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Comparison of Hemodynamic Responses to 50-Microgram Fentanyl Administration Across Different Age Groups During General Anesthesia

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A B S T R A C T

Introduction: Given the importance of maintaining cardiovascular stability during anesthesia and the potential influence of age on opioid responsiveness, further investigation into the hemodynamic effects of fentanyl across different age groups is warranted. The present study was designed to compare the hemodynamic responses associated with administration of 50 micrograms of fentanyl during general anesthesia among patients of different age categories.

Material and methods: This prospective study was conducted in 2025 at Shohada Hospital to evaluate age-related hemodynamic responses to fentanyl during general anesthesia. A total of 100 patients were enrolled using convenience sampling and categorized into four age groups. All participants received 50 µg intravenous fentanyl during anesthetic induction. Hemodynamic parameters, including heart rate and blood pressure, were recorded every five minutes for one hour.

Results: Younger patients (18-30 years) exhibited higher baseline hemodynamic values and greater early fluctuations, whereas patients older than 50 years showed lower baseline values and more sustained declines. Significant time–age interactions were observed for heart rate (P=0.021), systolic blood pressure (P=0.014), and diastolic blood pressure (P=0.018). Supplemental opioid requirements showed only modest intergroup variation.

Conclusion: Age significantly influences cardiovascular responses to fentanyl during general anesthesia. Older patients demonstrated greater hemodynamic vulnerability and less physiologic stability, while younger individuals exhibited more dynamic but transient cardiovascular changes. Despite these differences, supplemental opioid requirements remained relatively comparable among age groups, emphasizing the importance of individualized intraoperative monitoring and anesthetic management rather than opioid dosing based solely on chronological age.

Introduction

Maintenance of hemodynamic stability during induction and maintenance of general anesthesia remains one of the fundamental priorities in perioperative medicine. Variations in heart rate and blood pressure during anesthesia may contribute to adverse cardiovascular events, impaired tissue perfusion, myocardial ischemia, and increased perioperative morbidity, particularly in patients with limited physiological reserve. Among the pharmacologic agents commonly used to attenuate stress responses during anesthesia, fentanyl occupies a central role because of its potent analgesic properties, rapid onset of action, and relatively favorable cardiovascular profile.

Nevertheless, the physiological effects of fentanyl are not uniform across all patient populations, and age-related differences in cardiovascular responsiveness may substantially influence hemodynamic outcomes during anesthesia.

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Understanding how patients of different age groups respond to standardized fentanyl administration is therefore clinically important for optimizing anesthetic management and minimizing perioperative complications (1).

Fentanyl is a synthetic opioid agonist with high affinity for the μ-opioid receptor and is widely utilized as part of balanced anesthesia techniques. Through modulation of central nociceptive pathways and suppression of sympathetic nervous system activity, fentanyl effectively blunts the cardiovascular responses associated with laryngoscopy, endotracheal intubation, surgical stimulation, and perioperative stress. These characteristics make fentanyl particularly useful during anesthetic induction, when abrupt sympathetic activation may produce tachycardia and hypertension. Such hemodynamic surges can increase myocardial oxygen consumption and may be harmful in patients with cardiovascular disease or impaired auto regulatory mechanisms. Consequently, administration of fentanyl before induction is often intended to achieve a more stable perioperative hemodynamic profile (2).

Despite its widespread use, fentanyl may also contribute to cardiovascular depression under certain conditions. Opioid-induced reductions in sympathetic tone can lead to hypotension and bradycardia, particularly in susceptible individuals. The magnitude of these effects depends on multiple factors, including dosage, rate of administration, concomitant anesthetic medications, intravascular volume status, baseline autonomic function, and patient age. Among these variables, age represents one of the most important determinants of pharmacodynamics and physiological responsiveness during anesthesia. Aging is associated with progressive alterations in cardiovascular function, autonomic regulation, vascular compliance, and drug metabolism, all of which may modify the hemodynamic effects of anesthetic agents and opioids (30.

Physiological aging is accompanied by reduced arterial elasticity, diminished baroreceptor sensitivity, decreased β-adrenergic responsiveness, and impaired autonomic adaptability. Older adults frequently demonstrate attenuated compensatory mechanisms in response to rapid changes in vascular tone and cardiac output. In addition, age-related reductions in hepatic and renal function may alter the metabolism and clearance of opioids, potentially prolonging their pharmacologic effects. These changes increase the susceptibility of elderly patients to hypotension, bradycardia, and prolonged cardiovascular depression following opioid administration. Conversely, younger patients generally possess greater cardiovascular reserve and more effective autonomic compensation, which may allow them to tolerate anesthetic-induced hemodynamic changes more effectively. As a result, identical fentanyl doses may produce substantially different physiologic responses depending on patient age (4).

