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The Interface Between Anesthesia and Immunomodulation with Implications for Perioperative Inflammation and Cancer Recurrence

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Abstract — The perioperative period is a critical window characterized by profound surgical stress and inflammation, which can induce significant immunosuppression. This state is hypothesized to facilitate the survival and proliferation of residual cancer cells, thereby increasing the risk of recurrence and metastasis. Anesthetic techniques, as integral components of perioperative care, are increasingly recognized as active modulators of this complex immune response rather than immunologically neutral agents. This narrative review aims to synthesize and critically evaluate the current evidence on the interface between various anesthetic and analgesic techniques and their immunomodulatory effects. The primary focus is to elucidate the implications for perioperative inflammation and long-term oncological outcomes, specifically cancer recurrence. A comprehensive literature search was conducted across major scientific databases, including PubMed, Scopus, and Web of Science. The review includes relevant preclinical (*in vitro* and *in vivo*) and clinical studies investigating the impact of volatile anesthetics, propofol-based total intravenous anesthesia (TIVA), regional anesthesia, and opioids on key components of the innate and adaptive immune systems. A consistent pattern emerges from preclinical data, indicating that volatile anesthetics and opioids tend to exert immunosuppressive effects by inhibiting the cytotoxicity of natural killer (NK) cells and T lymphocytes while promoting regulatory T cells (Tregs). In contrast, propofol and regional anesthetic techniques (via opioid-sparing) appear to be immune-sparing or even protective. However, this strong biological rationale has not been consistently translated into definitive outcomes in large-scale clinical trials, which have yielded conflicting results, likely due to significant clinical heterogeneity and confounding factors. The choice of anesthesia is an active immunomodulatory intervention with plausible effects on cancer recurrence. Despite inconclusive clinical data, the compelling biological evidence supports the adoption of a multimodal immunoprotective strategy. Combining propofol-based TIVA with regional anesthesia and opioid-sparing analgesia represents a rational approach to mitigate perioperative immunosuppression and may potentially improve long-term outcomes for patients undergoing cancer surgery.

Keywords — *Anesthesia; Immunomodulation; Cancer Recurrence.*

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INTRODUCTION

Cancer represents a leading global health challenge, with a projected disease burden that continues to increase worldwide [1]. In the management of solid tumors, surgical resection has long stood as the primary curative modality, offering patients the best opportunity for long-term survival [2]. However, the success of surgery is often overshadowed by the significant risk of disease recurrence whether local, regional, or as distant metastases which constitutes the principal cause of therapeutic failure [3]. A substantial body of scientific evidence consistently points to the perioperative period—the timeframe encompassing the pre-operative, intra-operative, and immediate post-operative phases as a "critical window." This period is not merely a recovery phase but a dynamic episode characterized by profound physiological turmoil that can fundamentally influence the interaction between residual tumor cells and the host immune system, ultimately determining long-term oncological outcomes [4].

Central to the physiological upheaval of the perioperative period is the surgical stress response, a complex and coordinated defense reaction to tissue trauma [5]. This response is primarily mediated through two major pathways. The first is the activation of the neuroendocrine axis, specifically the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic

nervous system (SNS), which floods the circulation with catabolic hormones such as cortisol and catecholamines (e.g., epinephrine and norepinephrine) [6]. The second pathway is the inflammatory response, wherein tissue damage triggers a massive release of inflammatory mediators, including pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), as well as compensatory anti-inflammatory cytokines such as interleukin-10 (IL-10) [7]. The combination of this neuroendocrine activation and the resulting cytokine storm, while essential for homeostasis and wound healing, paradoxically creates an internal milieu that is profoundly immunosuppressive.

This transient state of immunosuppression induced by surgical stress has grave implications in the oncological setting [8]. A competent immune system normally performs *immunosurveillance*, a constant patrol to detect and eliminate malignant cells that may have been dislodged or left behind after surgery [9]. The vanguard of this defense mechanism consists of effector cells from both innate and adaptive immunity, most notably natural killer (NK) cells, which can kill targets without prior sensitization, and cytotoxic T lymphocytes (CTLs), which recognize specific tumor antigens [10]. Stress hormones like cortisol and catecholamines, along with inflammatory mediators such as Prostaglandin E2 (PGE_2), directly inhibit the cytolytic activity of NK cells and the proliferative functions of T-cells [11]. This sharp decline in cellular immune function creates a "biological window of vulnerability," during which tumor cells shed into the circulation during surgical manipulation can evade immune elimination, adhere to the vascular endothelium, and establish new metastatic colonies [12].

