Anaesthesia affects immune function and impact on long-term cancer prognosis: a review

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Abstract. The effect of anaesthesia on the immune system has been the focus of research over the last decade, particularly in cancer patients. Anaesthetic procedures, which are essential in surgical management, can affect the body's immune response through direct and indirect mechanisms. Anti-tumour immunity is compromised by local and systemic immunosuppression, which may ultimately contribute to tumor survival and the long-term prognosis of cancer patients. This article aims to identify and evaluate the evidence on the effects of anaesthesia-induced immunosuppression, to determine the mechanisms by which anaesthesia affects the immune system during surgery, and the implications for cancer proliferation, metastasis, and recurrence. In addition, this article also evaluates the type of anaesthesia and explores the relationship between immune modulation during anaesthesia and long-term survival. This article uses the literature review method with the PICO and JBI tools analysis approach of 15 journals found through database searches on PubMed, ScienceDirect, and EBSCO. The study population is cancer patients, and the research reviewed provides an overview of research into the biological pathways involved, the effects of immunosuppression associated with anaesthesia, and the potential for anaesthetic interventions to minimize the negative impact on cancer prognosis. The review showed a significant association between the type of anaesthesia and modulation of the immune system and its impact on long-term survival. Conclusions from the literature highlight the importance of the appropriate choice of anaesthetic to improve clinical outcomes and long-term survival in cancer patients.

1 Introduction

The genetic disease often referred to as cancer is caused by uncontrolled cell proliferation that spreads wildly throughout the body. Cancer is known as a malignant tumor that continues to evolve, competing with fibroblasts, staying away from immune cells, and absorbing pro-tumor components to produce angiogenesis products and normalize acid conditions in the body [1]. Clinical manifestations include an abnormal lump or mass, significant weight loss, prolonged fatigue, pain, and decreased function of certain organs, depending on the location and variety of cancer [2]. In 2020, the World Health Organization projects 396,914 instances

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of cancer and 234,511 deaths in Indonesia [3]. Worldwide, this deadly disease kills up to 10 million people every year, requiring curative therapies such as immunotherapy, chemotherapy, and radiotherapy, and even surgery to treat it [4].

Gene expression and tumor cell behavior are altered by surgery, which also modifies the surrounding tumor microenvironment. The body's reaction to cancer is significantly influenced by inflammation, with both intrinsic and extrinsic inflammation playing a part in the development of tumors. Extrinsic inflammation includes factors such as infection, smoking, and obesity, while intrinsic inflammation is triggered by mutases that promote cancer cell proliferation [5]. The naturally occurring killer (NK), polymorphonuclear, and lymphocytic cells are components of the body's immune system that fight cancer and preserve tissue homeostasis [6-8]. This creates an environment that is less supportive of the body's own immune system and promotes metastatic spread [9].

Immune response and blood clotting are also important in cancer progression, as tumors produce substances similar to TFs that cause blood clotting and increase blood clotting risk [10]. Homeostatic thrombosis also helps cancer cells hide from immune surveillance and supports their colonization of new tissue [11]. Some anaesthetics, particularly those used during surgery, affect the immune response and may have a long-term impact on cancer outcomes. A few studies have indicated that regional anaesthesia tends to limit the production of stress hormones and inhibit metastasis, while anaesthetics such as propofol have potential antitumor benefits by controlling the expression of immune response-related mRNAs [12], [13], [14].

A previous review by Brogi E. and Forfori F. (2022) outlined those neuroendocrine responses, whose dysregulation occurs with the creation of immunosuppression or decreased immune system, can directly affect cancer cell proliferation and metastasis. The stimulation of the hypothalamic-pituitary-adrenal and the sympathetic nervous system during anesthesia is a combination of surgical and hormonal responses that can have a major impact on immune function and cancer outcome. Anaesthetic agents can alter the immune system's response to surgical stress. These drugs affect cortisol levels, which depress the immune system through the HPA axis [14].

Watson et al. (2021) reviewed the interaction of anesthetic medications and chemotherapy medicines in the context of cancer. The study concentrated on the pharmacological element rather than the direct effects on cancer patients' immunity and long-term prognosis. Furthermore, Alexa et al. (2024) conducted a review study on the influence of anesthetic agents on neutrophils and their potential in onco-anesthesia regulation. The study focuses on the effects of specific anesthetic agents but is limited to perioperative effects and does not provide a picture of long-term clinical outcomes. The author's review will provide a new perspective by focusing on immunological impacts, such as diverse immune-related cell biological molecules immunoadjuvants during the operating phase, and the long-term prognostic influence of anesthesia on cancer patients, in addition to drug interactions.

