Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers: A Quality Improvement Educational Module

A DNP Project Presented to the Faculty of the
Nicole Wertheim College of Nursing and Health Sciences

Florida International University

In partial fulfillment of the requirements
For the Degree of Doctor of Nursing Practice

By

Tatiana Amaya, MSN, RN, CCRN-CSC-CMC

Supervised By

Jorge A. Valdés, DNP, CRNA, APRN, FAANA
Guillermo Garcia, MD

Approval Acknowledged: DocuSigned by: Ann Miller A986D8685093471..., DNA Program Chair

Date: 11/30/2023

Approval Acknowledged: DocuSigned by: 27267E9FF76F460..., DNP Program Director

Date: 12/1/2023

Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers: A Quality Improvement Educational Module

Abstract

Background: Current data indicates that anesthetic agents can modulate the immune system and response. The extent of anesthesia's contribution to immunosuppression and the proliferation and migration of circulating tumor cells, resulting in an increased risk of cancer metastasis, recurrence, and morbidity, is unclear. Emerging evidence suggests Sevoflurane may accelerate tumor growth and recurrence in oncology patients. Conversely, recent studies demonstrate Propofol's ability to preserve or enhance immune function. 39.5% of men and women will be diagnosed with cancer at some point in their lifetime, and over 60% of cancer patients will undergo surgery as a form of treatment. However, there are currently no standard recommendations for the anesthesia management of these patients. The three most common cancers worldwide responsible for the most deaths are breast, lung, and colorectal. Therefore, comparative studies of anesthesia modalities in these deadly cancers were analyzed to generate perioperative anesthetic management guidelines most beneficial for the surgical oncology population.

Aim: This study aims to educate anesthesia providers on the harmful effects of anesthesia modalities on cancer patients and provide evidence-based recommendations to improve clinical decision-making and patient outcomes.

Methods: The educational intervention will be conveyed by a 10-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. Once results are collected, and data synthesized, a statistical analysis of findings will reveal correlations.

Results: The findings generated positive outcomes, anesthesia provider knowledge on the harmful effects of anesthesia modalities on cancer patients was enhanced, inclination to utilize Propofol TIVA on patients with deadly cancers was increased, and overall enriched clinical decision-making. Ultimately, the Quality Improvement was able to answer to the research question.

Discussion: Further research is indicated. However, the performed QI is promising. A paradigm shift in the anesthetic management of surgical oncology patients could signify an overall reduction in cancer recurrence rates, tumor metastasis, and mortality rates, particularly in deadly cancers. Increased participant knowledge of the harmful effects of anesthesia modalities and evidence-based recommendations for these cancer patients will improve clinical decision-making and patient outcomes.

Keywords: *Cancer, recurrence, immunosuppression, tumor, tumorigenic, Anesthesia modality, techniques, Propofol-based, Sevoflurane-based, immunomodulation, Flow Cytometry*

Table of Contents

PICO

In oncology patients undergoing cancer surgery, how does using Propofol-based anesthesia compared to Sevoflurane-based anesthesia affect immunosuppression in oncology patients within the perioperative period?

Population (P): Oncology patients undergoing cancer surgery

Intervention (I): Propofol-based anesthesia

Comparison (C): Sevoflurane-based anesthesia

Outcome (O): Affect immunosuppression

Time (T): Perioperative period

Problem Identification

Factors altering patient outcomes is critical when planning to provide anesthesia for surgical oncology. *In vivo* and *in vitro* experimentation analyses reveal that anesthetic agents immunosuppress the functionality of macrophages, T-cells, and, most notably, natural killer cells after surgery.[1] Belonging to the innate immune system, natural killer (NK) cells are effector lymphocytes notoriously understood for their distinctive anti-tumorigenic ability to eliminate tumor cells.[2] NK cells are the primary effector cells against cancer and aid in restricting cancer spread and tissue damage by destroying circulating tumor cells.[1,2] Anesthesia's involvement in decreasing NK cells' cytotoxic function and proliferative effects on cancer cells warrant investigative efforts to enhance the perioperative management of surgical oncology patients.

Cancer recurrence after tumor resection is not entirely understood but heavily researched. Various hypotheses have been formulated over the years, a leading theory being increased tumor cell counts due to surgical manipulation.[2] Current data establishes that anesthetic agents, to varying degrees, can inhibit immune response. Thus, it is reasonable to hypothesize that

anesthesia can directly contribute to the proliferation of circulating tumor cells and have pro-tumorigenic effects via immune response attenuation, resulting in an augmented risk of cancer recurrence and morbidity. To effectively manage oncology patients perioperatively, investigating the immunomodulatory effects of individual anesthetic agents in the presence of circulating tumor cells is crucial to determining the best modality in tumor resection and cancer surgery.