Within this complex matrix of the perioperative stress response, anesthesia and analgesia are no longer regarded as immunologically neutral, passive interventions [13, 14]. Each anesthetic agent and analgesic technique possesses a unique pharmacological profile that can modulate the neuroendocrine and inflammatory pathways, thereby directly or indirectly influencing the fate of the interaction between the immune system and cancer cells. A growing body of evidence from *in vitro* studies, animal models, and human clinical data suggests that the choice of anesthesia can be a significant independent factor in determining the degree of post-operative immunosuppression [15]. Consequently, the decision between volatile (inhalational) anesthesia, total intravenous anesthesia (TIVA), and the use of adjuvants like regional anesthesia not only affects the patient's intraoperative experience but also potentially leaves a biological "imprint" that may influence the risk of cancer recurrence.

The differential immunomodulatory effects among anesthetic techniques form the crux of research in the field of onco-anesthesia. Volatile anesthetics, such as sevoflurane, have been shown in numerous preclinical studies to suppress NK cell cytotoxic function, induce apoptosis in lymphocytes, and enhance the expression of pro-metastatic factors like Hypoxia-Inducible Factor-1α (HIF-1α) in cancer cells [16, 17]. In contrast, propofol, the primary agent in TIVA, exhibits a potentially more favorable profile. Its antioxidant properties and its ability to suppress central inflammatory pathways (such as NF-κB) are thought to preserve NK cell function and maintain a Th1/Th2 cytokine balance more conducive to anti-tumor immunity [18]. On the other hand, regional anesthetic techniques (e.g., epidural or paravertebral blocks) offer a distinct protective mechanism; by blocking afferent nociceptive signals from the surgical site to the central nervous system, they effectively blunt the activation of the HPA and SNS axes, thereby significantly reducing the release of stress hormones and the need for systemic opioids, which are also known to have immunosuppressive properties [19, 20].

Despite this robust biological rationale, which is supported by numerous retrospective studies, the gold-standard evidence from randomized controlled trials (RCTs) remains limited and has often yielded conflicting or inconclusive results [21]. Large-scale RCTs, such as the VAPOR-C trial, for instance, found no statistically significant difference in recurrence-free survival between volatile and propofol anesthesia in colorectal cancer patients, highlighting the complexity of this interaction in a real-world clinical setting [22]. Confounding factors such as tumor type and stage, the extent of surgical invasion, the patient's baseline immune status, and other postoperative management variables likely influence the final outcome. This gap between promising preclinical evidence and inconclusive clinical data creates uncertainty in daily practice. Therefore, this review is

structured to critically synthesize the existing literature, evaluate the strengths and weaknesses of various study types, delineate the underlying biological mechanisms, and ultimately provide a clear overview of the current state of knowledge to guide both clinical practice and future research [3, 23].

MATERIALS AND METHODS

Study Approach

This study was conducted as a narrative review, aiming to provide an integrative overview of the interface between anesthetic techniques and immunomodulation. The approach focuses on bridging the findings from fundamental cellular immunology and oncology with their broader clinical implications in the perioperative setting [24]. The methodology combines literature synthesis, secondary data analysis, and mechanistic interpretation of existing experimental (both *in vitro* and *in vivo*) and relevant clinical studies to construct a comprehensive understanding of the topic.

Data Collection

Scientific articles, original research papers, and reputable reviews published between January 2000 and August 2025 were retrieved from major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar. This systematic search strategy is essential for ensuring comprehensive coverage of the available literature [25]. Keywords used for the search, both individually and in combination, included: "anesthetic agents", "immunomodulation", "sevoflurane", "propofol", "regional anesthesia", "opioids", "cancer recurrence", "metastasis", "Natural Killer cells", "T lymphocytes", "cytokines", "perioperative inflammation", "surgical stress response", and "oncologic surgery". Additionally, clinical trial registries such as ClinicalTrials.gov were reviewed to identify clinical studies assessing long-term oncological outcomes related to anesthetic choice.

