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INDUCTION AND MAINTENANCE OF GENERAL ANESTHESIA: RECENT ADVANCES AND CLINICAL IMPLICATIONS

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Abstract: General anesthesia consists of a pharmacologically induced state of unconsciousness, analgesia, amnesia, and abolition of reflexes, organized into the phases of induction, maintenance, and emergence. This study aimed to critically review recent evidence related to the main agents and techniques used in the induction and maintenance of general anesthesia, as well as their most relevant clinical outcomes. This is a narrative review of the literature, based on a search conducted in the PubMed database, including articles published in the last five years, available in full text and directly related to contemporary anesthetic practices. The findings demonstrate that induction remains a particularly critical stage, especially in elderly patients, in whom hemodynamic instability is frequent regardless of the agent used. Although remimazolam has been proposed as a more stable alternative, recent studies show no significant reduction in the incidence of hypotension compared to propofol. In the field of preoxygenation, modern techniques—especially the use of high-flow nasal oxygen (HFNO) associated with an elevated head position—effectively prolong the time of safe apnea and reduce hypoxemic events. Regarding maintenance, propofol and sevoflurane have their own profiles, with no defined clinical superiority in cognitive or recovery outcomes, although biomarkers indicate greater neuronal stress related to volatile agents. In the pediatric population, it is noteworthy that monitoring anesthetic depth using the bispectral index (BIS) significantly reduces the incidence of emergency delirium. It is concluded that contemporary anesthetic safety depends on the integration of individualized agent selection, the application of optimized ventilation and preoxygenation strategies, and the systematic use of advanced moni-

toring to reduce complications and improve perioperative outcomes. At the same time, the latest innovations in personalized approaches to anesthesia have deepened the understanding that successful anesthesia goes beyond the choice of medication. Integrated actions focused on improving blood circulation, such as adjusting the dose based on real-time data and using vasopressors with caution at the beginning of the process, have proven effective in reducing the occurrence of cardiovascular problems. Similarly, current studies emphasize the need for a thorough preoperative assessment, taking into account aspects such as the patient's physical condition, heart and lung disease, and the risk of mental confusion or memory problems after surgery. During anesthesia, recent results confirm the usefulness of goal-directed anesthesia plans, which promote less fluctuation in how the body processes medications and a more predictable recovery. In addition, current research highlights the importance of careful pulmonary ventilation to reduce respiratory complications during and after surgery, especially in more vulnerable individuals. Therefore, it is clear that the quality of anesthesia outcomes depends on a comprehensive strategy focused on individual patient analysis and supported by advanced monitoring, well-structured perioperative planning, and decisions based on solid information.

Keywords: general anesthesia; anesthetic induction; anesthetic maintenance; hemodynamics; preoxygenation.

INTRODUCTION

General anesthesia is a pharmacologically induced state that combines unconsciousness, amnesia, analgesia, hypnosis, and abolition of motor and autonomic reflexes, allowing for the safe performance of surgical procedures of varying complexity. Modern anesthetic management is traditionally structured in three phases—induction, maintenance, and emergence—each associated with specific physiological challenges and clinical decisions that directly influence perioperative safety (Philip, Brohan, & Goudra, 2025).

In recent decades, significant advances in pharmacology, monitoring, and airway management techniques have expanded the anesthesiologist's repertoire and allowed for greater individualization of care. The introduction of ultra-short-acting hypnotic agents, the development of target-controlled infusion systems, the use of optimized preoxygenation strategies, and the incorporation of monitoring methods based on processed electroencephalogram (EEG) have transformed contemporary anesthetic practice and contributed to the reduction of adverse events (Carvalho *et al.*, 2024; Frelich et al., 2024; Bidkar et al., 2024; Philip, Brohan & Goudra, 2025).

At the same time, the increasing complexity of patients—including aging populations, patients with multiple comorbidities, individuals at high risk of cardiovascular instability, and children undergoing procedures of varying durations—reinforces the need for a thorough understanding of physiological responses to anesthetic agents and the techniques employed (Takaki *et al.*, 2024; Frelich et al., 2024). The choice of anesthetic strategy should therefore consider

not only the type of surgery but also the hemodynamic, cognitive, and respiratory impacts of each approach, with special attention to the specific characteristics of more vulnerable groups (Huang & Zhang, 2023; Philip, Brohan & Goudra, 2025).