Background

Anesthesia varies from provider to provider, most commonly, anesthesia providers utilize General Anesthesia (GA) with Sevoflurane for cancer surgery.[3] *In vivo* studies isolated immune cells and tumor-infiltrating lymphocytes via flow cytometry, staining, and assay analysis to assess the effects of Sevoflurane on immune cell counts in the presence of circulating tumor cells. In the same studies, a control group was given Propofol, and cell counts were compared. Perioperatively drawn blood samples in a randomized control trial (RCT) by Hovaguimian et al. found that the administration of Sevoflurane resulted in a 36% increase in maximal tumor cell counts in the postoperative period, and a decrease in NK cell counts in comparison to Propofol.[2] These results were consistent with a multitude of RCTs and retrospective studies.[1,2,4-9]

The immunosuppressive consequences rendered by Sevoflurane are postulated to accelerate cancerous cell migration and recurrence in oncology patients. Furthermore, another RCT revealed enhanced NK cell cytotoxic-induced effects in oncology patients who underwent surgical procedures anesthetized with Propofol instead of Sevoflurane.[4] In the presence of cancer cell BGC-823, as expected, NK cell-induced cytotoxic functions were suppressed; however, this inhibition was eradicated with Propofol's administration, and function was restored.[4] Anesthesia providers should consider these microcellular shifts in all surgical oncology patients undergoing

surgery, particularly tumor resection surgery, to preserve immune function and reduce the risk of negative outcomes.

The rate of cancer recurrence and morbidity after surgery varies depending on the type of cancer histology, diagnosis, and prognosis.[5,7] Numerous patient characteristics are additionally examined to determine treatment options and surgery. Anesthesia providers should emulate this approach to cancer surgery. Oncology is a vast and intricately complex field, and extrapolated conclusions about a single cancer type or study should not be generalized for all cancers. In this regard, anesthesia personnel should make the necessary adjustments to their anesthetic plan considering the patient *and* the cancer characteristics.

To enhance external validity, a study should incorporate a subgroup analysis of the anesthetic modality, cancer type, and surgery performed. Certain cancers are more prone to recurrence after surgical intervention. For example, at nearly 100% recurrence, glioblastoma malignancy is the highest among cancers and the most common brain tumor, with less than 5% of patients achieving a 5-year survival.[10] Due to glioblastoma's high mortality, studies investigating anesthesia's role in immunosuppression and its impact on cancer survival, recurrence, and metastasis have gained incredible attention in the research community.

Research endeavors in neurosurgical oncology revealed that patients who received total intravenous anesthesia (TIVA) using Propofol as the primary anesthetic during glioblastoma surgery, as opposed to inhaled agents, had improved survival rates and less postoperative cancer recurrence.[10] Ovarian cancer is also highly malignant, with recurrence rates up to 85% in patients after surgery.[11] Retrospective cohort studies yielded similar results, concluding that Propofol TIVA resulted in increased survival rates compared to patients who underwent elective open ovarian cancer surgery with inhaled agents.[11] The need to reduce the incidence of recurrence with

these cancers is of heightened importance, making it essential to take preventative steps in perioperative management and prevent further immunosuppression from anesthesia a priority.

Scope of Problem

The three most common cancers worldwide are breast, lung, and colorectal, accounting for approximately more than half of all new cancer diagnoses in 2020.[13] According to the National Institute of Health (NIH) and the National Cancer Institute (NCI), 39.5% of men and women will be at some point in their lifetime diagnosed with cancer. Currently, the mortality rate of cancer is more than 158 deaths per 100,000 people.[13]

Breast cancer is the most common type, making up more than 1 of every 10 new cancer diagnoses yearly.[14] Due to its silent progression, breast cancer is undeniably one of the deadliest in all oncology. It is the second most common cause of death from cancer among all women worldwide.[14] Lung cancer is the second most common cancer diagnosis in the United States. It is known to be the most diagnosed cancer globally, with the highest percentage of cancer-related deaths and accounting for 12.4% of all cancers diagnosed worldwide.[15]

Colorectal cancer is the third leading cause of cancer and the second deadliest malignancy for both men and women.[16] The incidence of new cases and mortality has not decreased over the years for people younger than 50. An increase in cancer screening and modality options could contribute to the lack of decline.[16] The statistical significance of these three cancers combined encompass nearly 60% of all cancer diagnoses.