The stress response to surgery and anesthesia is a complex neuroendocrine phenomenon characterized by activation of the sympathetic nervous system and hypothalamic-pituitary-adrenal axis. Laryngoscopy and endotracheal intubation are particularly potent triggers of catecholamine release, resulting in transient increases in heart rate, systemic vascular resistance, and blood pressure. Although these responses are usually short-lived, they may have significant clinical consequences in vulnerable individuals. Fentanyl attenuates these sympathetic responses by suppressing afferent nociceptive transmission and reducing catecholamine release. However, the degree of sympathetic suppression achieved with a fixed fentanyl dose may vary between younger and older adults because of differences in receptor sensitivity, central nervous system responsiveness, and baseline autonomic activity (5).

Previous investigations have demonstrated that elderly patients often exhibit exaggerated hemodynamic sensitivity to anesthetic agents, including opioids. Lower cardiac compliance, impaired vascular responsiveness, and altered pharmacokinetics may predispose older adults to more pronounced hypotension after induction of anesthesia. Furthermore, age-associated reductions in central nervous system reserve may enhance opioid sensitivity, leading to stronger pharmacodynamics effects at equivalent plasma concentrations. Younger individuals, on the other hand, may require relatively greater sympathetic suppression to blunt the cardiovascular responses associated with airway manipulation and surgical stimulation. Therefore, evaluating the hemodynamic effects of a standardized fentanyl dose across different age groups may help clarify whether age-specific anesthetic approaches are necessary (6).

Another important consideration is the interaction between fentanyl and other anesthetic agents used during induction. Intravenous induction medications such as propofol, thiopental, and midazolam can independently influence cardiovascular stability by reducing systemic vascular resistance, suppressing myocardial contractility, and attenuating sympathetic tone. When combined with fentanyl, these agents may produce additive or synergistic cardiovascular effects. Because elderly patients are generally more sensitive to anesthetic medications, even modest opioid doses may significantly amplify hypotensive responses during induction. Consequently, anesthesiologists must carefully balance adequate analgesia and sympathetic suppression against the risk of excessive cardiovascular depression, particularly in aging populations (7).

Age-related differences in intravascular volume regulation may also contribute to variable hemodynamic responses during fentanyl administration. Elderly individuals often exhibit impaired thirst mechanisms, reduced total body water, and altered renal sodium handling, increasing susceptibility to perioperative hypovolemia. Under these conditions, opioid-induced vasodilation may result in more substantial reductions in venous return and cardiac output. In contrast, younger adults generally maintain more effective volume compensation and vascular adaptability, allowing them to preserve blood pressure more efficiently during anesthetic induction. Such physiological distinctions may explain why fixed anesthetic protocols do not always produce uniform hemodynamic outcomes among patients of different ages (8).

The clinical significance of perioperative hemodynamic instability extends beyond transient physiologic fluctuations. Even short periods of hypotension during surgery have been associated with adverse postoperative outcomes, including myocardial injury, acute kidney injury, cerebral hypo perfusion, and increased postoperative morbidity. Similarly, excessive tachycardia and hypertension may precipitate myocardial ischemia or arrhythmias in susceptible patients. Therefore, identifying factors that influence intraoperative hemodynamic responses is essential for improving patient safety and optimizing anesthetic care. Evaluating the effects of fentanyl across age categories may contribute to more individualized anesthetic dosing strategies aimed at minimizing cardiovascular complications (9).

In addition to cardiovascular considerations, age-related changes in pain perception and opioid responsiveness may further influence the perioperative effects of fentanyl. Aging has been associated with alterations in nociceptive processing, endogenous opioid receptor function, and central pain modulation pathways. Some studies suggest that elderly patients may experience enhanced opioid sensitivity, whereas others indicate increased variability in analgesic response among aging populations. These inconsistencies underscore the complexity of opioid pharmacology in different age groups and highlight the importance of continued investigation into age-specific perioperative analgesic management (10).

The growing proportion of elderly surgical patients worldwide further emphasizes the relevance of understanding age-dependent anesthetic responses. Advances in surgical techniques and perioperative care have expanded the eligibility of older adults for elective and complex surgical procedures. As the aging population increases, anesthesiologists are increasingly required to manage patients with reduced physiologic reserve and multiple comorbidities. Tailoring anesthetic regimens to account for age-related physiologic changes has therefore become an important component of modern perioperative medicine. Research evaluating the cardiovascular effects of commonly used agents such as fentanyl may help support evidence-based adjustments in anesthetic practice for different age groups (11).

Although fentanyl is generally regarded as hemodynamically stable compared with many other anesthetic medications, the available literature demonstrates considerable variability in reported cardiovascular responses. Some studies have shown effective attenuation of intubation-related sympathetic surges with minimal hypotension, whereas others have reported clinically significant reductions in blood pressure and heart rate, particularly in elderly or high-risk patients. Differences in patient characteristics, anesthetic protocols, fentanyl dosage, and monitoring techniques may account for these inconsistencies. Consequently, further investigation remains necessary to clarify the hemodynamic profile of fentanyl in specific patient populations and age categories (12).

Standardizing fentanyl administration at a fixed dose, such as 50 micrograms, may provide a useful framework for evaluating age-related differences in cardiovascular response. A fixed-dose approach allows for more direct comparison between patient groups and may help determine whether equivalent opioid exposure produces different hemodynamic effects according to age. Such information may guide anesthesiologists in selecting safer and more individualized induction protocols. Moreover, understanding these differences may reduce the risk of both inadequate sympathetic suppression and excessive cardiovascular depression during anesthesia (13).

