)**. Ketamine and peripheral inflammation. *CNS Neuroscience & Therapeutics*, *19*(6), 403–410.

[5] Domagalska, M., Ciftsi, B., & Janusz, P. **(2023)**. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) following erector spinae plane block (ESPB) in posterior lumbar decompression: A randomized, controlled trial. *European Spine Journal*, *32*(12), 4192–4199.

[6] Gorlin, A. W., Rosenfeld, D. M., & Ramakrishna, H. **(2016)**. Intravenous sub-anesthetic ketamine for perioperative analgesia. *Journal of Anaesthesiology Clinical Pharmacology*, *32*(2), 160–167.

[7] Gumus, F., Solak, I., & Eryilmaz, M. A. **(2018)**. The effects of smoking on neutrophil/lymphocyte, platelet/lymphocyte ratios. *Bratislavske Lekarske Listy*, *119*(2), 116–119.

[8] Ishizuka, M., Shimizu, T., & Kubota, K. **(2013)**. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *International Surgery*, *97*(4), 299–304.

[9] Kaur, S., Saroa, R., & Aggarwal, S. **(2015)**. Effect of intraoperative low-dose ketamine on management of postoperative analgesia. *Journal of Natural Science, Biology and Medicine*, *6*(2), 378–382.

[10] Mohammadi, K . (**2026**). CHA_2DS_2 VASc, anticoagulation, echocardiographic, thrombosis. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(1), 17-25.
[11] Kissin, I. **(2000)**. Preemptive analgesia. *Anesthesiology*, *93*(4), 1138–1143.
[12] Köksal, H., Ateş, D., Nazik, E. E., Küçükosmanoğlu, İ., Doğan, S. M., & Doğru, O. **(2018)**. Predictive value of preoperative neutrophil-to-lymphocyte ratio for detecting bowel resection in hernia with intestinal incarceration. *Turkish Journal of Trauma & Emergency Surgery*, *24*(3), 207–210.
[13] Kwok, R. F. K., Lim, J., Chan, M. T. V., Gin, T., & Chiu, W. K. Y. **(2004)**. Preoperative ketamine administration improves postoperative analgesia after gynecologic laparoscopic surgery. *Anesthesia & Analgesia*, *98*(4), 1044–1049.
[14] Lee, J. S., Kim, N. Y., Na, S. H., Youn, Y. H., & Shin, C. S. **(2018)**. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. *Medicine (Baltimore)*, *97*(26), e11138.
[15] McNicol, E. D., Schumann, R., & Haroutounian, S. **(2014)**. A systematic review and meta-analysis of ketamine for the prevention of persistent post-surgical pain. *Acta Anaesthesiologica Scandinavica*, *58*(10), 1199–1213.
[16] Mertoglu, C., & Gunay, M. **(2017)**. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as useful predictive markers of prediabetes and diabetes mellitus. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *11*(Suppl. 1), S127–S131.
[17] Reinpold, W. **(2017)**. Risk factors for chronic pain after inguinal hernia repair: A systematic review. *Innovative Surgical Sciences*, *2*(2), 61–68.
[18] Milanifard, M and Hashemloo, A. (**2025**). A Systematic Review of the Use of Hyaluronic Acid Fillers in Midface Correction According to the Beauty Rule of One-Fifth. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(1), 10-16.
[19] Serban, D., Stoica, P. L., & Dascalu, A. M. **(2023)**. Significance of preoperative neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammatory index (SII) in predicting severity and adverse outcomes in acute calculous cholecystitis. *Journal of Clinical Medicine*, *12*(21), 6946.
[20] Silva, M. D., Cleghorn, M. C., Elnahas, A., Jackson, T. D., Okrainec, A., & Qureshi, F. A. **(2016)**. Postoperative day 1 neutrophil-to-lymphocyte ratio as a predictor of 30-day outcomes among bariatric surgery patients. *Surgical Endoscopy*, *31*(6), 2645–2650.
[21] Singh, H., Kundra, S., Singh, R. M., Grewal, A., Kaul, T. K., & Sood, D. **(2013)**. Preemptive analgesia with ketamine for laparoscopic cholecystectomy. *Journal of Anaesthesiology Clinical Pharmacology*, *29*(4), 478–484.
[22] Surhonne, N., Hebri, C., Kannan, S., Duggappa, D. R., Rs, R. R., & Mapari, C. G. **(2019)**. Effect of anesthetic techniques on the neutrophil-to-lymphocyte ratio in patients undergoing infraumbilical surgeries. *Korean Journal of Anesthesiology*, *72*(5), 458–465.
[23] Suzuki, M., Haraguti, S., Sugimoto, K., Kikutani, T., Shimada, Y., & Sakamoto, A. **(2006)**. Low-dose intravenous ketamine potentiates epidural analgesia after thoracotomy. *Anesthesiology*, *105*(1), 111–119.
[24] Turkmen, K., Erdur, F. M., & Ozcicek, F. **(2013)**. Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in patients with end-stage renal disease. *Hemodialysis International*, *17*(3), 391–396.
[25] Tzikos, G., Alexiou, I., & Tsagkaropoulos, S. **(2023)**. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as predictive factors for mortality and length of hospital stay after cardiac surgery. *Journal of Personalized Medicine*, *13*(3), 473.
[26] Vaughan-Shaw, P. G., Rees, J. R. E., & King, A. T. **(2012)**. Neutrophil lymphocyte ratio as a predictor of outcome after emergency abdominal surgery in the elderly. *International Journal of Surgery*, *10*(3), 157–162.
[27] Walsh, S. R., Cook, E. J., Goulder, F., Justin, T. A., & Keeling, N. J. **(2005)**. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. *Journal of Surgical Oncology*, *91*(3), 181–184.
[28] Westerdijk, K., Simons, K. S., Zegers, M., Wever, P. C., Pickkers, P., & de Jager, C. P. C. **(2019)**. The value of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in patients admitted to the intensive care unit: A retrospective cohort study. *PLoS One*, *14*(2), e0212861.
[29] Yildirim, O. T., Aydin, F., Aydin, A. H., Dagtekin, E., Aksit, E., & Hasirci, S. H. **(2018)**. The neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are independent predictors of blood pressure variability. *Journal of Hypertension*, *36*(Suppl. 1), e12.