Consequences of the Problem

Anesthesia providers caring for surgical oncology patients are responsible for selecting the most appropriate anesthetic agents to facilitate health and improve outcomes. The *Hippocratic Oath* by Hippocrates is a philosophy that states, "*primum non nocere*" in Latin,

meaning "Do no harm," is a doctrine that every healthcare provider should strive for.[12] If Bench to Bedside translational research is equivocally compelling, a paradigm shift in the anesthetic management of cancer patients could signify an overall reduction in cancer recurrence rates and morbidity among surgical oncology patients. This is of immense importance for two reasons: a standard of care would call for Propofol TIVA to be the drug of choice in surgical oncology, and a decrease in cancer rates may be observed in the long term. The consequences of not further investigating current *in vivo* and *in vitro* findings could lead to increases in cancer recurrence rates, tumor metastasis, mortality, and overall provider negligence of the *Hippocratic Oath*.

Anesthesia providers are highly educated on the pharmacological mechanisms of anesthetic agents; therefore, enhancing the knowledge of providers on the harmful effects of agents, like inhaled volatile agents, on the oncology population should nurture discussion that challenges the current mainstay of anesthesia management, improves clinical decision-making, and drives research for further investigation.

SEARCH PROCESS

The study question was structured according to PICOT. Population: Patients undergoing cancer surgery. Intervention: Propofol-based anesthesia. Comparison: Sevoflurane-based anesthesia. Outcome: affect immunosuppression in oncology patients. Time: perioperative period. Studies that satisfied the PICOT criteria were considered eligible for data inclusion. Limitations were set forth on study design and publication year to produce randomized controlled trials within the last 10 years. Language limitation to English was implemented.

The exclusion criteria removed: immunosuppressive therapy, immune and autoimmune disorders, steroid treatment, known metastasis of cancer, chemotherapy before surgery, animal studies, studies in languages where translation was insufficient for data retrieval, and

simultaneous anesthetic interventions in conjunction with Propofol- or Sevoflurane- based anesthesia that is not regional anesthesia or opioid. PubMed, MEDLINE, and Embase were searched for relevant published literature. The search was performed on September 1, 2022. Medical Subject Heading (MeSH) terms in addition to the free text were utilized for the search. After exclusion criteria, the search yielded 84 articles, of these 27 were found to be relevant. Duplicates were eliminated and 13 studies utilized for this study.

KEYWORDS: *Cancer, Propofol-based, Sevoflurane-based, recurrence, immunosuppression, tumor, tumorigenic, immunomodulation, Flow Cytometry, Cluster Differentiation*

REVIEW OF LITERATURE

The process of cancer cell proliferation and overwhelming of an immune system and permeation of tissues is known as metastasis.[17] The surgical removal and resection of cancerous tumors and metastatic lymph nodes are the pinnacles of treatment for oncology patients and are intended to be curative. Although success has been seen in primary tumors, surgical intervention does not entirely eradicate circulating tumor cells. Anesthetic agents are known to cause immunosuppression, creating a tumorigenic environment for remaining cancer cells inducing malignancy, micro-metastases, and overall recurrence in oncology patients.[17]

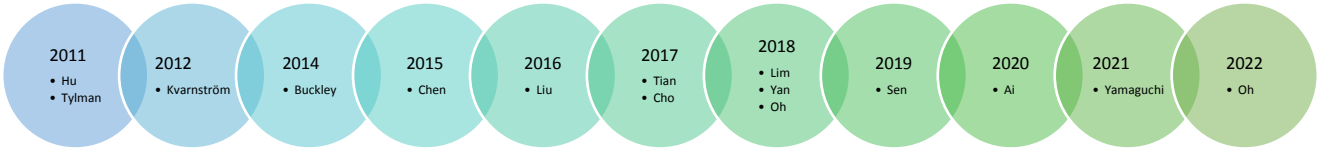
Perioperative stress stimulates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS) which releases prostaglandin E2 (PE2) and catecholamines. The release of these factors activates immunosuppressive and proinflammatory cytokines, such as interleukins (IL-4,6,8,10), vascular endothelial growth factor (VEGF), and transforming growth factor beta (TGF-β), which are further suppressed with most anesthetics, enabling metastasis and tumor angiogenesis.[1] Newer data is now supporting that regional anesthesia interrupts the HPA pathway preventing the cascade altogether.[1,8,17] Cluster of differentiation