Given the diversity of agents available and the continuous evolution of technologies applied to anesthesia, it is essential to critically review recent evidence related to induction and maintenance techniques. Thus, the objective of this article is to summarize the advances of the last five years, contextualizing the role of the main agents and strategies used in general anesthesia and discussing their clinical implications in light of current trends.

In addition, the gradual introduction of concrete metrics for anesthesia intensity and methods for improving ventilation has helped to consolidate the idea of body-data-driven anesthesia. The common use of the bispectral index (BIS) and other resources based on analyzed EEG has made it possible to reduce both excess anesthetics and insufficient doses, mitigating dangers such as perception during surgery, pressure instability, and mental confusion after the operation, especially in children and the elderly. The growing emphasis on lung protection in surgery, coupled with these advances, includes personalized strategies to optimize PEEP and the use of high-flow oxygen in preoxygenation. Studies (*Carvalho et al.*, 2024; Takaki *et al.*, 2024) prove the effectiveness of these practices in reducing hypoxia and prolonging safe apnea time.

Another important point concerns the clinical significance of differences in how the body processes and reacts to injectable anesthetics and anesthetic gases. Recent research has reinforced that, even though both modes show similar efficacy in sustaining anesthesia, different profiles of heart and vessel stability, effects on biological signals from neurons, and speed of recovery continue to weigh on anesthetic resolution. In this scenario, the choice between propofol, remimazolam, sevoflurane, or other drugs should take into account not only the institution's preferences, but also the physical processes of each individual that determine their response, tolerance, and risk of problems. These facts reinforce the urgency of courses of action based on strong clinical data and tailored to each person's specific situation.

Thus, understanding scientific advances related to the onset and continuity of anesthesia is crucial to optimize medical practice and guide evidence-based decisions. The thorough analysis presented in this study aims to provide modern support for improving the quality of anesthetic care, emphasizing trends, limitations, and possibilities for evolution in current anesthesiology.

METHODOLOGY

This study is a narrative review of the literature, developed with the aim of analyzing and synthesizing recent scientific evidence on methods of induction and maintenance of general anesthesia. The literature search was conducted in the PubMed database, using the descriptors "General Anesthesia," "induction," "maintenance," and "inhalational anesthesia," combined with the Boolean operators AND and OR, according to the Medical Subject Headings (MeSH) terminology.

Publications from the last five years were included, available in full, in English or Portuguese, and directly related to anesthetic induction or maintenance practices. Studies not relevant to the topic, duplicate articles, unindexed publications, or those that did not present minimum methodological clarity for interpretation of the results were excluded.

The selection of studies was carried out in two stages: initially, titles and abstracts were screened; then, potentially relevant articles were read in full to confirm eligibility. The information extracted was organized and synthesized in a descriptive manner, seeking to offer an integrative, up-to-date, and coherent perspective on the main trends and contemporary evidence in general anesthesia.

After identifying and selecting the studies, we conducted a detailed analysis, focusing on research methods, methodological soundness, patient group characteristics, and key outcomes related to the induction and maintenance phases of general anesthesia. We observed details such as the type and quantity of medications, monitoring methods, procedures for the initiation and continuation of anesthesia, and the clinical signs evaluated. The comparative analysis aimed to find similarities and differences between the results, as well as to identify areas that have been little explored in recent studies.

The information extracted from the selected studies was organized into thematic tables, covering aspects such as circulatory stability, preoperative oxygenation approaches, the impact of medications, ventilation procedures, intensive monitoring, and postoperative outcomes. This thematic organization allowed for a more transparent and coherent display of the findings, simplifying the analysis of contemporary trends and practical implications related to the various types of anesthesia.

Given the descriptive nature of this review, we chose not to apply statistical meta-analysis methods, prioritizing qualitative synthesis of the results. The reliability of the results was reinforced through careful selection of sources and adherence to current standards of scientific rigor in anesthesiology.