Support for the immune system in the perioperative situation can be achieved by adequate anaesthetic recovery and more tailored anesthesia procedures, which have been demonstrated to lower the risk of immunosuppression and enhance clinical outcomes in patients [15], [16]. This article intends to give a complete evaluation of the literature that can be used as a reference or review of the latest evidence-based theories relating to the effects of anaesthesia on immune function and cancer prognosis. Hopefully, this article will provide insight and understanding of how this approach may improve clinical outcomes and reduce morbidity and mortality in cancer patients.

2 Methods

Searches for this review were undertaken in EBSCO, Science Direct, and PubMed until September 2024 using keywords: ('Anesthesia' [All Field] AND 'Cancer' [All Field]. OR, 'A general anesthesia for Cancer' [Network Terms] OR 'General Anesthesiology for Cancer Recurrence' (All Sections) OR, ('Regional Anesthesia for Cancer Recurrence' [All Fields]. OR 'Onco-anesthesia for Cancer Surgery' (All Areas) OR ('immunosuppressive' [All Areas] AND 'anesthesia' [Palliative Care] OR 'immunotherapy' [MESH term]) OR ('anesthesia techniques' [All Areas] AND 'cancer surgery' [All Areas]). To discover relevant trials, we searched journals in the above electronic databases. The search strategy concentrated on randomized controlled experiments and prospective research on humans published in English.

The review looked solely at publications published in the recent five years (September 2018 to September 2024). We omitted papers in other languages, reviews of systems, meta-analyses, case studies, individual viewpoint articles, and appeals to the editor. Both titles and abstracts were evaluated in the first round based on the requirements for inclusion and exclusion. The article looked at studies involving cancer patients and the effects of anesthesia on the immune response and cancer prognosis. The qualifying criteria were solely applied to the primary study.

The screening procedure involved two stages, a preliminary evaluation by the abstracts and titles according to inclusion and exclusion criteria, subsequent to a full-text review to determine final eligibility. The analysis was conducted using the PICO approach to ensure that only studies that were relevant to cancer patients undergoing anaesthesia interventions and their impact on immune system function and long-term cancer outcomes were included in this review. The primary outcomes assessed were the response of immune system function to anaesthetic exposure and long-term cancer prognosis. The complex interactions between anaesthesia and cancer biology were also examined, with mechanistic studies focusing on immune cell function, cytokine production, hypoxia-inducible factors, neuroendocrine responses, inflammatory pathways, and gene expression, in order to clarify how anaesthesia affects the immune response in the context of cancer. The study's quality was evaluated utilizing the Joanna Briggs Institute (JBI) Critical Appraisal Tools to obtain RCT Potential of Bias Assessment, which was utilized to evaluate the quality of the methodology of each randomized trial.

3 Results

Our literature search yielded 1650 studies, but only 15 matched the inclusion requirements. The PRISMA standards were used to screen and select these studies (Figure 1). Table 1 summarizes the features of these trials. The majority of these studies examined the role of anesthesiology in cancer patients, specifically with regard to long-term results and immune system impacts. The association between the type of anesthetic used and post-operative alterations in immunological markers, which may impact the likelihood of malignancy relapse or metastatic resistance, is among the most significant findings.