(CD) are antigens expressed on the surface of leukocytes and immune cells when in contact with monoclonal antibodies; this process is known as immunophenotyping and can be achieved via flow cytometry.[1] $CD4^+$ and $CD8^+$ are common markers for helper, cytotoxic, regulatory T cells, NK cells, and lymphocytes. Analyzing these monitored factors during perioperative periods provides insight into the degree of immunomodulation caused by anesthetic agents in cancer patients in trials. Subsequently, outlining results generated in these studies will aid in understanding which modality creates the least tumorigenic conditions and is recommended for each cancer.

STANDARDIZATION

All included studies examined the immunomodulating effects of using Propofol TIVA versus Sevoflurane-based anesthesia in the most common cancers. All studies were RCTs that satisfied the criteria outlined by the John Hopkins Nursing Evidence-Based Practice tool for Level 1 research classification. All included articles consisted of experimental studies yielding quantitative data, which underwent ELISA or flow cytometry analysis, and extrapolated conclusive results for clinical implementation. Standardization of multiple variables enhance power, validity, and reliability.

Figure 1.1 Timeline of Research Progression by Author's name



LUNG CANCER

2011

Hu et al. in 2011, explored the immunologic consequences of sevoflurane-based anesthesia compared to Propofol-based TIVA on lung cancer patients.[18] Based on *in-vitro*

research, in *The effect of sevoflurane inhalation anesthesia only and propofol total intravenous anesthesia on perioperative cytokine balance in lung cancer patients,* Hu et al. concluded that Propofol-based anesthesia had a lesser impact on cytokines when analyzing perioperative IL-6, IL-8 , IL-10 levels.[18] Hu studied 90 patients with lung cancer undergoing a lobectomy, they were randomly separated into one of two groups; the sevoflurane-based anesthesia group or the propofol-based group, with (n=45) participants in each. Flow cytometry and ELISA analyzed serum concentrations of IL-6, IL-8 and IL-10 of blood samples drawn perioperatively at (T0) before induction of anesthesia, (T1) before initiating one-lung ventilation, (T2) before the cessation of one-lung ventilation, (T3) after chest closure, and (T4) 24 hours after surgery. [18] Hu et al. concluded that Propofol-based anesthesia caused a lesser inflammatory-mediated response in cancer patients and aided in the immunomodulated balance of cytokines perioperatively. The researchers recommended propofol-based anesthesia over sevoflurane for lung cancer patients.[18]

The attempt to standardize new recommendations that challenge common practice undergo extensive scrutiny prior to its acceptance and implementation. The bold claims made in 2011 peaked the interest of numerous fields including hematology-oncology, anesthesia, and surgery. In the years that followed, similar studies further investigated its plausibility and applicability in other forms of cancer.

2014-2016

From 2014 to 2016, Tian et al. furthered Hu's research by investigating the effects of propofol-based versus sevoflurane-based anesthesia on the inflammatory response, and pulmonary and cognitive function of 62 lung cancer patients undergoing a lobectomy.[19]

The RCT randomly divided (n=31) patients into the propofol group and (n=31) into the sevoflurane group. Lung cancer patients in the propofol-based anesthesia group received

propofol as the primary anesthetic for the lobectomy. In contrast, those in the sevoflurane-based group received the inhaled agent for the same procedure.[19] All patients undergoing Tian et al.'s study had the surgical resection of the lobes performed by the same surgeon to preserve validity.

In continuation of Hu et al.'s research, Tian also scrutinized the immunological impact of anesthetic agents on IL-6 and IL-10 throughout the perioperative timeline depicting critical junctures. Blood samples mirrored the previous study and were drawn at (T1) before induction of anesthesia, (T2) before initiating one-lung ventilation, (T3) after sternal closure, and (T4) 24 hours after surgery.[19] In addition to pulmonary and immunosuppressive analysis, Tian et al. further investigated the time to eye-opening, extubation, and the time to respond of the two groups. Participants were evaluated for changes in cognitive function via mini-mental state examination (MMSE) and serum concentration levels of S100 calcium-binding protein β (S100β) in (T1) and (T4).[19] Used as an immunohistochemical identifier of malignancy, the S100 calcium-binding proteins β are expressed in various elements within cells, involved in calcium and proliferation regulation, cluster differentiation, cell apoptosis, energy expenditure, inflammatory response, migration, and invasion via target proteins. Enzyme-linked immunosorbent assay (ELISA) is the biochemical testing methodology utilized in this study, which demonstrated serum concentrations of IL-6 and S100β in the propofol group to be lower than that of the sevoflurane group ($p<0.05$).[19]

