



Review Article

The Effects of Anesthetic Agents on Perioperative Glucose Homeostasis in Patients with Diabetes: A Narrative Review

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Abstract

Anesthesia plays a critical role in modern surgical care by ensuring patient comfort, safety, and physiologic stability. However, the effects of anesthetic agents extend beyond sedation and analgesia and include important, yet often underrecognized, influences on perioperative glucose metabolism. This consideration is particularly relevant in patients with diabetes mellitus, a growing surgical population in whom perioperative hyperglycemia is strongly associated with increased risks of infection, delayed wound healing, cardiovascular complications, and prolonged hospital stay. This narrative review synthesized current clinical and mechanistic evidence regarding how commonly used anesthetic agents and techniques influence perioperative glucose homeostasis. Volatile anesthetics have been shown to impair pancreatic β -cell insulin secretion and promote peripheral insulin resistance through the effect on cellular ion channels, mitochondrial function, and stress hormone pathways, frequently resulting in intraoperative hyperglycemia. In contrast, propofol-based total intravenous anesthesia (TIVA) appears to exert comparatively milder effects on insulin dynamics in many clinical contexts. Adjunctive agents such as dexmedetomidine and clonidine may further stabilize glucose levels through sympatholytic and stress-attenuating mechanisms. Additionally, regional and neuraxial anesthesia consistently demonstrate an ability to blunt the neuroendocrine stress response to surgery, thereby promoting improved glycemic stability. By integrating physiologic mechanisms with clinical findings, this review highlights how anesthetic choice can meaningfully influence perioperative glucose trends. Understanding these interactions is essential for optimizing anesthetic planning, intraoperative monitoring, and glycemic management strategies in diabetic surgical patients.

Keywords

Anesthetic Effects on Glucose Metabolism, Perioperative Glucose Homeostasis, Surgical Stress and Hyperglycemia, Glucose Regulation During Anesthesia, Anesthesia and Glycemic Control, Anesthesia Impact on Blood Glucose

1. Background

Diabetes Mellitus is a prevalent comorbidity among surgical patients worldwide and represents a major perioperative management challenge. The national prevalence of diabetes in the United States has risen steadily over the past decades. A 2021 review showed a crude estimate that 11.6% of the United States population had diabetes and a substantial percentage of

patients who undergo elective and emergency surgeries present with diagnosed diabetes or impaired glucose tolerance [1]. Perioperative hyperglycemia in diabetic patients increases mortality and morbidity and has been connected to increased risk of surgical site infection, delayed wound healing, longer length of stay, and cardiovascular complications. These factors make glucose management

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a cornerstone of perioperative care [2].

The metabolic disturbances that underlie perioperative hyperglycemia are multifactorial. Surgery injury elicits a complex neuroendocrine response: nociceptive afferent signals and tissue injury activate the sympathetic nervous system and hypothalamic-pituitary-adrenal (HPA) axis, producing elevated circulating catecholamines, cortisol, glucagon, and growth hormone. These hormones increase hepatic gluconeogenesis and glycogenolysis, reduce peripheral glucose uptake, and promote insulin resistance in skeletal muscle and adipose tissue [3, 23], a physiologic process extensively described in mechanistic analyses of the perioperative neuroendocrine stress response. In patients with diabetes, baseline deficits in insulin secretion and/or action reduce metabolic reserve and widen the amplitude and duration of hyperglycemic excursions during and after surgery.

Anesthetic agents influence glucose metabolism through neuroendocrine and cellular mechanisms. Management of these anesthetic agents exert a modulatory effect on this stress response and on glucose homeostasis through several mechanisms. First, the anesthetic agents differ in their effects on neuroendocrine activation: techniques or drugs that blunt nociceptive transmission and sympathetic outflow (e.g. neuraxial blockade, regional anesthesia) typically attenuate the rise in counter-regulatory hormones and thereby mitigate intraoperative hyperglycemia [4]. Conversely, agents that increase sympathetic tone or catecholamine release (e.g. ketamine and high-dose volatile agents in some contexts) can exacerbate hyperglycemia [6]. Second, anesthetic drugs may have direct actions on pancreatic beta cell function, insulin signaling pathways, or hepatic and peripheral glucose metabolism. Experimental and clinical data indicate that volatile anesthetics (isoflurane, sevoflurane, desflurane) can impair insulin secretion and promote peripheral insulin resistance via effects on ion channels, mitochondrial function, and cellular signaling cascades [9, 11]. Propofol, the backbone of total intravenous anesthesia (TIVA), has been variably reported to produce less insulin resistance than volatiles in some clinical contexts, though findings are not uniform and may depend on dose, infusion duration, and the clinical circumstance [5, 16].