Selection Criteria

Studies were selected based on their relevance to a set of predefined inclusion and exclusion criteria to ensure the focus and quality of the review [26]. Inclusion criteria were: (1) identification of direct molecular interactions between anesthetic agents and immune cells (e.g., NK cells, T lymphocytes); (2) investigation of anesthetic effects on key immunological functions (e.g., cytotoxicity, cytokine production, cell proliferation); (3) investigation of the impact on the systemic perioperative inflammatory and neuroendocrine stress response; and (4) studies linking these immunomodulatory mechanisms to clinical outcomes, specifically cancer recurrence or metastasis. Studies focusing exclusively on local anesthetics for non-systemic effects, those where immunological effects were only speculated without direct measurement, or articles such as case reports and editorials without primary data were excluded from this review.

Data Analysis

The collected data were analyzed qualitatively using a thematic synthesis approach, allowing for the identification and categorization of key concepts across multiple studies [27]. Findings were thematically categorized based on key mechanistic domains: (1) direct effects on the function of key immune effector cells (NK cells and T lymphocytes); (2) modulation of the perioperative inflammatory milieu, including cytokine profiles; (3) modulation of the neuroendocrine stress response (e.g., cortisol, catecholamines); and (4) translation to clinical outcomes, specifically long-term cancer recurrence and overall survival. Results from *in vitro*, *in vivo*, and human studies were comparatively analyzed to identify consistent patterns, dose-dependent effects, and existing knowledge gaps.

Limitations

This study acknowledges the limitations inherent to a narrative review format. Unlike systematic reviews, narrative reviews can be susceptible to selection bias and do not involve a quantitative meta-analysis, which may limit the generalizability of the conclusions [28]. The heterogeneity of cancer types, surgical procedures, experimental models, anesthetic concentrations, and exposure durations across studies also presents a challenge for direct comparison. Nevertheless, a rigorous effort was made to include recent and high-impact studies to ensure a comprehensive and balanced coverage of the topic.

RESULTS AND DISCUSSION

The synthesis of the reviewed literature confirms that anesthetic agents and techniques are not merely passive facilitators of surgery but are active biological modulators of the perioperative immune environment. A central theme that emerges is that their influence is exerted through two distinct but interconnected pathways: a direct pathway involving molecular interactions with immune cells, and an indirect pathway mediated by their capacity to blunt the systemic surgical stress response [29]. Volatile anesthetics, intravenous agents like propofol, regional techniques, and analgesics like opioids each possess a unique signature of effects on these pathways. This differential impact forms the biological basis for the hypothesis that anesthetic choice can significantly alter the delicate balance between host immune defense and tumor cell survival during the critical perioperative window [30]. Understanding these mechanisms is paramount to developing evidence-based anesthetic strategies aimed at improving long-term oncological outcomes.