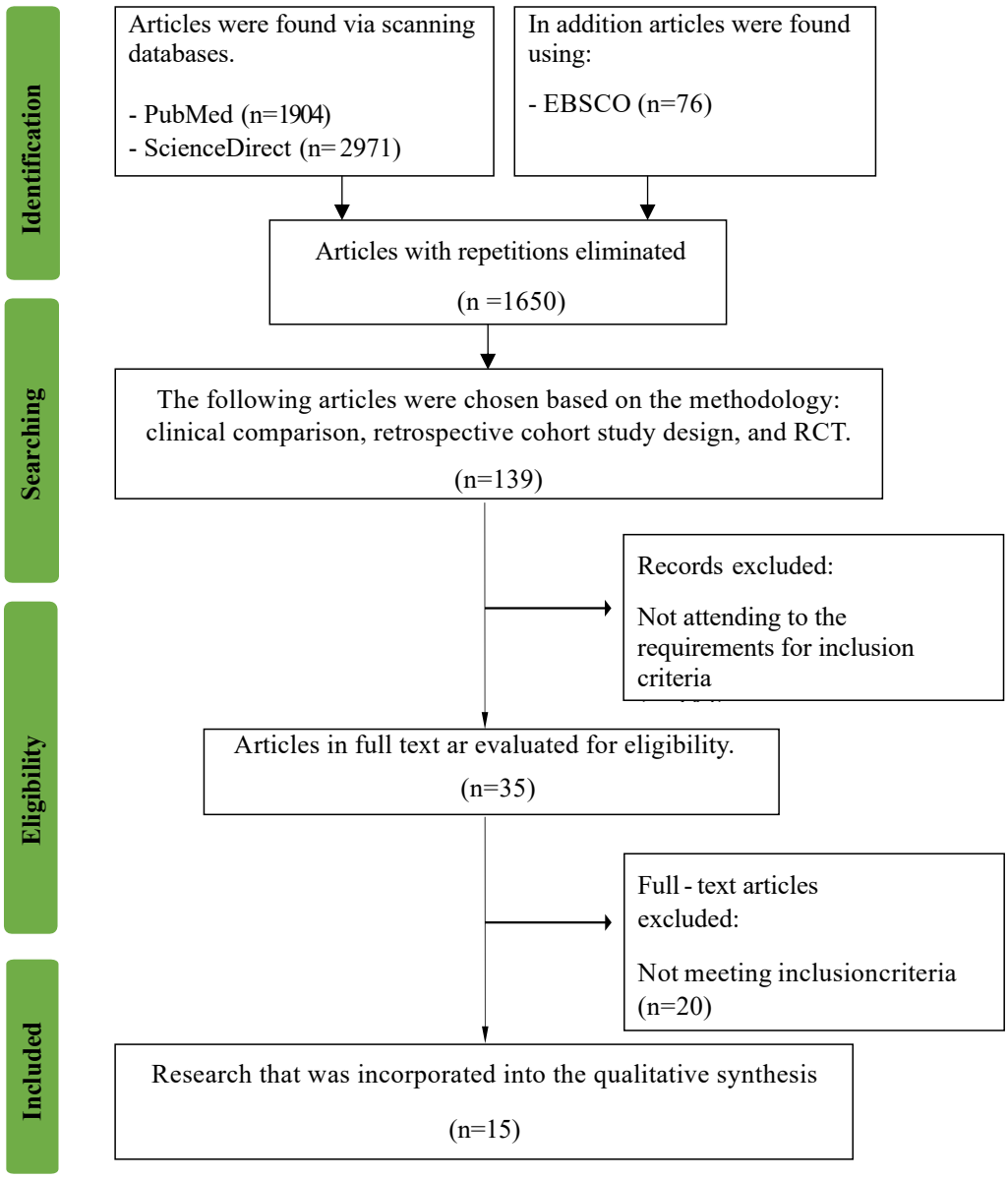

Fig 1. PRISMA Schema

Table 1. Literature Review

Purpose	Authors	Study design	Group (n)	Control Group	Tools	Primary Outcome
Analyze the complex relationship between anesthetic technique and cancer recurrence	Brogi E. and Forfori F.	Original article	N/A	N/A	Overview during operation	This article presents findings on the interaction between anesthetic technique, immune response, and cancer recurrence, selecting appropriate anesthetic for cancer patients requires significant attention.
Investigate the impact of anesthetic methods on afterward cancer survival and assess the feasibility of performing a large randomized controlled trial.	Dubowitz et al.	RCT with comparative clinical	Cancer patient (n=146)		DASI dan QoL, POMS, and Clevein-Dindo.	The successful recruitment rate was 67.3% with 146 patients enrolled. With an overall compliance rate of 99.3%, Patient characteristics and surgical complications were similar among the treatment groups.
Compare epidural RA vs. GA in the outcomes of ovarian cancer surgery. Evaluate analgesic effects, safety and recovery benefits, and investigate post-anesthesia cortisol and C-reactive protein levels in the two groups.	Zhong et al.	Comparative clinical	RA Epidural (n=158)	GA TIVA (n=140)	RA Epidural, GA TIVA, Visual Analog Scale (VAS), and Aldrete Score	Epidural RA had a better analgesic effect and fewer adverse effects. The epidural RA group had lower VAS scores and faster recovery time. The COR and CRP levels got substantially reduced in the epidural RA category. Neither of the groups had comparable one-year quality of life.
Compare TIVA vs. sevoflurane anesthesia	Yan T. et al.	RCT with comparative	TIVA (n=40)	Sevoflurane (n=40	Kit ELISA VEGF-C dan TGF-	Sevoflurane raised postoperative VEGF-C levels, whereas TIVA