Adjunct medications commonly employed in modern anesthetic practice, such as dexmedetomidine, clonidine, and multimodal analgesics, have received increasing attention for their potential to stabilize perioperative glucose by reducing catecholamine release and inflammatory mediators [14]. Dexmedetomidine has been shown in several clinical studies to attenuate stress hormone surges and to reduce intraoperative and early postoperative hyperglycemia in surgical cohorts, including some diabetic subgroups [20]. Conversely, widely used agents such as perioperative corticosteroids and certain vasopressors may induce or worsen hyperglycemia and necessitate anticipatory insulin adjustments.

Beyond individual agents, anesthetic techniques, especially the use of regional or neuraxial anesthesia as an adjunct or al-

ternative to general anesthesia, consistently demonstrates a capacity to blunt the neuroendocrine response to surgical stimulation, reduce perioperative insulin resistance, and improve glycemic stability [24], as described in comprehensive reviews of perioperative catabolic and metabolic stress pathways. These physiologic effects are especially relevant in diabetic patients, where reducing hormonal surges may translate to fewer hyperglycemia-related complications.

Despite the physiologic plausibility and accumulating clinical data, existing literature is heterogeneous. Studies vary by patient population (type 1 vs type 2 vs mixed diabetes), type and duration of surgery, anesthetic regimens, perioperative glucose targets, and monitoring frequency, limiting generalizability. Many trials are small, single-center, or focused on non-diabetic cohorts, and direct randomized comparisons of anesthetic regimens specifically in diabetic surgical patients are sparse. Moreover, the clinical significance of modest intraoperative differences in glucose (infection rates, myocardial events, or length of stay) remain incompletely defined [2, 4].

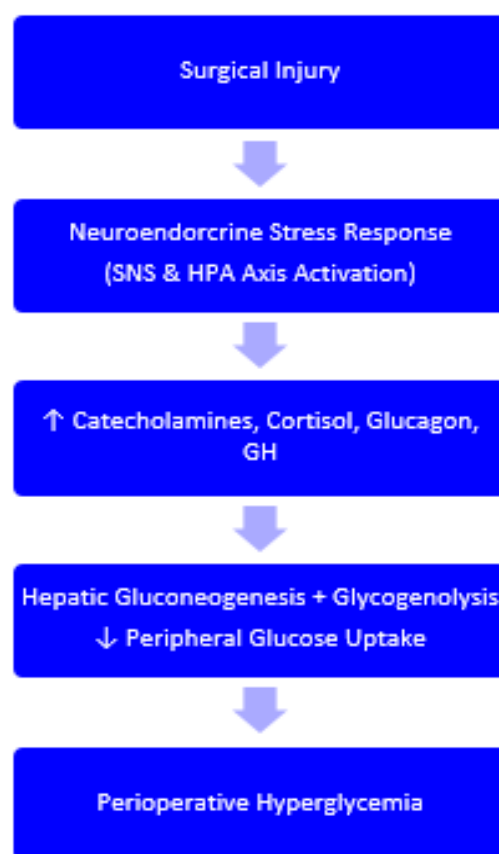


Figure 1. Schematic representation of the neuroendocrine stress response to surgery and the sites at which anesthetic agents and techniques modulate perioperative glucose homeostasis.

Given the high prevalence of diabetes in surgical populations and the well-documented association between perioper-

ative hyperglycemia and poor outcomes, clarifying how anesthetic choices influence glucose homeostasis has meaningful implications for perioperative planning and glycemia management protocols. This narrative review synthesizes current evidence on volatile and intravenous anesthetics, adjunctive agents, and regional techniques, with the goal of informing intraoperative monitoring strategies and individualized management plans for patients with diabetes undergoing surgery.

Figure 1. Mechanisms by Which Anesthetic Techniques Influence Perioperative Glucose Homeostasis.