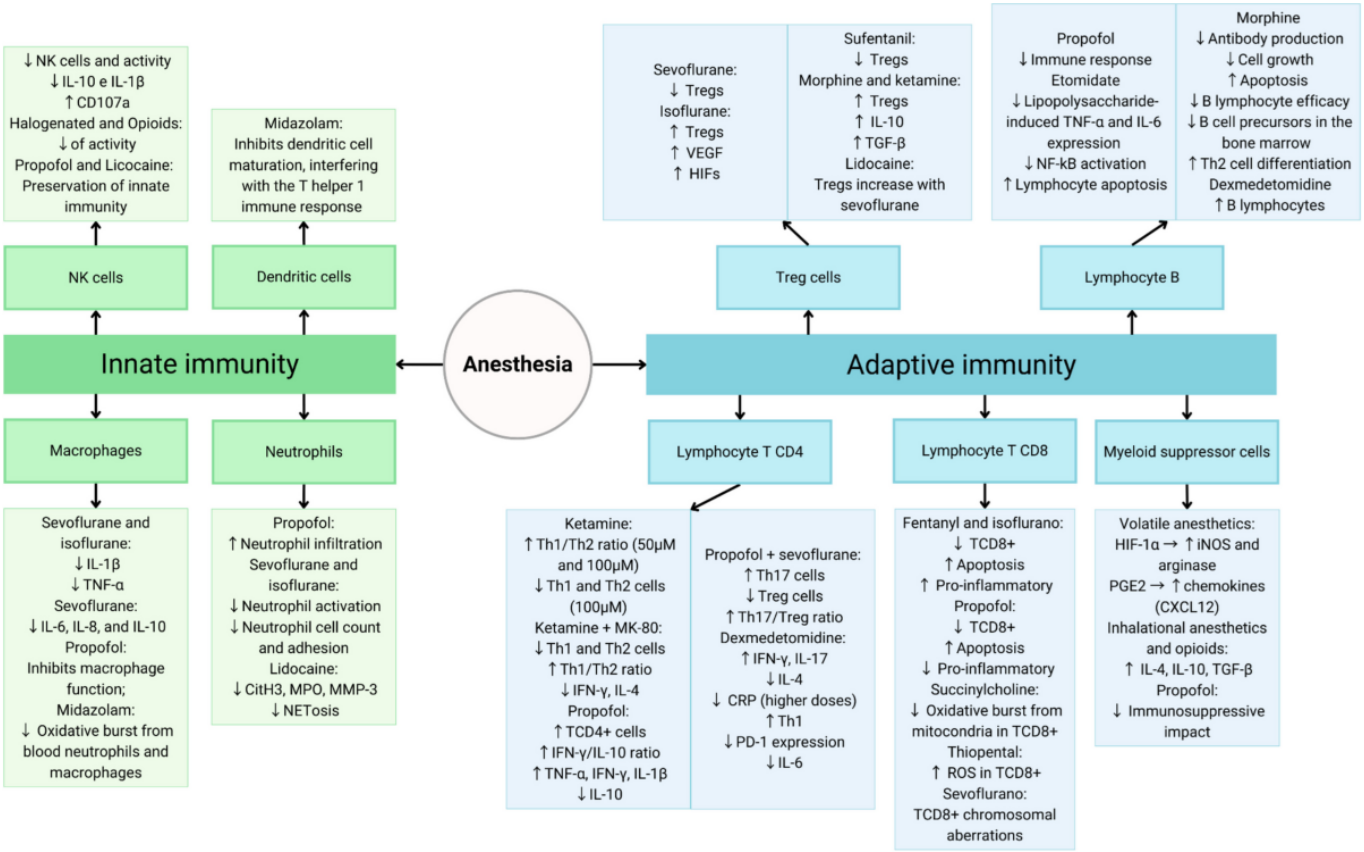


Figure 1. The Interface Between Anesthesia and Immunomodulation with Implications for Perioperative Inflammation and Cancer Recurrence.

It positions "Anesthesia" as a central intervention with broad and diverse effects on the two primary arms of the immune system: innate immunity and adaptive immunity. Each pathway from the central anesthetic hub to specific immune cells (e.g.,

NK cells, macrophages, T lymphocytes, and B lymphocytes) is annotated with specific data on how different anesthetic and analgesic agents such as sevoflurane, propofol, opioids, and ketamine modulate cellular function. The implications of this modulation are directly relevant to the title; interactions with cells like neutrophils and macrophages directly impact "perioperative inflammation," while interactions with cells like NK cells, cytotoxic T lymphocytes (CD8+), and regulatory T cells (Tregs) fundamentally determine the body's ability to fight "cancer recurrence" [47].

On the innate immunity axis, the diagram highlights how various anesthetic agents can either bolster or weaken the body's first line of defense. Natural killer (NK) cells, which are crucial for eliminating circulating tumor cells, demonstrate a clear vulnerability to volatile anesthetics and opioids, which are noted to decrease (↓) NK cell activity and function [48]. In contrast, Propofol and Lidocaine are shown to preserve innate immunity, suggesting a protective effect on these vital cells. Similarly, regarding inflammatory cells such as neutrophils and macrophages, Propofol exhibits potentially beneficial effects by decreasing (↓) excessive neutrophil infiltration and activity, whereas Sevoflurane can inhibit macrophage function [49]. The implications for "perioperative inflammation" are evident: anesthetic choice can determine whether the inflammatory response to surgery is a controlled, healing process or a detrimental, pro-tumorigenic inflammatory storm. Furthermore, the negative effect of midazolam on dendritic cells, inhibiting their maturation; demonstrates how certain anesthetics can disrupt the critical communication bridge between the innate and adaptive immune systems [50].