in breast cancer surgery outcomes, analyze VEGF-C and TGF-β release, and examine the effect of angiogenic factors on proliferation and quality of life.		clinical		)	β	remained steady. TGF-β levels were not significantly different between the Sevoflurane nor TIVA groups. TIVA inhibited angiogenesis, while sevoflurane enhanced it. There was no substantial difference in quality of life across the two groups.
Evaluation of the impact of the anesthetic type on the outcome of gastric cancer surgery, as well as a comparison of QoL outcomes between TIVA and inhalation therapies.	Wu W. et al.	Retrospective cohort study with comparative clinical	TIVA (n=323)	Inhalasi (n=645)	TIVA and inhalation	Anesthesia type has no impact on quality of life during procedures for cancer. However, TIVA anesthesia may increase long-term survival in cancer of the abdomen. Propofol in TIVA inactivates oncogenes and suppresses tumor angiogenesis.
Inspection of the impact of general and local anesthesia on serum malignant behavior in HCC patients.	Shi Y. et al.	RCT with comparative clinical	GA (n=14)	LA (n=11)	Transwell Test, Kit CCK-8, and ELISA.	Serum GA promotes HepG2 invasion, migration and proliferation. Serum GA has higher pro-inflammatory cytokines and lower lymphokines. GA may affect metastasis and prognosis of HCC through serum changes.
The study looks at how anesthesia affects cancer relapse and metastasis, as well as the impact of anesthetic procedures and drugs	Montejano J. et al.	Narrative Review	N/A	N/A	Intraperitoneal chemotherapy during cytoreductive surgery, and a literature database with keywords related to	Anesthesia's impact on cancer growth and spread is unclear. There are no definitive recommendations for the choice of anesthesia. In particular, regional anesthesia has been discussed for its potential to reduce cancer recurrence by limiting the use

on patient outcomes.					anesthesia and cancer.	of systemic opioids, which are thought to promote tumor progression.
Examine the impact of propofol alongside sevoflurane anesthesia on colon cancer outcomes, including postoperative neutrophil/lymphocyte ratio and clinical results.	Lee S. et al.	Retrospective cohort study with comparative clinical	Propofol (n=84)	Sevoflurane (n=90)	GA propofol and Sevoflurane	The type of anesthesia did not affect clinical outcomes. Propofol showed a lower postoperative NLR, but no clinical association. There was no substantial variation in the standard of life among various kinds of anesthesia.
Examine the impact of anesthesia techniques on urethral carcinoma recurrence and analyze factors affecting prognosis after transurethral resection.	Xue R. et al.	Retrospective cohort study with comparative clinical	GA (n=280)	RA (n=280)	GA dan RA Epidural	Anesthesia technique was not an independent factor and did not affect the recurrence of urethral cancer. The epidural group had longer QoL. General anesthesia provides comfort and relaxation during surgery.
Examine how anesthetic influences immunological activity in carcinoma of the breast patients, particularly NK cell cytotoxicity.	Cho J. et al.	RCT	Propofol-Ketorolac (n=25)	Sevoflurane-Fentanyl (n=25)	NK Cell Cytotoxicity (NKCC) and ELISA	The propofol-ketorolac group increased postoperative NK cell cytotoxicity. Sevoflurane fentanyl may decrease postoperative NK cell cytotoxicity. In general, propofol anesthesia may reduce perioperative immunosuppression.
Evaluate the impact of opioids on inflammatory responses during surgery, evaluate cytokine release and	Titon O. et al.	RCT	Opioid-Inclusive (n=23)	Opioid-Free (n=22)	Test in vitro	Aesthetics affect immunomodulation and cancer recurrence. Opioids inhibit the immune system, while local anesthetics can reduce cancer recurrence.