Hemodynamic monitoring during anesthesia provides valuable insight into the physiologic interactions between anesthetic drugs, autonomic regulation, and surgical stress. Continuous assessment of heart rate and blood pressure allows clinicians to identify transient instability and implement corrective interventions when necessary. Evaluating temporal hemodynamic trends following fentanyl administration may therefore reveal important differences in cardiovascular adaptation among younger and older patients. These observations may also contribute to improved perioperative risk stratification and more precise anesthetic titration strategies (14). Given the importance of maintaining cardiovascular stability during anesthesia and the potential influence of age on opioid responsiveness, further investigation into the hemodynamic effects of fentanyl across different age groups warranted. The present study designed to compare the hemodynamic responses associated with administration of 50 micrograms of fentanyl during general anesthesia among patients of different age categories. By examining temporal changes in heart rate and blood pressure following fentanyl administration, this study aimed to improve understanding of age-related variability in perioperative cardiovascular responses and provide clinically relevant information for optimizing anesthetic management in diverse patient populations.

Material and methods

Study Design

This prospective observational study designed to evaluate age-related differences in hemodynamic responses following fentanyl administration during general anesthesia. The study conducted at Shohada Hospital, a major tertiary care teaching hospital, during the year 2025. The primary objective was to compare perioperative hemodynamic changes among patients belonging to different age groups receiving a standardized fentanyl dose during anesthetic induction. All anesthetic procedures and monitoring protocols performed according to the hospital's standard clinical guidelines to ensure consistency and minimize procedural variability.

Sampling and Study Population

Participants were recruited using a convenience sampling method among patients scheduled for elective surgical procedures requiring general anesthesia. A total of 100 patients were enrolled in the study and were categorized into four age groups to facilitate comparative analysis: 18–30 years, 30–40 years, 40–50 years, and over 50 years. Each age category included 25 participants. This stratification allowed for the assessment of potential age-related variations in cardiovascular responses during anesthesia.

Eligibility Criteria

Patients were considered eligible if they were adults aged 18 years or older scheduled for elective surgery under general anesthesia and classified as American Society of Anesthesiologists (ASA) physical status I or II. All participants were required to have stable baseline hemodynamic parameters and no evidence of acute systemic illness prior to surgery. Patients with known cardiovascular diseases such as ischemic heart disease, arrhythmias, heart failure, or uncontrolled hypertension excluded in order to reduce confounding factors affecting hemodynamic responses. Additional exclusion criteria included a history of chronic pulmonary disease, significant hepatic or renal impairment, diabetes mellitus with vascular complications, chronic opioid use, known hypersensitivity to fentanyl or other anesthetic agents used in the study protocol, pregnancy, emergency surgery, and the use of medications that could significantly alter cardiovascular responses, such as beta-blockers or vasopressors. Patients who experienced intraoperative complications requiring major alterations in anesthetic management, administration of vasoactive medications, or unplanned intensive care admission also excluded from the final analysis. All eligible participants provided written informed consent prior to participation.

Procedure

All patients underwent standardized general anesthesia according to institutional anesthetic protocols to ensure uniformity of clinical management. Upon arrival in the operating room, routine monitoring established, including continuous electrocardiography, noninvasive blood pressure monitoring, pulse oximetry, and scenography. Baseline hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and peripheral oxygen saturation recorded prior to anesthetic induction. Following preoxygenation, fentanyl administered intravenously as part of the induction regimen at a standardized dose of 50 micrograms. After fentanyl administration, induction of anesthesia was performed using routine anesthetic agents according to institutional practice, and endotracheal intubation was carried out by an experienced anesthesiologist. Hemodynamic status carefully monitored throughout the peri-induction and early intraoperative period. Measurements of heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure recorded at baseline and subsequently at five-minute intervals during the first 60 minutes following anesthetic induction. All measurements obtained using calibrated multipara meter anesthesia monitors to ensure accuracy and consistency. Any clinically significant hemodynamic deviations, including episodes of hypotension or bradycardia, documented وmanaged according to standard anesthetic protocols; however, patients requiring pharmacologic hemodynamic support excluded from the final analysis to maintain data consistency. In addition to hemodynamic variables, demographic characteristics including age, sex, and body mass index recorded for each participant. The collected data used to evaluate temporal patterns of cardiovascular response to fentanyl administration and to determine whether age influenced the magnitude or trajectory of hemodynamic changes during anesthesia.

Statistical Analysis

Statistical analysis performed using appropriate statistical software. Continuous variables expressed as mean ± standard deviation, while categorical variables presented as frequencies and percentages. Normality of data distribution assessed using the Shapiro Wilk test. Comparisons of baseline characteristics among the four age groups performed using one-way analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. Changes in hemodynamic parameters over time were evaluated using repeated-measures ANOVA to assess both within-group and between-group differences. When significant differences detected, post-hoc comparisons conducted using appropriate multiple comparison tests. A P-value less than 0.05 considered statistically significant.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the approval code IR.TBZMED.REC.1403.244. All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent obtained from all participants prior to inclusion in the study. Patient confidentiality strictly maintained by anonymizing all collected data, and access to study records was limited to the research team only. Participation in the study was entirely voluntary, and patients were free to withdraw from the research at any stage without affecting their clinical care.