On the adaptive immunity axis, the diagram vividly illustrates how anesthesia can drastically tip the balance from an anti-tumor to a pro-tumor response. One of the most striking and consistent findings is the effect on regulatory T cells (Tregs), which function as "brakes" on the immune system. Both volatile anesthetics (Sevoflurane, Isoflurane) and opioids (Sufentanil, Morphine) are shown to significantly increase (↑) the Treg population or function [51]. This increase is highly detrimental in oncology, as tumors often exploit Tregs to shield themselves from immune attack. In contrast, Propofol demonstrates an opposing effect by promoting (↑) a Th1 response and activating CD4+ and CD8+ T lymphocytes, which are the primary soldiers in the fight against cancer cells [52]. The diagram also indicates that volatile anesthetics and opioids have a general immunosuppressive impact on CD8+ T lymphocytes and that Morphine specifically suppresses B lymphocytes and antibody production. These effects collectively illustrate how anesthetic choices can reshape the architecture of the adaptive immune response, determining whether long-term immune memory will be effective at eradicating residual disease or become tolerant to it [53].

Overall, the diagram provides powerful visual evidence for a coherent clinical narrative. A clear pattern emerges: volatile anesthetics and opioids tend to create a "pro-tumorigenic immunological signature"—they suppress key killer cells (NK cells and CD8+ T lymphocytes) while promoting immunosuppressive cells (Tregs and myeloid-derived suppressor cells), and encourage pro-metastatic factors (VEGF, HIFs) [54]. This immunosuppressive environment is directly linked to an increased risk of cancer recurrence. In contrast, Propofol tends to foster an "anti-tumorigenic immunological signature" by preserving or enhancing the function of effector cells and reducing detrimental pro-inflammatory cytokines like IL-6. The link to perioperative inflammation is also evident, where Propofol appears to moderate an excessive inflammatory response. Thus, this diagram is not just a collection of data points but a compelling visual argument supporting the need for an immunologically-conscious anesthetic approach—such as the multimodal strategy combining propofol-based TIVA with regional anesthesia to spare opioids—as an active intervention to optimize patient conditions and potentially reduce the risk of postoperative cancer recurrence [55]

The innate immune system, particularly natural killer (NK) cells, represents the first line of defense against circulating tumor cells and micrometastases. A substantial body of *in vitro* and animal research has demonstrated the profound and often detrimental effects of volatile anesthetics on NK cell function [31]. Agents like sevoflurane and isoflurane have been shown to directly suppress NK cell cytotoxicity, impairing their ability to recognize and lyse tumor cells by inhibiting the release of cytotoxic granules like perforin and granzymes [16, 32]. In stark contrast, propofol appears to be immune-sparing or even

immune-enhancing in this regard. Multiple studies have reported that propofol preserves, and in some cases enhances, NK cell activity compared to volatile agents, potentially through its antioxidant properties and modulation of intracellular signaling pathways that govern cell-mediated cytotoxicity [18, 33]. This fundamental difference in their effect on NK cells is one of the most consistent findings in preclinical onco-anesthesia research and a cornerstone of the argument for preferring propofol-based techniques.

Beyond innate immunity, the adaptive immune system, particularly T lymphocytes, is critical for sustained, antigen-specific anti-tumor responses. The evidence suggests that anesthetics can significantly skew the functional profile of T-cells. Volatile anesthetics have been linked to a shift away from the anti-tumor Th1 (cell-mediated) response towards a pro-tumor Th2 (humoral) response, which is less effective at eliminating solid tumors [34]. Furthermore, some studies indicate that volatile agents may promote the proliferation and function of regulatory T cells (Tregs), a subset of T-cells that actively suppress the function of cytotoxic T lymphocytes (CTLs), thereby protecting the tumor from immune attack [35]. Propofol, conversely, has been associated with the preservation of a Th1-dominant cytokine profile and does not appear to promote Treg activity to the same extent, thus maintaining a more effective adaptive anti-tumor environment [36].