2. Methods

This narrative review was conducted to synthesize current evidence regarding the effects of anesthetic agents and techniques on perioperative glucose regulation in patients with diabetes mellitus. A comprehensive literature search was performed using PubMed, Embased, and Google Scholar for studies published in English through October 2025. The following key terms and their combinations were used: *diabetes mellitus, perioperative hyperglycemia, anesthetic agents, volatile anesthesia, total intravenous anesthesia (TIVA), propofol, sevoflurane, isoflurane, desflurane, regional anesthesia, neuraxial block, dexmedetomidine, clonidine, insulin resistance, stress response, and surgical outcomes.*

Both clinical studies (randomized controlled trials, cohort studies, case-control studies) and experimental investigations (animal and cellular models) were included to capture mechanistic and translational data relevant to anesthetic-glucose interactions. Systematic reviews and meta-analyses were

screened for additional references. Articles were excluded if they (1) focused solely on non-surgical or critical care populations, (2) did not include glucose or insulin-related outcomes, or (3) were editorials or non-peer-reviewed sources.

The selection process involved an initial title and abstract review followed by full text assessment for eligibility. Data were extracted on study by design, population, characteristics (including diabetic type), anesthetic agents or techniques used, glycemic outcomes (intraoperative glucose, insulin levels, stress hormone changes), and postoperative clinical endpoints (infection rates, cardiovascular events, length of stay).

Given the heterogeneity in study designs and outcome measures, findings were summarized descriptively rather than pooled quantitatively. Emphasis was placed on identifying trends in anesthetic-related effects on glucose homeostasis, differences between volatile and intravenous agents, and the potential modulatory roles of adjunctive and regional anesthetic techniques. The synthesis aimed to integrate physiologic mechanisms with clinical outcomes to inform perioperative management strategies for diabetic surgical patients.

3. Results

A total of approximately 120 studies met inclusion criteria, encompassing randomized controlled trials, observational studies, and experimental investigations. Evidence consistently demonstrated that perioperative hyperglycemia remains a frequent and clinically relevant occurrence in diabetic patients, even under established glucose management protocols.

Table 1. Comparative Effects of Common Anesthetic Agents and Techniques on Perioperative Glucose Homeostasis.

Anesthetic Agent/Technique	Effect on Insulin Secretion	Effect on Insulin Resistance	Effect on Stress Hormones	Net Effect on Glucose	Key Mechanism	Overall Glycemic Impact
Sevoflurane/Isoflurane/Desflurane	↑ Impaired β -cell function	↑ Increased	Minimal suppression	↑ Hyperglycemia	Ion channel & mitochondrial effects	Least favorable
Propofol (TIVA)	Mild ↓ or neutral	Mild ↑ (dose dependent)	Blunts SNS modestly	↔ / ↓ compared to volatiles	Less β -cell suppression	More favorable
Dexmedetomidine	Neutral	↓	↓↓ Cortisol & catecholamines	↓	Sympatholysis	Highly favorable adjunct
Clonidine	Neutral	↓	↓	↓	Sympatholysis	Favorable adjunct
Ketamine	↓	↑↑	↑↑ Catecholamines	↑↑	SNS stimulation	Unfavorable in diabetics
Perioperative Steroids	Neutral	↑↑	↑	↑↑	Gluconeogenesis	Requires insulin planning
Vasopressors (epi-containing)	Neutral	↑	↑	↑	Adrenergic stimulation	Transient hyperglycemia

Anesthetic Agent/Technique	Effect on Insulin Secretion	Effect on Insulin Resistance	Effect on Stress Hormones	Net Effect on Glucose	Key Mechanism	Overall Glycemic Impact
Regional/Neuraxial	Preserved	↓	↓↓	↓	Blocks afferent stress response	Most favorable technique

Table 1. Summary comparison of how commonly used anesthetic agents and techniques influence insulin physiology, stress hormone, release, and perioperative glucose trends in diabetic patients.

3.1. Volatile vs. Intravenous Anesthetics

Across multiple studies, volatile agents, including sevoflurane, isoflurane, and desflurane, were associated with dose-dependent impairments in insulin secretion and peripheral

glucose utilization [8-10]. Mechanistic investigations attributed these effects to altered pancreatic beta cell ion channel function, mitochondrial oxidative activity, and interference with insulin signaling pathways [8]. Conversely, propofol-based total intravenous anesthesia (TIVA) was generally associated with lower intraoperative glucose levels and reduced postoperative insulin resistance compared with volatile agents, [5, 7] although results varied. Some studies noted that prolonged infusions or higher doses of propofol could attenuate these benefits [12].

Table 2. Volatile Anesthesia vs. Propofol-Based TIVA in Diabetic Surgical Patients.