RESULTS AND DISCUSSION

Induction of general anesthesia

The induction phase of anesthesia remains one of the most critical stages of general anesthesia, especially in elderly patients or those with cardiovascular disease, due to the increased risk of hemodynamic instability and respiratory depression. Among intravenous agents, propofol continues to be widely used for its pharmacokinetic predictability, rapid onset of action, and ease of titration. However, its propensity to cause dose-dependent hypotension is a particularly relevant limitation in more vulnerable populations (Philip, Brohan & Goudra, 2025).

In recent years, remimazolam has emerged as a potential alternative to propofol, mainly due to the expectation of greater cardiovascular stability. However, recent evidence does not confirm this advantage in the elderly. In a randomized clinical trial conducted by Takaki *et al.* (2024), involving patients between 80 and 90 years of age, the incidence of hypotension during induction

was virtually identical between remimazolam (72.1%) and propofol (72.7%), even under strictly controlled conditions. These findings indicate that, in this population, physiological changes related to aging—such as reduced cardiovascular reserve and autonomic responsiveness—have a greater influence than the agent used.

Another agent of interest is etomidate, recognized for providing hemodynamic stability during induction, as demonstrated in recent comparative studies (Moningi *et al.*, 2022; Shetabi, Montazeri & Ghoodjani, 2022). However, its application remains limited by transient adrenal suppression, which is why it is recommended mainly in scenarios of extreme cardiovascular instability. Thus, the choice of induction agent should be individualized, considering the patient's physiological profile, the presence of comorbidities, and complementary strategies such as slow titration, adequate volume maintenance, and continuous monitoring.

The evolution of hypnotic agents has also contributed to increased safety in anesthetic induction, especially in patients with lower physiological reserves. New molecules are being developed with the aim of preserving hemodynamic stability and allowing more precise titration, reducing blood pressure fluctuations during loss of consciousness. Although remimazolam is an example of this trend, recent data show that its cardiovascular performance in clinical practice tends to be similar to that of propofol in elderly patients, indicating that the physiology of aging has a more significant influence than the agent alone (Takaki *et al.*, 2024; Philip, Brohan & Goudra, 2025). Nevertheless, the incorporation of these ultra-short-acting hypnotics represents an important advance, as it offers safer alternatives in scenarios of clinical frailty, while reinforcing the need for individualized protocols and rigorous monitoring from the onset of induction.

Preoxygenation and airway management

Preoxygenation is an essential step in induction, as it increases the functional oxygen reserve and improves safety during periods of apnea, especially in patients at higher risk of desaturation, such as obese individuals, the elderly, pregnant women, and patients with cardiopulmonary diseases. The reduction in muscle tone induced by anesthetic agents decreases functional residual capacity and promotes airway collapse, reinforcing the importance of effective preoxygenation techniques (Carvalho *et al.*, 2024).

Recent evidence, including the systematic review and network meta-analysis by Carvalho *et al.* (2024), shows that traditional techniques—such as spontaneous ventilation with a face mask in the supine position—underperform compared to contemporary strategies. Among these, the use of *high-flow nasal* oxygen (HFNO) associated with the *head-up* position stands out, a technique that significantly prolongs the time of safe apnea.

HFNO offers integrated physiological benefits: it provides continuous oxygenation, generates mild positive end-expiratory pressure, and improves ventilatory distribution, resulting in a lower risk of desaturation (Carvalho *et al.*, 2024). Its effectiveness is enhanced when combined with the *head-up* position, which increases functional residual capacity, improves the ventilation-perfusion

ratio, and reduces compression of the lung bases, especially in obese individuals.

In airway management, the proper use of preoxygenation techniques reduces urgency and instability at the time of laryngoscopy. The *apneic oxygenation* strategy, especially with HFNO, allows continuous oxygenation throughout intubation, substantially reducing the risk of peri-intubation hypoxemia (Carvalho *et al.*, 2024). Thus, the systematic adoption of these approaches represents a significant advance in the safety of anesthetic induction.