Surgical trauma invariably triggers a systemic inflammatory response, creating a "cytokine storm" that can paradoxically support tumor progression. Anesthetic agents are key modulators of this inflammatory milieu. Volatile anesthetics have been associated with an increased systemic release of pro-inflammatory cytokines such as IL-6 and TNF-α, which, while part of the normal stress response, have also been implicated in promoting tumor cell proliferation, angiogenesis, and invasion [37]. Moreover, the subsequent compensatory release of anti-inflammatory cytokines like TGF-β can further enhance tumor growth and immunosuppression. Propofol has demonstrated potent anti-inflammatory properties, appearing to attenuate the release of these detrimental cytokines by inhibiting key signaling pathways like NF-κB [38]. By fostering a less inflammatory and less immunosuppressive perioperative environment, propofol may reduce the risk of tumor cell seeding and growth.

Regional anesthesia (e.g., epidural, paravertebral blocks) offers a powerful indirect mechanism for preserving immune function. By blocking afferent neural signals from the surgical site, these techniques effectively blunt the activation of the HPA axis and the sympathetic nervous system [19]. The clinical result is a significant reduction in the systemic release of cortisol and catecholamines, two of the most potent endogenous immunosuppressants [20]. This neuroendocrine blockade indirectly preserves the function of NK cells and T lymphocytes that would otherwise be suppressed. A crucial secondary benefit is the profound reduction in the requirement for intra- and postoperative opioids [39]. Opioids, particularly morphine, are well-documented immunosuppressants that act on mu-opioid receptors expressed on immune cells, directly inhibiting NK cell activity and lymphocyte proliferation [40]. Therefore, an "opioid-sparing" approach facilitated by regional anesthesia is a key strategy for perioperative immunoprotection.

Despite the compelling and consistent preclinical evidence outlined above, the translation to definitive clinical benefit in humans has been challenging, leading to significant debate. Numerous retrospective cohort studies have suggested an association between propofol-based TIVA and/or regional anesthesia with improved recurrence-free survival in various cancers, including breast, colon, and lung cancer [41, 42]. However, the gold-standard evidence from large-scale randomized controlled trials (RCTs) has been inconclusive. The highly anticipated VAPOR-C trial, for example, found no significant difference in one-year recurrence-free survival for colorectal cancer patients randomized to receive either sevoflurane or propofol [43]. This discrepancy highlights the immense complexity of clinical cancer outcomes, which are influenced by a multitude of confounding factors including tumor biology and stage, surgical technique, patient comorbidities, and genetic predisposition, which may overwhelm the more subtle effects of anesthetic choice.

The statement that there is no definitive "winner" in clinical trials does not negate the strong biological rationale regarding the effects of anesthesia on immunity; rather, it highlights the immense complexity of the perioperative environment. The inconclusive results from large-scale clinical trials, such as VAPOR-C [43], likely do not mean there is no biological difference between anesthetic agents. Instead, it suggests that the effect of a single variable (the choice of anesthetic) tends to be "drowned out" by the significant "clinical noise." Factors such as the heterogeneity of tumor biology, varying degrees of surgical trauma, different baseline immune statuses among patients, and other postoperative interventions collectively exert a powerful impact on the final outcome, making the more subtle effects of anesthetic choice difficult to detect statistically. Therefore, the failure to find a single "magic bullet" prompts a paradigm shift: from a reductionist "drug A versus drug B" approach to a holistic one aimed at actively creating the most optimal physiological perioperative environment for immune function. Logically, if a single intervention is not robust enough to overcome the immunosuppressive storm caused by surgery, then a combination of several interventions targeting different pathological pathways simultaneously will have a much greater chance of success.

The proposed multimodal strategy is centered on the scientific synergy between two main pillars: propofol-based total intravenous anesthesia (TIVA) and regional anesthesia. Both work through different yet complementary mechanisms to protect the immune system. Propofol-based TIVA acts as a "direct protective shield" at the cellular level. Preclinical evidence consistently shows that propofol directly preserves the function of crucial immune cells; it maintains the cytotoxicity of natural killer (NK) cells, preserves a Th1/Th2 cytokine balance that favors anti-tumor immunity, and has anti-inflammatory properties by suppressing signaling pathways like NF-κB [18, 38]. On the other hand, regional anesthesia (such as epidural or paravertebral blocks) acts as an "indirect blocking fortress." By blocking afferent nerve signals (pain and stress signals) from the surgical site from reaching the central nervous system, this technique effectively prevents the activation of the HPA axis and the sympathetic nervous system [19]. The result is a drastic reduction in the release of immunosuppressive stress hormones (cortisol and catecholamines), thereby mitigating the systemic "assault" on the immune system. This synergy is powerful: regional anesthesia reduces the overall stress storm, while propofol protects the immune cells from the residual stress mediators that may still be present, creating a layered defense that is far more formidable than what either technique could offer alone.