After data extrapolation, compared to the sevoflurane-based group, lung cancer patients in the propofol-based anesthesia group exhibited lesser recovery times, enhanced pulmonary and cognitive function, and a significant reduction in the perioperative inflammatory response as well as the rate of adverse events intraoperatively.[19] Tian et al.'s research demonstrated propofol-based anesthesia in lung cancer patients undergoing a lobectomy to be superior to sevoflurane-

based anesthesia. Tian published his findings in the *Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection*.[19]

2016-2018

Following Hu and Tian et al.'s research, from January 2016 to December 2018, Sen Y et al. advanced research in the immunomodulatory effects of Propofol and Sevoflurane-based anesthesia lung cancer patients. However, Sen et al. speculated adding a paravertebral nerve block would further reduce the amount of Propofol required for general anesthesia and provide better outcomes.[20] Therefore, the study evolved into a comparison of Propofol with paravertebral-nerve block-based anesthesia (PPA) to sevoflurane-based anesthesia and its influence on vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGF-β) in lung cancer patients undergoing radical lung resection. The study consisted of 82 patients, (n=41) were placed randomly into the PPA group and (n=41) in the sevoflurane group.[20]

Lung cancer is promoted by tumor angiogenesis-related factors VEGF and TGF-β and are crucial in the pathogenesis and progression of malignancy. Subsequently, perioperative blood samples were collected, and serum concentrations were evaluated via ELISA.[20] Sen et al. also investigated the amount of opioid consumption between the two groups since opioids are known as immunosuppressive drugs. The extensive analysis also revealed both VEGF and TGF-β expression levels to be remarkably lower in the propofol-paravertebral-based group than in the sevoflurane-based group 24 hours after surgery ($P < 0.05$).[20] Compared to preoperative radical lung resection levels, VEGF and TGF-β at 24 hours postoperative were significantly higher in the sevoflurane group than in the propofol-paravertebral-based group ($P < 0.05$). Lower levels

may diminish the risk of tumor cell invasion, proliferation, and metastasis of the residual cancer cells, thus correlating with improved long-term lung cancer prognosis. Moreover, the PPA group also had fewer breakthrough Sufentanil and Remifentanil dosage requirements for pain management. [20]

Sen et al. suggest that propofol-paravertebral-based anesthesia is the preferred anesthetic modality due to its ability to decrease the consumption of opioids, enhance analgesia influence postoperatively, and lower the postoperative VEGF and TGF-β levels in lung cancer patients undergoing radical lung cancer surgery.[20] Sen et al.'s findings contributed a new element to fill a gap in the existing literature by creating a clinical basis for its implementation.

2018-2019

Yamaguchi et al. built upon previous works by analyzing the distinct immunological impact of propofol-based anesthesia and sevoflurane-based anesthesia. This study examined perioperative regulatory T cells, CD4+ and CD8+ T cells, and apoptosis or programmed death 1 (PD-1) via flow cytometry in lung cancer patients undergoing resection.[21]

Yamaguchi et al. emulated prior conducted research designs by randomly placing a total of 64 patients with lung cancer into a propofol-based anesthesia group and a sevoflurane-based anesthesia group. [21] Blood samples of collected immune cells demonstrated higher ratios of regulatory T cells in the postoperative Sevoflurane group compared to preoperative levels ($P < 0.05$). there was no disparity among PD-1 on CD4+ and CD8+ T cells following lung resection in either group. However, in the propofol-based group, CD8+ T cell levels were notably lower postoperatively compared to preoperative levels ($P < 0.05$).[21] Flow cytometry results also found both Propofol and sevoflurane-based anesthesia groups did not increase the proportion of PD-1 on CD4+ and CD8+ T cells status post lung resection surgery.[21] By analyzing immune cells

through different aspects, in *Propofol decreases CD8+ T cells and sevoflurane increases regulatory T cells after lung cancer resection: a randomized controlled trial* Yamaguchi et al. determined both groups may cause immunosuppression via differing mechanisms. Ultimately, research indicated Sevoflurane might further contribute to cancer progression by increasing regulatory T cells.[21]