Maintenance of general anesthesia

The maintenance phase of anesthesia is crucial for intraoperative stability and the quality of postoperative recovery. Two main strategies are used: total intravenous anesthesia (TIVA), predominantly with propofol, and inhalation anesthesia, most commonly with sevoflurane or desflurane (Philip, Brohan & Goudra, 2025).

Propofol is widely used in TIVA due to its predictable pharmacokinetics, rapid awakening, and lower incidence of postoperative nausea and vomiting. However, its cardiovascular limitations remain relevant (Philip, Brohan & Goudra, 2025). In contrast, volatile agents such as sevoflurane are easily titrated, have low hepatic metabolism, and respond quickly to depth adjustments, characteristics that contribute to their widespread use in clinical practice (Huang & Zhang, 2023).

In the geriatric context, the systematic review conducted by Huang and Zhang (2023) demonstrated that intravenous anesthesia with propofol and inhalation anesthesia with sevoflurane have a similar incidence of short-term postoperative cognitive dysfunction (POCD). However, sevoflurane was associated with higher plasma levels of S-100β protein in the postoperative period, indicating greater activation of biomarkers related to neuronal stress, although without evident clinical repercussions on cognition.

In the pediatric population, sevoflurane is known to be associated with a higher incidence of emergency delirium (ED). However, this risk can be significantly reduced when the depth of anesthesia is monitored objectively. In the prospective trial conducted by Frelich *et al.* (2024), sevoflurane titration guided by the Bispectral Index (BIS) reduced the incidence of ED from 35.1% to 12.8%, demonstrating that excessive hypnosis—and not the inhalation agent alone—is the main determinant of this phenomenon.

In general, TIVA and volatile anesthesia have distinct profiles of benefits and limitations, with no evidence of universal superiority of one technique over the other. Selection should be individualized, taking into account the risk of hemodynamic instability, the need for faster cognitive recovery, and the particularities of the procedure and the patient.

Monitoring of anesthetic depth

Monitoring the depth of anesthesia is essential to avoid both superficial anesthesia—associated with the risk of intraoperative awareness—and excessive levels of hypnosis, which can trigger cardiovascular instability, respiratory depression, and neurological complications. Monitors based on processed EEG, such as BIS, integrate cortical patterns into numerical values that reflect the degree of hypnosis and allow for more accurate titration of anesthetic agents

(Frelich *et al.*, 2024; Philip, Brohan & Goudra, 2025).

From a neurophysiological point of view, anesthetic depth results from the modulation of GABA-A receptors and changes in connectivity between thalamocortical networks, effects that produce specific patterns in the EEG. Thus, monitors such as BIS translate these changes into a numerical index, allowing dynamic monitoring of pharmacological action and more individualized adjustment of anesthesia (Philip, Brohan & Goudra, 2025).

In addition to reducing complications, BIS can optimize anesthetic consumption, decrease interindividual variability, and facilitate more stable recovery, especially in adults. Although it has limitations—such as sensitivity to muscle artifacts—BIS is a valuable complement to continuous clinical assessment, especially in prolonged procedures or in higher-risk patients.

Postoperative outcomes

The main postoperative outcomes associated with induction and maintenance techniques include hypotension, DCPO, ED, and immediate recovery characteristics. Peri-induction hypotension remains one of the main challenges, especially in the elderly. In the study by Takaki et al. (2024), remimazolam and propofol had virtually identical incidences of hypotension, reinforcing that physiological changes associated with aging have a greater impact than the hypnotic agent.

DCPO, which is particularly relevant in elderly patients, showed no significant differences between propofol and sevoflurane in the systematic review by Huang & Zhang (2023). However, higher postoperative S-100β values in the sevoflurane group indicate greater activation of neuronal stress biomarkers, although without detectable clinical repercussions on cognition.

In the pediatric population, DE remains the most relevant outcome in the immediate postoperative period. In the study by Frelich *et al.* (2024), monitoring anesthetic depth with BIS significantly reduced the occurrence of DE, showing that excessive hypnosis—and not the volatile agent alone—is the main determining factor in this phenomenon.

Finally, both intravenous and volatile agents exhibit distinct profiles in terms of recovery quality, reinforcing the need for individualized technique selection and adequate monitoring. Anesthetic customization, combined with the use of modern monitoring tools, is essential to reduce complications and optimize perioperative outcomes.