changes in tumor angiogenesis, and analyze systemic inflammatory and immunological patterns in patients.						
Compare the effects of propofol TIVA anesthesia with desflurane on surgical outcomes for osteosarcoma, to assess the relationship between anesthesia type and clinical outcomes, and to identify potential risk factors for mortality.	Sun Ting-Yi et al.	Retrospective cohort study with comparative clinical	Propofol (n=85)	Desflurane (n=76)	TIVA Propofol dan volatile desflurane	Propofol-based TIVA enhances survival and lowers the chance of cancer returning and spreading in comparison to defloration. The TIVA group experienced decreased overall and cancer-specific death rates.
Compare the effects of TIVA and VA on prostate cancer recurrence with colloid input and prostate specific antigen (PSA) levels.	Kim N. et al.	RCT	TIVA (n=64)	Volatile (n=64)	N/A	At all time points after RALP, both the TIVA and VA groups had equivalent biochemical relapse-free survival rates, and their impacts on cancer prognosis were comparable.
This page summarizes the effects of anesthesia on immune responses and malignancies, in addition to clinical	Xia S. et al.	Retrospective	N/A	N/A	Ketamin dan NSAID	Surgery increases angiogenesis, suppresses immunity, and affects clinical outcomes. Anesthetics such as TIVA and propofol showed variable effects on cancer outcomes.

data on cancer-related mortality and relapse.						
The study contrasts the impacts of propofol and sevoflurane on the function of regulatory T cells, evaluates the immunosuppressive effects of anesthesia following breast cancer surgery, and assesses the association with cancer returning.	Oh C. et al.	RCT	Propofol (n=99)	Sevoflurane (n=102)	Bispectrality index, Flow cytometry dan uji immunosorbent	Cytokine levels showed no difference between groups, propofol and sevoflurane. NLR was found to be within normal limits, and there was no difference in immune function between the two groups.

4 Discussions

Adaptive immune responses are significant because they involve the conversion of B cell lymphocytes towards circulating cells, which can produce particular antibodies against certain infections. Antibodies produced by plasma cells neutralize pathogens, which can be inhibited or targeted for destruction by other immune components. When B cells recognize a specific antigen, they become activated and differentiate, resulting in the production of plasma cells and antibodies to fight the infection [17]. The T cell receptor (TCR) must activate effector T cells for the immune system to respond more specifically. T cells generate a cascade of signals by activating intracellular signaling proteins and responding to antigenic peptides presented by MHC molecules on target cells recognized by the TCR. These signals activate T cells, which can either produce deadly compounds or modulate immunological responses. TCR activation that is precise and effective guarantees a focused response while minimizing the negative effects on healthy tissues [18].

Numerous biological components, such as lymphocytes, mast cells, NK cells, and polymorphonuclear leukocytes, mediate the immune system. T cells, which are immune cells, grow in the thymus gland, and B-cells are what grow in the marrow of the spine to become lymphocytes. Each lymphocyte uses its B-cell receptor (BCR) and TCR on the cell surface to recognize particular antigens. When B cells develop into plasma cells, they generate antibodies that can kill infections and improve macrophage phagocytosis. They also manufacture antigens and release T-cell cytokines [7]. Furthermore, effector T cells use signaling proteins to activate target cells. NK cells generate cytokines such as IFN-γ, IL-1, and TNF-α, which cause inflammatory processes and attract antibodies into the infection site [8]. Polymorphonuclear leukocytes containing neutrophil, eosinophil, and basophil components chemotaxis via interleukin-8 (IL-8) chemokine signaling as a first response to

infection. This allows them to rapidly eliminate infections by phagocytizing them, creating reactive oxygen species (ROS), and building extracellular neutrophil traps (NETs). Macrophages remove apoptotic neutrophils. To avoid tissue damage from chronic inflammation, these diseases must be managed [7].

Furthermore, the coagulation system helps to maintain bodily homeostasis [19]. Hemostasis is a natural mechanism that stops bleeding by causing vascular spasms, activating the clotting cascade, releasing thrombin, and initiating fibrinolysis [11]. The interaction factors, such thrombin, may trigger immune cells and increase the release of inflammatory cytokines [20]. Cancer patients frequently develop hypercoagulability, which leads to a risk of thrombosis [10]. Tumors emit chemicals like the Tissue Factor (TF), which activate the coagulation system. Some coagulation components, including thrombin and fibrinogen, have the potential to promote the proliferation of tumor cells, infiltrate other tissues, produce metastases, and alter the body's response to surgery or anesthesia [21].

Platelets are an important component of the host's innate immune system in the circulation because they coordinate both adaptive immunity and adaptive antimicrobial defense. Platelet activation leads to a release of growth-promoting angiogenic agents, cytokines, and chemokines. This molecule, once produced, regulates inflammatory chemotaxis and vasomotor function. These processes are essential for angiogenesis, which rebuilds damaged blood vessel walls [11]. Immunotherapy and/or chemotherapy can affect platelet counts throughout treatment, particularly by reducing platelet synthesis in the bone marrow or generating an imbalance of platelets in circulation [22].