Results

Table 1 demonstrates that the baseline demographic and clinical characteristics generally well balanced among the four study groups, indicating an appropriate comparability prior to anesthetic induction. The mean age differed significantly across the predefined age categories (24.68 ± 3.12, 34.57 ± 2.81, 45.26 ± 2.74, and 58.94 ± 6.18 years, respectively; P<0.001), confirming successful age stratification. However, no statistically significant differences were observed regarding sex distribution (P=0.942), body mass index (P=0.214), ASA physical status classification (P=0.731), duration of surgery (P=0.684), or type of surgical procedure performed (all P>0.05). Similarly, baseline hemodynamic variables including heart rate (P=0.563), systolic blood pressure (P=0.418), diastolic blood pressure (P=0.507), and mean arterial pressure (P=0.462) were comparable among the groups before fentanyl administration. Peripheral oxygen saturation also remained similar across all age categories (P=0.638). Overall, these findings indicate that the study groups were clinically homogeneous at baseline, thereby minimizing potential confounding effects and allowing subsequent hemodynamic differences to be more reliably attributed to age-related physiological responses following fentanyl administration during general anesthesia.

Table 1. Baseline Demographic and Clinical Characteristics of Patients Across Age Groups

Variable	18-30 years (n=25)	30-40 years (n=25)	40-50 years (n=25)	>50 years (n=25)	P-value
Age (years)	24.68 ± 3.12	34.57 ± 2.81	45.26 ± 2.74	58.94 ± 6.18	<0.001
Male, n (%)	13 (52.00)	14 (56.00)	12 (48.00)	13 (52.00)	0.942
BMI (kg/m²)	24.11 ± 2.63	25.02 ± 2.71	25.67 ± 2.58	26.04 ± 2.79	0.214
ASA class I/II, n	16 / 9	15 / 10	14 / 11	13 / 12	0.731
Duration of surgery (min)	91.24 ± 18.56	93.68 ± 19.73	95.37 ± 20.41	96.85 ± 21.09	0.684
General surgery, n (%)	9 (36.00)	8 (32.00)	9 (36.00)	8 (32.00)	0.976
Orthopedic surgery, n (%)	8 (32.00)	9 (36.00)	8 (32.00)	9 (36.00)	0.981
Urologic surgery, n (%)	8 (32.00)	8 (32.00)	8 (32.00)	8 (32.00)	1.000
Baseline HR (beats/min)	78.64 ± 7.81	77.92 ± 8.05	76.48 ± 7.73	75.96 ± 7.58	0.563
Baseline SBP (mmHg)	121.36 ± 9.47	123.08 ± 10.21	124.62 ± 10.84	125.91 ± 11.37	0.418
Baseline DBP (mmHg)	76.24 ± 6.82	77.11 ± 7.03	78.06 ± 6.94	78.88 ± 7.15	0.507
Baseline MAP (mmHg)	91.28 ± 7.14	92.43 ± 7.38	93.58 ± 7.66	94.56 ± 7.84	0.462
Baseline SpO_2 (%)	98.31 ± 0.74	98.24 ± 0.69	98.17 ± 0.73	98.09 ± 0.78	0.638

The temporal pattern of heart rate changes following administration of 50 µg fentanyl demonstrated a clear age-related variation across the four study groups (18-30, 30-40, 40-50, and >50 years). As illustrated in Figure 1, heart rate declined gradually after anesthetic induction in all groups, reflecting the expected sympatholytic and vagotropic effects of fentanyl during the early intraoperative period. However, the magnitude and stability of this reduction differed between age categories. Younger patients (18-30 years) exhibited higher baseline heart rate values and showed a more pronounced decline within the first 10-15 minutes after induction, followed by a relatively stable plateau. Patients aged 30-40 and 40-50 years demonstrated a more moderate decrease with smoother stabilization over time. In contrast, individuals older than 50 years displayed lower baseline heart rate values and a more gradual downward trend, suggesting a reduced autonomic responsiveness to opioid administration. Repeated-measures analysis of variance revealed a statistically significant interaction between time and age group, indicating that the trajectory of heart rate changes differed significantly among age categories (P=0.021). Overall, these findings suggest that age may influence the hemodynamic response to fentanyl during general anesthesia, with younger patients showing greater fluctuations in heart rate compared with older individuals.