In addition to the findings already discussed, something interesting is the direction that current approaches to induction and maintenance of anesthesia seem to be taking. They seek more tailored methods, designed for each patient's physiology.

Recent studies show that the reaction to anesthetics, whether injected or inhaled, is highly dependent on the condition of the heart and breathing, the individual's physical fitness, and neurological changes with age. This shows how crucial it is to tailor doses individually and increase them gradually at the beginning.

Modern medicine is also increasingly embracing systems that make decisions based on real-time data, such as blood pressure and how the body responds to fluids. This helps prevent a drop in blood pressure du-

ring induction, especially in the elderly or people with neurological deficits.

When it comes to maintaining anesthesia, recent research indicates that stability during surgery is closely related to the balance between the depth of anesthesia, pain relief, and support for the circulatory system.

Target-controlled anesthesia (TCA) techniques are on the rise. These techniques enable more precise control of drugs, minimizing discrepancies between patients and, moreover, simplifying a more predictable recovery.

Similarly, advances in protective intraoperative ventilation—using smaller air volumes, lower pressures, and moderate PEEP—have shown encouraging results in reducing areas of lung collapse, hypoxia, and post-surgical respiratory complications.

Furthermore, there is a growing use of various monitoring tools that complement the assessment of anesthesia depth. Methods based on heart rate variability, pain perception, and brain activity analysis are being tested as promising alternatives for refining anesthetic plans. Such approaches not only help mitigate problems but also optimize awakening, reducing agitation, nausea, and time in the recovery room.

After all, a broad view of studies reveals that post-surgical outcomes depend more on the combination of anesthesia applied, monitoring, and the patient's clinical condition than on the choice of a particular anesthetic. Therefore, current research suggests that contemporary general anesthesia should be personalized, relying on sophisticated monitoring technologies and science-based methods to enhance the safety and excellence of patient care throughout the surgical journey.

Modern anesthetic practice is based on a variety of drugs, most of which are GABA receptor agonists (Philip, Brohan & Goudra, 2025). Propofol, an intravenous agent, remains the mainstay of induction and maintenance of anesthesia (TIVA), despite its known disadvantages, such as injection pain and dose-dependent cardiovascular depression (Philip, Brohan & Goudra, 2025).

The induction phase, which precedes maintenance, is a high-risk period that requires optimization of patient safety. Preoxygenation is a standard step to increase oxygen reserve and prolong safe apnea time. A recent systematic review compared different preoxygenation techniquesoxygenation techniques and concluded that the use of high-flow nasal oxygen (HFNO) with the patient in a head-up position was the most effective technique, associated with a significantly longer safe apnea time compared to the traditional face mask, both in the supine and elevated positions (Carvalho *et al.*, 2024).

When choosing an induction agent, hemodynamic stability is a key concern, especially in elderly patients. Propofol is known for its hypotensive potential. Newer agents, such as remimazolam—an ultra-short-acting benzodiazepine—have been investigated as alternatives with greater cardiovascular stability (Philip, Brohan & Goudra, 2025). However, a randomized clinical trial focused on geriatric patients (aged ≥80 years) compared induction with remimazolam versus propofol (both followed by maintenance with sevoflurane and remifentanil) (Takaki *et al.*, 2024). Surprisingly, the study found no statistically significant difference in the incidence of hypotension

(defined as MAP < 65 mmHg) between the groups. The incidence was high in both, reaching 72.1% in the remimazolam group and 72.7% in the propofol group, suggesting that in very elderly patients with diminished physiological reserves, the theoretical hemodynamic benefit of remimazolam may not translate into clinical superiority over propofol (Takaki *et al.*, 2024).

During the maintenance phase, the choice between intravenous (propofol) and inhalation (sevoflurane) anesthesia impacts different postoperative outcomes. In elderly patients undergoing non-cardiac surgery, postoperative cognitive dysfunction (POCD) is a feared complication. A meta-analysis comparing propofol and sevoflurane for this outcome found no significant difference in the occurrence of POCD in the short term (1 to 7 days) (Huang & Zhang, 2023). However, the same study noted that plasma levels of S-100ß protein, a biomarker of central nervous system damage, were significantly lower in the group receiving propofol. This suggests that, although the functional clinical outcome may be similar, sevoflurane may be associated with a higher degree of subclinical neural injury (Huang & Zhang, 2023).