Cancer immunosuppressive mechanisms are mediated by complex pathophysiological mediators, including an increase in regulatory T cells (Treg) that reduce the effectiveness of anti-tumor immune systems by releasing cytokines that suppress inflammation Instances are IL-10 and the expression of TGF-β. Tregs typically regulate immune responses and avoid autoimmunity. An increase in Treg suppresses cytotoxic T cells (cytotoxic T cells), rendering them incapable of killing cancer cells (16). Another mediator, NK cells, known to be responsible for identifying and destroying tumor cells, also get inhibited. Tumors produce ligands such as PD-L1, that interact to PD-1 on NK cell surfaces, leading in the production about pro-tumor mediators including Interleukin-6 (IL-6) and IL-10. This hinders T lymphocytes from recognizing tumor cells and promotes the tumor a microenvironment (17). These cytokine modulators work synergistically to block the growth and maturation of effector T and NK cells, resulting in a more suppressive tumor microenvironment in which cancer cells can grow freely [23].

A variety of anesthetics can significantly impact the physiological stress reactivity mediated by the HPA axis. Certain anesthetics, for example, can decrease the metabolism of stress hormones such as hormone cortisol and catecholamines, resulting in a reduction in total tension during surgery. This modulation process not only affects the patient's perception of pain and discomfort, but also creates a more stable and balanced physiological state for the patient during the perioperative period. By managing and minimizing the stress response, the appropriate use of anesthesia improves clinical outcomes and accelerates patient recovery after surgery. This highlights the importance of selecting the appropriate type of anesthesia to minimize the negative effects of physiological stress and improve the overall patient experience in a medical context [24].

The sympathetic nervous system plays a crucial role in activating neural signaling pathways that support the HPA axis. Stressors including surgical trauma, cold, and patient anxiety can activate these pathways and release catecholamines like adrenaline and norepinephrine to prepare the body for potential threats. Other stress-related chemicals elevate pulse, cardiac output, and activate this HPA axis, leading to a positive feedback cycle that enhances one's stress response [25].

Anesthetics affect neutrophil numbers and function, inflammation, immune surveillance, and perioperative outcomes. Anesthetics also indirectly modulate the host immune response, which may affect neutrophil activity. This modulation can alter how neutrophils respond to cancer cells and infections, potentially affecting the patient's clinical outcome. Direct interference with cancer cell biology by anesthetics for example propofol has been demonstrated to increase the action of certain chemotherapeutic drugs. This may indirectly impair neutrophil function by affecting the tumor microenvironment. The Neutrophil-Lymphocyte Ratio (NLR) is a promising biomarker for evaluating the immunological state of surgical patients. The occurrence of changes in NLR during the perioperative period may reflect the effect of anesthetics on neutrophil activity and the overall immune response [12].

Comparative clinical by Lee S. et al. (2022) observed how the anesthetic reactions to propofol with sevoflurane had no impact on colorectal cancer outcomes. Propofol caused a significant inflammatory response with reduced postoperative NLR on days 2 and 5, The means of variations are 0.71 ($p < 0.001$) and 0.52 ($p < 0.001$), accordingly. However, there was no clinical correlation. In general, there was no substantial difference in quality of life across anesthetic kinds [26]. Wu W. et al. (2021) found an absence of significance in survival rates among both TIVA and inhalation groups ($P = 0.566$). The results remained constant after propensity score matching ($P = 0.679$) [27].

The pathway of HPA initiates a hormonal cascade that secretes several hormones with a major impact on the organism. In addition to cortisol, hormones such as catecholamines and glucocorticoids are released, all of which play a role in modulating various physiological functions. One important effect of these hormones is their influence on the immune system. Research by Brogi E and Forfori F (2022) showed that increased levels of cortisol and other stress hormones can lead to a downregulation of NK cell activation and cytotoxic T cell function. This decrease is critical, as these cells represent a crucial part of long-term tumor investigations, and control, affecting long-term postoperative clinical outcomes, including the risk of infection and cancer progression [14].