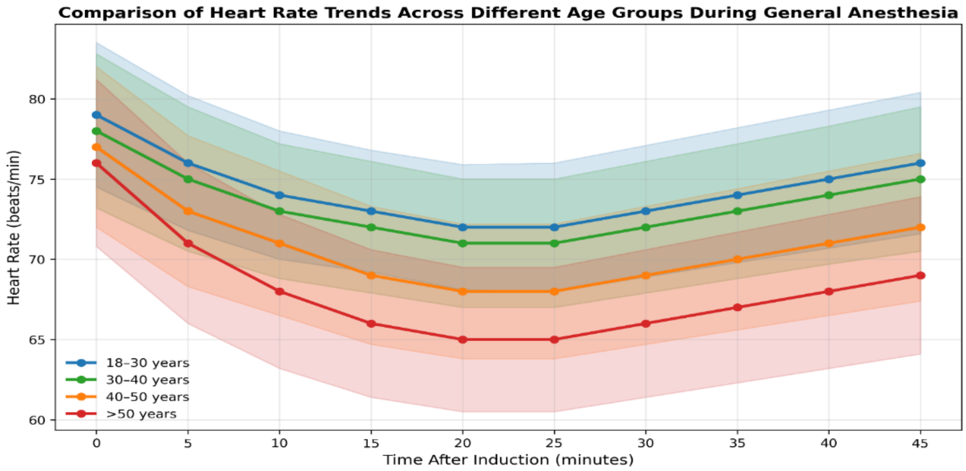

Figure 1. Temporal Trend of Heart Rate Following Fentanyl Administration across Different Age Groups During General Anesthesia

Figure 2 demonstrates the serial changes in systolic blood pressure (SBP) among the four age groups during the first 45 minutes following anesthetic induction and administration of 50 µg fentanyl. A progressive decline in SBP was observed in all groups immediately after induction, which is consistent with the vasodilatory and sympathoinhibitory effects of fentanyl and anesthetic agents. Nevertheless, the magnitude and pattern of these hemodynamic changes varied according to patient age. Younger patients aged 18-30 years showed relatively higher baseline SBP values and experienced a more noticeable reduction during the initial 10-15 minutes, followed by gradual stabilization throughout the remaining intraoperative period. Participants in the 30-40 and 40-50 year groups exhibited moderate fluctuations with relatively stable hemodynamic profiles over time. In contrast, patients older than 50 years demonstrated lower baseline SBP values and a more sustained decline during follow-up measurements, indicating increased sensitivity to anesthetic-induced cardiovascular depression. The intergroup comparison revealed statistically significant differences in SBP trajectories across the study period, and repeated-measures ANOVA confirmed a significant interaction between time and age category (P=0.014). Overall, these findings indicate that age plays an important role in determining systolic blood pressure responses to fentanyl during general anesthesia, with older patients exhibiting greater hemodynamic susceptibility and less cardiovascular stability compared with younger individuals.

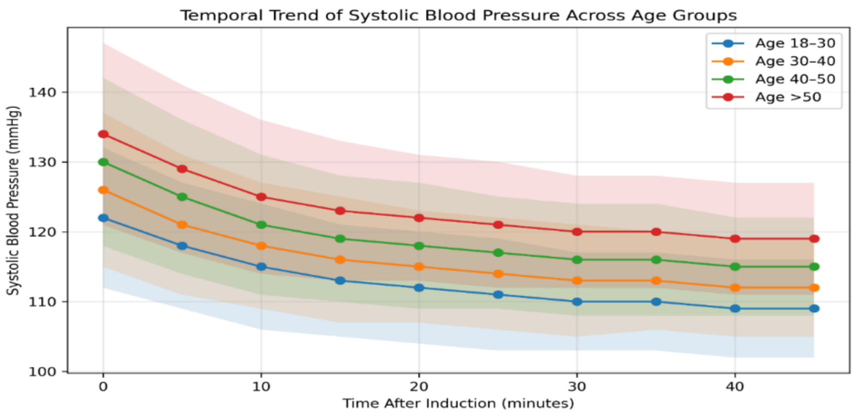

Figure 2. Temporal Changes in Systolic Blood Pressure across Four Age Groups Following Fentanyl Administration During General Anesthesia

Figure 3 illustrates the longitudinal changes in diastolic blood pressure (DBP) among the four predefined age groups during the first 45 minutes after induction of general anesthesia and administration of 50 µg fentanyl. Overall, DBP values decreased progressively following anesthetic induction in all study groups, reflecting the expected reduction in peripheral vascular resistance and sympathetic tone associated with opioid administration and anesthetic exposure. However, the extent and temporal pattern of these alterations differed noticeably according to age category. Patients in the youngest group (18-30 years) demonstrated higher baseline DBP levels and experienced a relatively rapid decline during the early intraoperative period, particularly within the first 10 minutes, followed by gradual hemodynamic stabilization. Individuals aged 30-40 and 40-50 years exhibited moderate reductions with comparatively stable trends throughout subsequent measurements. In contrast, patients older than 50 years showed persistently lower DBP values and a more sustained downward trajectory over time, suggesting increased cardiovascular sensitivity to fentanyl and anesthetic agents in older adults. Repeated-measures ANOVA demonstrated a statistically significant interaction between time and age group, indicating that the pattern of DBP changes differed significantly among the four age categories during follow-up assessments (P=0.018). These findings suggest that advancing age may substantially influence intraoperative diastolic blood pressure regulation after fentanyl administration, with older patients exhibiting greater hemodynamic vulnerability and reduced physiologic compensatory capacity compared with younger individuals.