COLORECTAL CANCER

2011

Tylman et al. conducted an RCT in 2011 investigating the immunosuppressive and inflammatory impacts of different anesthetic modalities on colorectal cancer patients undergoing surgery. Pain management is crucial in the oncology patient population; therefore, implementing opioids into research was essential. In the study *Inflammatory response in patients undergoing colorectal cancer surgery: the effect of two different anesthetic techniques*, Tylman et al selected 50 patients with colorectal cancer undergoing surgery and randomly allocated them into two groups, a Propofol-based anesthesia with remifentanil group (n=25) and a Sevoflurane-based anesthesia with fentanyl group (n=25).[22]

Blood samples were obtained perioperatively, before induction of anesthesia (T0), 60 minutes after the surgery start time (T1), 30 minutes after surgery (T2), and 24 hours after surgery (T3). Serum plasma concentrations of IL-8 and IL-17 and corresponding factors such as ICAM-1, L-selectin, and MPO were then dissected and quantified utilizing ELISA methodology.[22]

Tylman et al. discovered colorectal cancer patients undergoing surgery in the sevoflurane-fentanyl anesthesia group exhibited significantly higher levels of the pro-inflammatory cytokine IL-17 compared to the propofol-remifentanil anesthesia group.[22] In

addition, in the Propofol-remifentanil anesthesia group, reduced levels of IL-17 were observed at (T3) compared to the sevoflurane-fentanyl group.[22] Tylman et al. noted the suppression of inflammatory response may be due to Propofol's potent antioxidant and anti-inflammatory properties indirectly creating a less detrimental environment for colorectal cancer patients. Propofol's antioxidant effects include lipid peroxidation inhibition and endothelial cell protection from harmful toxic free radicals.[22]

2011-2012

Kvarnström et al. mirrored Tylman et al.'s research design a year later in 2012, he published *Complement activation and interleukin response in major abdominal surgery* where he also scrutinized the immunosuppressive and inflammatory effects of Propofol-based anesthesia with remifentanil versus Sevoflurane-based anesthesia with fentanyl in 50 colorectal cancer patients undergoing surgery.[23]

The article hypothesized that colorectal surgery induced the activation of complement factors resulting in the release of pro-inflammatory interleukins; Kvarnström et al. believe this process could be mediated with the administration of Propofol-based anesthesia with remifentanil, compared to patients receiving sevoflurane-based anesthesia with fentanyl.[23] After randomization via sealed envelopes, (n=25) colorectal cancer patients were designated to each group before their scheduled elective open colorectal surgery. Analogous to previous research, blood samples were collected perioperatively, before induction of anesthesia (T0), 60 minutes after the surgery start (T1), 30 minutes after surgery completion (T2), and 24 hours after surgery end time (T3).[23] In addition to IL-6 and IL-8, pro-inflammatory cytokines TNF-α, IL-1β, and anti-inflammatory cytokines IL-4 and IL-10 were examined. Levels of C3a and SC5b-9 were also dissected from samples to assess complement involvement.[23]

After an in-depth analysis, data revealed that major colorectal surgery was found to induce complement as evidence of heightened C3a levels perioperatively. Subsequently, interleukin levels were also elevated in both groups. Unfortunately, the activation of complement and release of pro-inflammatory and anti-inflammatory cytokines could not be attenuated to a large enough degree by either anesthetic to be considered clinically or statistically relevant.[23]

The use of opioids became an increasingly controversial topic provoking new investigations into the depth of immunosuppression caused- not by the anesthetic, but by the narcotic, on cancer patients.

2012-2015

Subsequent years, from 2012 to 2015, studies confirming opioid-induced immunosuppression in oncology patients became increasingly evident. Therefore, Chen et al. studied the immunosuppressive effects of sole Propofol-based versus Sevoflurane-based anesthesia in colorectal cancer patients undergoing laparoscopic radical resection.[24]

Colorectal cancer patients were randomly assigned to each anesthetic group (n=30) prior to surgery. By obtaining perioperative blood samples, Chen et al. were able to closely dissect NK cell counts and cluster differentiation levels via flow cytometry.[24] Precise $CD3^+$, $CD4^+$ $CD19^+$, and $CD4^+$ /$CD8^+$ ratios were quantified. Blood samples were acquired before induction of anesthesia (T1), at the end of surgery (T2), and 24 hours after the surgical end time (T3).[24]