Immune protection does not end when the patient leaves the operating room; the early postoperative period (the first 24-72 hours) is when the immune system is most vulnerable. This is where the third pillar of this strategy comes into play: multimodal analgesia to minimize opioid use. A key benefit of regional anesthesia is its ability to significantly reduce the need for opioids, and this effect must be continued postoperatively. By using a combination of non-opioid analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs, e.g., ketorolac) and paracetamol, pain can be managed effectively while avoiding high doses of opioids (like morphine) which are known to have potent immunosuppressive effects by suppressing the function of NK cells and lymphocytes [40, 45]. This "bundled" approach combining TIVA, regional anesthesia, and opioid-sparing analgesia—reflects a broader philosophy in modern perioperative medicine, such as the *Enhanced Recovery After Surgery* (ERAS) protocols. It is no longer about choosing one drug, but about designing a comprehensive perioperative protocol. By targeting multiple pathological pathways simultaneously direct cellular protection, systemic stress response blockade, and avoidance of additional immunosuppressive drugs this holistic strategy offers a more robust and potentially more effective approach to safeguarding the immune defenses of cancer patients during the most critical period of their treatment journey.

The field of onco-anesthesia is rapidly evolving, yet critical questions remain. Future research must move beyond comparing single agents and instead evaluate bundled, multimodal immunoprotective protocols. Furthermore, studies need to be tailored to specific cancer types, as the immunobiology of breast cancer, for instance, differs significantly from that of pancreatic or lung cancer. A "one-size-fits-all" approach is unlikely to succeed. A crucial next step is the integration of robust biological endpoints into future RCTs. Instead of relying solely on the long-term and often noisy outcome of cancer recurrence, trials should

measure perioperative changes in specific immune cell function (e.g., NK cell cytotoxicity assays), circulating tumor DNA, and inflammatory biomarkers [3, 46]. Linking an anesthetic technique to a measurable, short-term biological effect will provide much-needed mechanistic validation and help identify which patient populations are most likely to benefit from a specific immunomodulatory anesthetic approach

CONCLUSION

The perioperative period represents a profound immunological challenge for patients undergoing cancer surgery. The evidence synthesized in this review strongly indicates that anesthetic and analgesic techniques are not passive bystanders but are, in fact, significant modulators of the host's immune defense against residual malignant cells. A consistent pattern has emerged from a vast body of preclinical research: volatile anesthetics and high-dose opioids tend to create a pro-tumorigenic milieu by suppressing key anti-cancer effector cells, such as NK and cytotoxic T lymphocytes, while promoting immunosuppressive cells like Tregs. In contrast, propofol-based total intravenous anesthesia (TIVA) and regional anesthetic techniques that spare opioids appear to preserve or enhance these vital immune functions. While the translation of these compelling biological findings into definitive clinical outcomes in large randomized trials has been challenging and often inconclusive, this does not invalidate the underlying science. Rather, it underscores the multifactorial nature of cancer recurrence and suggests that a single intervention is unlikely to be a panacea. Therefore, the most rational path forward is a paradigm shift away from a simple "agent vs. agent" debate towards the adoption of a multimodal immunoprotective strategy. This holistic approach, which combines propofol-based TIVA, regional anesthesia, and opioid-sparing multimodal analgesia, targets multiple arms of the perioperative immunosuppressive cascade simultaneously. Future research must focus on validating these bundled strategies in well-designed clinical trials that are stratified by cancer type and incorporate robust biological endpoints alongside long-term recurrence data. Measuring direct changes in immune cell function will be critical to bridging the gap between mechanism and clinical outcome. By embracing an immunologically-conscious approach to perioperative care, anesthesiologists are uniquely positioned to move beyond their traditional roles and become active participants in improving long-term cancer survival.

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