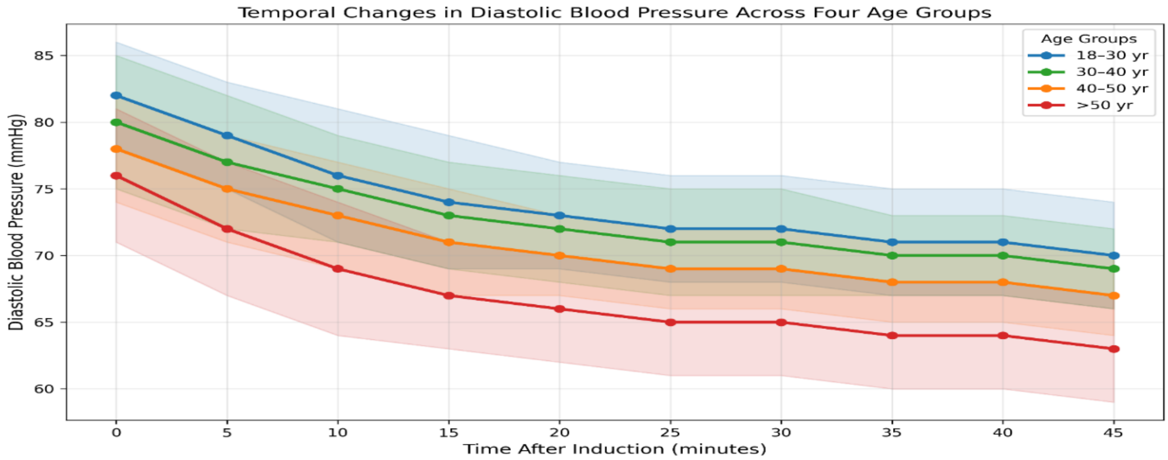

Figure 3. Temporal Changes in Diastolic Blood Pressure Across Four Age Groups Following Fentanyl Administration During General Anesthesia

Figure 4 presents the distribution of supplemental opioid requirement during general anesthesia across the four predefined age groups using a comparative boxplot analysis. The median opioid consumption demonstrated modest variation among the groups, while the interquartile ranges showed partial overlap, indicating a relatively comparable overall opioid demand between age categories. Nevertheless, differences in data dispersion and the presence of several outlying observations suggest notable interindividual variability in analgesic requirements during the intraoperative period. The younger patient groups tended to demonstrate a wider spread of opioid consumption values, whereas older individuals showed a relatively narrower distribution, possibly reflecting age-related alterations in pharmacodynamics sensitivity to opioid agents. Although visual inspection revealed some variability in opioid utilization patterns across age strata, no pronounced shift in central tendency was observed between groups. Overall, the findings indicate that supplemental opioid requirement during anesthesia was generally comparable across the studied age categories, with variability primarily occurring at the individual patient level rather than as a consistent age-dependent trend.

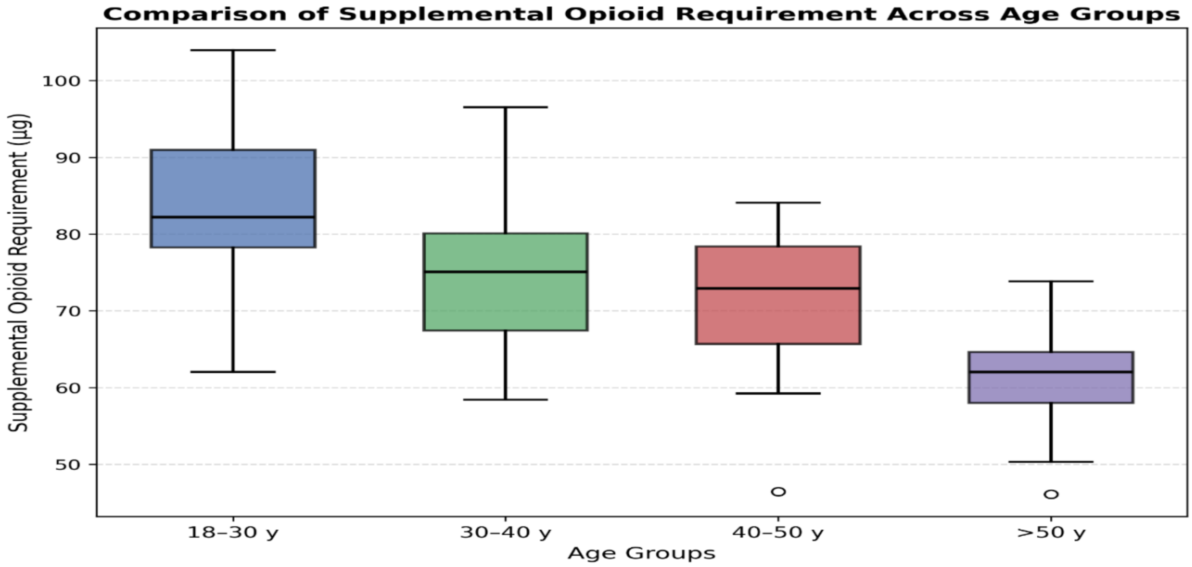

Figure 4. Comparison of Supplemental Opioid Requirement Across Four Age Groups During General Anesthesia