In another vulnerable population, children, inhalation anesthesia with sevoflurane is associated with a high incidence of emergency delirium (ED) (Frelich *et al.*, 2024). A prospective study investigated whether the *method* of administering sevoflurane could mitigate this risk. The results showed that individualizing the depth of anesthesia through Bispectral Index (BIS) monitoring, with the goal of maintaining values between 40-60, dramatically reduced the incidence of ED (12.8%) compared to the control group, where the dosage was determined by minimum alveolar concentration (MAC) (35.1%) (Frelich *et al.*, 2024). This evidence suggests that excessive depth of anesthesia (dose-dependent) may be a more critical factor for delirium than the inhalation agent itself (Frelich *et al.*, 2024).

CONCLUSION

The induction and maintenance of general anesthesia have evolved significantly in recent decades, driven by the development of new agents, the expansion of monitoring techniques, and a growing understanding of the neurophysiological mechanisms involved in hypnosis and autonomic modulation. The most recent evidence shows that, although pharmacological alternatives such as remimazolam have emerged with the promise of greater hemodynamic stability, their efficacy in high-risk populations—especially the elderly >80 years of age—remains comparable to that of propofol. (Philip, Brohan & Goudra, 2025) In fact, a randomized clinical trial found no significant difference in the incidence of hypotension (MAP < 65 mmHg), which was high in both groups (72.1% for remimazolam and 72.7% for propofol). This reinforces that the physiological changes of aging are important factors (Takaki *et al.*, 2024).

Similarly, the choice of maintenance method should prioritize individualized care. A review of studies comparing propofol (TIVA) and sevoflurane (inhalation) shows distinct profiles, but no absolute superiority in cognitive or clinical outcomes, although biomarkers indicate possible greater neuronal stress associated with volatile agents (Huang & Zhang, 2023). In pediatrics, anesthetic depth is important to pre-

vent emergency *delirium* (ED); advanced monitoring by the bispectral index (BIS) to maintain values between 40-60 drastically reduced the incidence of ED from 35.1% (in the control group) to 12.8%, proving to be an effective strategy in reducing this complication.

Preoxygenation, in turn, remains a central step in induction, with clear advances thanks to the adoption of strategies such as high-flow nasal oxygen (HFNO) combined with head elevation, which significantly increase the time of safe apnea and reduce hypoxemic events.

Overall, the findings of this review indicate that contemporary anesthetic safety depends less on the isolated choice of agent and more on the integration of appropriate techniques (such as HFNO and positioning), accurate monitoring (such as BIS in pediatrics), and understanding of each patient's physiological particularities. The continuous advancement of monitoring technologies, combined with evidence-based practice, tends to further improve perioperative outcomes and the quality of anesthetic care.

Apart from the evidence presented, it is clear, without a doubt, that improving general anesthesia today is linked to the use of personalized approaches and tools that increase safety at every stage of surgery.

Recent studies show that differences between individuals, especially in the elderly, children, and those with multiple diseases, require more specific methods, combining detailed prior assessments, precise adjustment of medications, and good cardiovascular support.

Thus, techniques such as slow induction, correct use of blood pressure medications, and application of special ventilation protocols have a major impact on reducing problems during and after surgery.

Furthermore, we are seeing a growing demand for anesthesia with defined goals, using modern monitoring systems that assess not only the depth of anesthesia, but also the body's response, pain perception, and respiratory health.

These methods help reduce excessive or insufficient application of anesthetics, facilitating a faster recovery, with fewer unforeseen events and superior physiological stability after surgery.

Therefore, recent developments now show that good anesthesia care goes beyond selecting a medication or maintaining a technique, involving general, person-centered care, supported by current studies and modern monitoring devices. The combination of these factors strengthens a more reliable, effective, and appropriate model of care for the current needs of anesthesiology, leading to better medical outcomes and improving overall care around surgery.

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