Feature	Volatile Anesthesia	Propofol TIVA
β-cell insulin secretion	Significantly impaired	Mild or variable effect
Peripheral insulin resistance	Increased	Less pronounced
Intraoperative glucose levels	Higher	Lower
Postoperative insulin requirements	Increased	Reduced in several studies
Mechanistic basis	Mitochondrial dysfunction, ion channel effects	Less β-cell interference
Clinical trend	Greater glucose variability	Improved glucose stability

Table 2. Direct comparison of physiologic and clinical glycemic effects between volatile anesthetics and propofol-based total intravenous anesthesia.

3.2. Adjunctive and Sympathetic Agents

The alpha-2 adrenergic agonists: dexmedetomidine and clonidine demonstrated reproducible reductions in intraoperative glucose excursions and serum cortisol levels in both diabetic and

non-diabetic cohorts [13, 15]. Dexmedetomidine's attenuation of catecholamine release and inflammatory mediators correlated with improved glycemic stability and, in several studies, reduced postoperative insulin requirements [19]. In contrast, perioperative corticosteroids, epinephrine-containing local anesthetics, and vasopressor infusions were consistently associated with transient hyperglycemia, often necessitating insulin titration or glucose monitoring adjustments [17, 18].

3.3. Regional and Neuraxial Techniques

Table 3. Impact of Regional and Neuraxial Anesthesia on the Surgical Stress Response and Glycemic Stability.

Mechanism	Effect	Glycemic Result
Blockade of nociceptive afferents	↓ SNS activation	↓ Catecholamines
Reduced HPA axis stimulation	↓ Cortisol, glucagon	↓ Hepatic glucose output

Mechanism	Effect	Glycemic Result
Improved peripheral insulin sensitivity	↓ Insulin resistance	Stable glucose levels
Reduced inflammatory mediators	↓ Cytokines	Reduced postoperative hyperglycemia
Observed clinical outcomes	↓ Infection rates, ↓ LOS	Improved recovery metrics

Studies evaluating epidural and spinal anesthesia, either as primary techniques or adjuncts to general anesthesia, demonstrated attenuated stress hormone surges and reduced perioperative insulin resistance [20, 21]. These findings were most pronounced in abdominal, orthopedic, and lower extremity procedures. Reduced sympathetic activation and lower circulating cortisol and catecholamine levels under regional anesthesia were associated with smaller glucose fluctuations and, in some cohorts, reduced postoperative infection rates and length of stay [22].

Table 3. Physiologic mechanisms by which regional and neuraxial anesthesia blunt the surgical stress response and improve perioperative glucose control.

3.4. Heterogeneity and Limitations

Despite consistent physiologic patterns, substantial heterogeneity was noted across studies regarding diabetes subtype, surgical type and duration, anesthetic regimens, and glycemia targets. Few randomized controlled trials directly compared anesthetic techniques specifically in diabetic surgical populations [12]. Moreover, many studies lacked standardized glucose monitoring protocols or robust reporting of clinical outcomes such as wound infection or myocardial events [5].

4. Conclusions

Current evidence supports a meaningful influence of anesthetic choice and technique on perioperative glucose homeostasis in patients with diabetes mellitus. Volatile anesthetics tend to impair insulin secretion and increase insulin resistance, while propofol-based TIVA and sympatholytic adjuncts such as dexmedetomidine may offer modest glycemic advantages. Regional and neuraxial anesthesia consistently attenuate the neuroendocrine stress response and promote more stable perioperative glucose profiles.

However, existing data are limited by small sample sizes, heterogeneous methodologies, and a paucity of trials specifically designed for diabetic surgical cohorts. The clinical significance of modest intraoperative glucose difference, particularly in relation to infection, cardiovascular outcomes, and recovery metrics, remains incompletely defined.

Future research should prioritize prospective, adequately powered trials comparing anesthetic regimens in diabetic patients, incorporating standardized glucose targets, insulin

management algorithms, and long-term outcome measures. Understanding the interplay between anesthetic technique, metabolic physiology, and glycemic control will be critical for optimizing perioperative care and improving outcomes in this growing surgical population.

Abbreviations

TIVA Total Intravenous Anesthesia

Author Contributions

Mariah Ganga: Data Curation, Formal Analysis, Investigation, Resources, Writing – Original Draft

Dan Erdman: Conceptualization, Writing – Review & Editing, Methodology

Conflicts of Interest

The authors declare no conflicts of interest.

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