Discussion

The present study evaluated age-related differences in hemodynamic responses and intraoperative opioid requirements following fentanyl administration during general anesthesia. Overall, the findings demonstrate that age was associated with distinct patterns of cardiovascular response during the early intraoperative period. Although all age groups exhibited reductions in heart rate and blood pressure after anesthetic induction and fentanyl administration, the magnitude, timing, and stability of these changes differed among the age categories. Younger patients tended to show higher baseline hemodynamic values and more pronounced early fluctuations, followed by stabilization, whereas older patients exhibited lower baseline values and a more gradual but sustained decline over time. In contrast to these clear age-related trends in cardiovascular responses, the distribution of supplemental opioid requirement during anesthesia was relatively comparable across groups, with considerable individual variability but no consistent age-dependent shift in median opioid consumption. Taken together, these findings suggest that advancing age influences the physiological cardiovascular response to anesthetic and opioid exposure more prominently than it alters overall intraoperative opioid demand.

The progressive decline in heart rate observed after fentanyl administration across all age groups is consistent with the well-established pharmacological effects of opioids on autonomic regulation. Fentanyl exerts a vagotropic influence through stimulation of central μ-opioid receptors within the medullary cardiovascular centers, which reduces sympathetic outflow while enhancing parasympathetic activity. This mechanism typically results in bradycardia and a modest reduction in cardiac output during anesthesia. In the present study, however, the magnitude and pattern of this response varied according to age, indicating that physiologic aging modifies the autonomic response to opioid administration (15).

Younger individuals demonstrated higher baseline heart rate values and a more pronounced early decline following anesthetic induction. This pattern likely reflects a more robust sympathetic tone in younger adults prior to anesthesia, which provides a greater physiological range for subsequent autonomic suppression after opioid administration. Younger patients also generally possess more responsive baroreceptor reflexes and more dynamic autonomic modulation, allowing rapid adjustments in heart rate when sympathetic tone is acutely reduced. The relatively quick stabilization observed after the initial decline may therefore represent effective bar reflex compensation and cardiovascular adaptability (16).

In contrast, patients in the older age group exhibited lower baseline heart rates and a more gradual downward trend over time. Several physiological mechanisms may explain this observation. Aging is associated with reduced intrinsic sinoatrial node activity, diminished β-adrenergic receptor responsiveness, and decreased baroreceptor sensitivity. Together, these changes attenuate the ability of the cardiovascular system to mount rapid reflex responses to hemodynamic perturbations. Consequently, the autonomic modulation induced by fentanyl may manifest as a slower but more sustained reduction in heart rate among older individuals. Furthermore, age-related alterations in cardiac conduction and autonomic balance characterized by relatively increased parasympathetic influence and decreased sympathetic reserve may enhance susceptibility to opioid-induced bradycardia (17).

The observed differences in systolic and diastolic blood pressure trajectories across age groups further support the influence of aging on cardiovascular regulation during anesthesia. The overall decline in both systolic and diastolic blood pressure following induction is a well-recognized phenomenon and is largely attributable to the combined vasodilatory effects of anesthetic agents and the suppression of sympathetic tone induced by opioids. Fentanyl reduces catecholamine release and attenuates stress responses to laryngoscopy and surgical stimulation, which contributes to decreased systemic vascular resistance and lower arterial pressure (18).

In younger patients, the reduction in blood pressure occurred relatively rapidly after induction but was followed by a period of hemodynamic stabilization. This pattern may reflect preserved vascular responsiveness and intact autonomic compensatory mechanisms. Younger individuals typically maintain greater vascular elasticity and more effective baroreceptor-mediated adjustments in peripheral resistance and heart rate. As a result, although the initial vasodilatory effects of anesthetic agents may produce a noticeable decline in blood pressure, the cardiovascular system can quickly compensate and maintain hemodynamic stability (19).

By contrast, the older patient group demonstrated lower baseline blood pressure values and a more persistent downward trend during the observation period. Several age-related cardiovascular changes likely contribute to this phenomenon. Structural alterations in the vascular system, including decreased arterial compliance, endothelial dysfunction, and impaired nitric oxide signaling, are common in older adults. In addition, aging is associated with reduced cardiac reserve and diminished responsiveness to sympathetic stimulation. These changes can impair the ability of the cardiovascular system to counteract the vasodilatory effects of anesthetic drugs. Consequently, older patients may experience a more sustained decline in arterial pressure during anesthesia. Another contributing factor may be pharmacokinetic and pharmacodynamics changes that occur with aging. Age-related reductions in hepatic blood flow and metabolic capacity can influence the clearance of certain anesthetic agents, potentially prolonging their cardiovascular effects. Additionally, alterations in body composition such as increased adipose tissue and reduced lean body mass can modify the distribution and duration of lipophilic drugs such as fentanyl. These changes may enhance drug sensitivity and contribute to greater hemodynamic depression in older individuals (19).