Another study by Chu J. et al (2017) describes the results of a comparison between propofol-ketorolac groups, which increased postoperative NK cell cytotoxicity, while sevoflurane fentanyl can reduce postoperative NK cell cytotoxicity. In general, propofol anesthesia can reduce perioperative immunosuppression ($p = 0.082$). Changes in NKCC over time differed considerably among the groups ($P = 0.048$). One participant in the sevoflurane-fentanyl group had a relapse of cancer in the opposite breast, but no metastases were detected within the group [28]. The immunosuppressive changes of propofol and sevoflurane against Treg cells were also investigated by Oh C. et al. (2018), with the result that there were no differences between groups in Treg cells, NK cells, cytotoxic T sets, cytokines, and NLR. The effect of anesthesia on immune activity during surgery is reported to be minimal [29].

Shi Y. et al. (2021) used cell culture transwell assays, CCK-8 kit and enzyme-linked immunosorbent analyze (ELISA) to quantify the impact of general and local anesthesia on the behavior of hepatocellular carcinoma (HCC) undergoing Radiofrequency Ablation (RFA). HepG2 cells grown via afterward serum of patients obtaining a general anesthesia demonstrated significant expansion, movement, and spread in contrast to prior-to-surgery serum. Following serum following general anesthesia patients presented significantly raised concentrations of cytokines that encourage inflammation and a decrease of lymphokines that are when compared to the prior serum [30].

Exploration of anti-cancer effects through direct toxicity stimulation to overcome cancer therapy resistance and analysis of the selection of immunostimulatory onco-anesthesia agents for good clinical outcomes were described by Carnet Le Provost K. et al. (2024) reviewed Dexmedetomidine shows potential in cancer therapy through immunostimulant and anti-tumor effects. Dexmedetomidine acts directly on malignant cells and shows anti-cancer effects by reducing migration, stopping proliferation and stimulating anti-tumor immunity,

reducing inflammatory pain and glucocorticoid stress during major surgery, promoting anti-tumor immune responses, and infiltrating the tumor microenvironment. Dexmedetomidine has a dual role in inducing tumorigenic pathways and cytotoxic responses [31].

Trauma associated with surgery not only affects the body physically but also triggers complex biological responses, one of which is stimulation over the HPA axis [32]. The hypothalamus releases corticotropin hormone (CRH), preparing the body for stress. CRH stimulates the adrenal glands to release the hormone adrenocorticotropic (ACTH). The substance stimulates those glands to produce cortisol, the basic stress hormone. Cortisol has several functions, including the regulation of metabolism and the immune response, which is particularly important in the context of postoperative recovery [33].

Propofol is a medium to modulate genetic signaling pathways that affect the carcinogenesis process. These signaling pathways include protein regulation, metastatic enzymes, angiogenesis factors, and epigenetic modifications to minimize cancer cell recurrence. Hypoxia-induced HIF-1α protein synthesis is suppressed by Propofol, resulting in reduced cancer cell survival. Propofol inhibits mRNA expression of MMP-2 (matrix metalloproteinases) and the p38 MAPK process, that influences cancer cell growth, gene motility, and survival. This reduces the likelihood of cancer cells spreading. Propofol inhibits the NF-kB pathway, potentially reducing cancer cell inflammatory responses such as proliferation and metastasis. Propofol modulates miRNA-controlled gene regulation by upregulating miRNAs as tumor suppressors and inhibiting miRNAs as oncogenes. Propofol also inhibits acetyl histones, which influence gene expression in cancer development [14], [34].

Propofol reduces S100A4 expression in endothelial cells and restricts Vascular Endothelial Growth Factor (VEGF). Yan T. et al. (2018) found that VEGF-C levels increased post-operatively in the Sevoflurane group from 105 pg./mL to 174 pg./mL (P=0.009). The TIVA group experienced minor changes in VEGF-C levels, ranging from 134 to 140 pg/mL (P=0.402). TGF-β amounts were not substantially different between the sevoflurane nor TIVA regimens. TIVA reduced angiogenesis, whereas sevoflurane promoted it. The relapse-free survival rate was not statistically different across either of the groups [35].

On the different view, study by Zhong et al. (2019) research suggests that combining epidural anesthesia with epidural analgesia may lead to enhanced recovery outcomes with fewer complications for patients undergoing progressive tumor removal surgery compared to general anesthesia plus intravenous anesthesia. The study also examined post-anesthesia cortisol and levels of C-reactivity in two groups. Following anesthesia, both groups had elevated levels of cortisol (COR) and C-reactivity protein (CRP). However, the epidural group had considerably lesser amounts in the general anesthesia mixed with analgesia control at 24 hours ($P < 0.05$) [36].