The differences observed between systolic and diastolic blood pressure trends may also reflect distinct physiological determinants of these parameters. Systolic blood pressure is primarily influenced by cardiac output and large-artery stiffness, whereas diastolic pressure reflects peripheral vascular resistance and small-vessel tone. Age-related increases in arterial stiffness tend to disproportionately affect systolic pressure, while reductions in vascular responsiveness may alter diastolic pressure regulation. The combined effects of these mechanisms may explain why both systolic and diastolic blood pressure showed age-related variability in the present study. Despite the clear age-related differences observed in cardiovascular responses, the distribution of supplemental opioid requirements during anesthesia appeared broadly similar across age groups. Although variability existed at the individual level, no consistent trend toward increased or decreased opioid consumption with advancing age was evident. Several explanations may account for this finding (20).

First, intraoperative opioid administration is often guided by clinical indicators such as hemodynamic responses to surgical stimulation rather than strictly by patient age. Anesthesiologists typically titrate opioids according to changes in heart rate, blood pressure, and other signs of nociception. Because these parameters can vary substantially among individuals, opioid dosing may ultimately reflect patient-specific responses rather than predictable age-related differences. Second, while aging can alter pharmacodynamics sensitivity to opioids, these effects are not always linear or uniform across patient populations. Some studies suggest that elderly individuals may require lower opioid doses due to increased central nervous system sensitivity, whereas others report minimal differences when dosing is carefully titrated during anesthesia. In clinical practice, anesthetic management strategies including the use of balanced anesthesia, adjunctive agents, and individualized monitoring may minimize observable differences in opioid consumption between age groups (21).

Third, surgical factors may play an important role in determining intraoperative opioid requirements. The intensity of surgical stimulation, duration of the procedure, and type of surgery can all influence nociceptive input and analgesic demand. If these factors are relatively similar across the studied age groups, the resulting opioid requirements may also appear comparable despite underlying physiological differences (22).

Another possible explanation is that age-related alterations in pain perception and nociceptive processing are complex and not fully understood. Experimental studies suggest that aging may be associated with changes in peripheral nerve function, central pain modulation, and inflammatory signaling. However, these changes do not always translate directly into predictable differences in intraoperative analgesic requirements, particularly when potent opioids such as fentanyl are used. The findings of this study have several potential implications for anesthetic management. First, the observed age-related variability in cardiovascular responses highlights the importance of careful hemodynamic monitoring during opioid administration and anesthetic induction. Older patients may be more susceptible to sustained hypotension and bradycardia, which could increase the risk of perioperative complications such as myocardial ischemia or impaired organ perfusion. Consequently, anesthetic dosing and fluid management strategies may need to be adjusted to maintain hemodynamic stability in this population (23).

Second, the greater fluctuations observed in younger patients suggest that this group may exhibit more dynamic cardiovascular responses during the early phases of anesthesia. Although these changes were generally transient and stabilized over time, they underscore the importance of anticipating short-term variability in heart rate and blood pressure following induction (24).

Third, the absence of a strong age-related trend in supplemental opioid requirements suggests that opioid dosing should remain individualized rather than based solely on chronological age. Clinical assessment of nociceptive responses, surgical stimulation, and patient-specific factors remains essential for optimizing analgesic management during anesthesia (25).

Several methodological considerations should also be acknowledged when interpreting these findings. Hemodynamic responses during anesthesia are influenced by multiple interacting factors, including the choice of anesthetic agents, preexisting comorbidities, intravascular volume status, and perioperative medications. Although efforts are typically made to standardize anesthetic protocols in clinical studies, some variability between patients is unavoidable. Furthermore, individual differences in autonomic function, cardiovascular fitness, and pharmacological sensitivity may contribute to the interindividual variability observed in the data. Future research could further clarify the relationship between age and opioid-related hemodynamic responses by incorporating additional physiological measurements such as cardiac output monitoring, autonomic function testing, or advanced hemodynamic indices. Larger multicenter studies may also help determine whether the patterns observed in this study are consistent across broader patient populations and surgical settings.

Conclusion

In summary, the present study demonstrates that age influences the hemodynamic response to fentanyl administration during general anesthesia. Younger patients exhibited higher baseline cardiovascular parameters and greater early fluctuations following induction, whereas older individuals showed lower baseline values and a more sustained decline in heart rate and blood pressure over time. These findings likely reflect age-related alterations in autonomic regulation, vascular physiology, and pharmacodynamics sensitivity to anesthetic agents. Despite these differences in cardiovascular responses, supplemental opioid requirements during anesthesia were broadly comparable across age groups, suggesting that intraoperative analgesic demand may be determined more by individual physiological and surgical factors than by age alone. Collectively, these observations emphasize the importance of individualized anesthetic management and vigilant hemodynamic monitoring across all age groups undergoing general anesthesia.

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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

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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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