Cancer recurrence rates were also studied by Xue R et al (2022), who discovered that anesthesia in the region is related to decreased relapse rates because it may reduce inflammatory responses and surgical stress, which may influence tumor recurrence, compared with general anesthesia [37]. Other regional techniques on cancer recurrence have also been described in a study by Montejano J et al (20-21), which described the potential of regional anesthesia to reduce cancer recurrence by limiting the use of systemic opioids, which are thought to promote tumor progression [38]. The effects of opioids on proliferation, metastasis and recurrence rates in cancer patients were also observed by Titon O. et al. (2024), with the result that anesthesia can influence tumor progression, with a significant decrease in IL-12 levels and a correlation between IL-12 and TNF found in the opioid-free group [39].

Other findings by Alexa L. et al. (2024) showed that intravenous lidocaine, due to its anti-inflammatory properties, has shown promise in reducing tumor proliferation and improving the efficacy of chemotherapy, which may benefit postoperative cancer patients. TIVA agents, notably propofol, have been linked to enhanced overall and disease-free survival rates in

various malignancies, including colorectal cancer [12]. The authors propose that the anesthetic approach used may impact long-term clinical outcomes and cancer prognosis.

Dubowitz et al. (2021) used the DASI instrument beginning at baseline and afterwards day 30 to assess the impact of anesthetic method on physical recovery. The study found that both intervention groups had comparable during surgery patient features and postoperative complications, indicating that the kind of anesthesia, which dates utilized did not significantly influence postoperative outcomes [40]. Another finding by Kim N. et al (2020) comparing biochemical recurrence after RALP showed that TIVA and sevoflurane had comparable effects on oncological outcomes. The results of the input colloid test ($P = 0.011$), PSA ($P = 0.006$) [41].

Health care workers' understanding of the potential impact of anesthesia rules on the return of cancer survivors is a significant consequence that deserves specific consideration. This understanding and/or knowledge will allow for more informed decision-making regarding anesthesia during surgical procedures and ultimately achieve better clinical outcomes. Brogi E. and Forfori F. (2022) have also reported that it is imperative for multidisciplinary collaboration for an oncologist, an Anesthesiologists and an Oncologist surgeon collaborate to produce procedures and/or guidelines that address the influence of anesthesia upon recurrences of cancer [14].

Research investigations are required to assess the impact of anesthetics on long-term cancer survival. In short, this paper underlines the importance of doing randomized controlled trials, longitudinal studies, comparative effectiveness research, multi-center trials, and mechanistic investigations in order to clarify the role of anesthesia on long-term cancer survival. This trial is critical for generating evidence-based guidelines to enhance patient outcomes in cancer surgery. Trials that focus on certain types of cancer can generate more significant results because the impact of anesthesia varies greatly depending on the specific kind of cancer. This tailored strategy can assist to elucidate the differences in how anesthetic affects various tumors.

5 Conclusion

This literature review presents compelling evidence about the relationship between anesthetic, immunological function, and cancer prognosis. The existence of consistent findings in various literature suggests that the administration strategies of anesthesia techniques, whether general, regional, or local, have varying effects on immunosuppressive effects and are oriented towards clinical outcomes related to cancer patients' standard of life, thus decreasing recurrence and mortality rates.

An anesthetic, especially during cancer surgery, has a substantial impact on the immune response. Some types of anesthetics, such as propofol and lidocaine, have been shown to lessen immunosuppression when compared to more immunosuppressive anesthesia, such as sevoflurane. Comparative research on the effects of anesthesia such as propofol and sevoflurane in cancer patients reveals significant differences in postoperative inflammatory responses and NLR ratio changes, but inadequate significant clinical correlation with survival rates has been established.

Clinically, selecting proper procedures and types of anesthetics has the potential to improve cancer patients' quality of life, reduce their chance of recurrence, and cut mortality rates. Although these findings support the use of specific anesthesia regimens to improve clinical outcomes, more study is needed to comprehend the inherent mechanisms of anesthetic agent-immune system interactions in distinct forms of cancer. More research will be required to determine the optimal the dosage and timing of administration to minimize the risk of immunosuppression while maintaining adequate pain management. Various variations of cancer are being examined, as well as the effects of a variety of anesthetics on distinct

immune responses. Close collaboration among surgeons, oncologists, and anesthesiologists is essential for developing safer and more effective anesthetic guidelines for cancer patients.

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