In *The effect of propofol and sevoflurane on the perioperative immunity in patients under laparoscopic radical resection of colorectal cancer*, Chen et al. detailed the RCT's findings. In the sevoflurane group, there was an increase in $CD3^+$, $CD4^+$, and $CD19^+$ levels immediately at the end of surgery (T2), compared to levels before surgery ($P<0.05$). At the same time, NK

cell count was notably reduced ($P<0.01$).[24] The immunomodulation observed in the sevoflurane group in $CD3^+$, $CD19^+$, and NK cells remained substantial at 24 hours postoperative (T3). However, in colorectal cancer patients placed in the propofol group, levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ ratios were significantly reduced from the end of surgery (T2) to 24 hours after surgery completion (T3), returning to their initial preoperative baseline levels ($P>0.05$). Moreover, NK cells also demonstrated recuperation by 24 hours (T3) when compared to immediate surgical end time (T2).[24]

The results uncovered by Chen et al. indicated that Propofol-based anesthesia may have lesser immunosuppressive consequences since immune cell function and counts were restored to preoperative baseline levels at 24 hours. In contrast, in the Sevoflurane group, levels remained suppressed.[24]

BREAST CANCER

2012-2014

Emerging retrospective studies identified several modifiable factors culpable for immunosuppression in oncology patients undergoing resection surgery. Among some of the highest agents responsible for NK cell suppression were inhaled volatile agents and opioids.[25] Alternatively, Propofol has antioxidant properties, and regional anesthesia has demonstrated a reduction in opioid consumption. Therefore, in 2014 Buckley et al., investigated if the anesthetic approach impacted breast cancer metastasis in the perioperative phase by comparing the effects of Propofol with paravertebral block anesthesia to Sevoflurane with fentanyl anesthesia in patients undergoing breast cancer surgery.[25]

The RCT design performed an electronic randomization of 10 participants with primary breast cancer undergoing cancer surgery into one of 2 anesthesia groups. Patients were allocated

into a Propofol with Paravertebral Block anesthesia (PPA) group or a Sevoflurane with Fentanyl (SFA) group as their primary anesthesia.[25] Blood samples were acquired from all study participants before surgery and then again 24 hours postoperatively. Unlike other studies that involved four critical perioperative times of sample collection, Buckley et al. centrifuged and stored the before and after-surgery blood specimens at -80 degrees Celsius for further in vitro examination. Serum extractions were scrutinized utilizing flow cytometry for NK cell isolation and counts, tumor cell culture analysis, ELISA for interleukin levels, NK cell receptor and CD107a expressions, and an apoptosis cell assay.[25] Serum levels of NK cells and their activating receptors: NKp30, NKp44, NKp46, 2b4, CD16, NKG2D, cytokine production, NK CD107a expression, and HCC1500 were among the immune factors quantified, and statistical data subsequently extrapolated in this study.[25]

Buckley et al. published their findings denoting the clinical significance of different anesthetic modalities in "*Effect of anesthetic technique on the natural killer cell anti-tumor activity of serum from women undergoing breast cancer surgery: a pilot study.*"[25] The study revealed that serum collected from patients with breast cancer undergoing cancer surgery in the PPA group had significantly higher NK cell cytotoxicity than those who received SFA. In addition, breast cancer patients in the PPA group better preserved healthy NK anti-tumor cell activity compared to the SFA group in the perioperative period.[25]

2017-2018

Lim JA[5] and Oh CS et al.[6] found the effect of propofol on cancer cells, NK cells and CTL functions did not differ from that of sevoflurane in breast cancer surgery. However, Yan T et al.[26] found Propofol effectively inhibited the release of VEGF-C induced by breast cancer

surgery compared to sevoflurane-based anesthesia. Cho et al.[27] concluded Propofol demonstrated a favorable impact on immune function by preserving NKCC compared with sevoflurane.

Table 1.1 Immunomodulation Effects of Propofol vs Sevoflurane based Anesthesia by Cancer Type (most common)

Citation	Cancer Type	Anesthetic	Design/ Level	Immune cells studied	Methodology	Findings	Results	Conclusions
Hu XL et al,[18] 2011	Lung	Propofol vs Sevoflurane	RCT /1 n=90	IL-6, IL-8 ,IL-10	ELISA	The IL-6 levels at T1 and T2 in the propofol group was lower than that of the sevoflurane ($P < 0.05$). The IL-8 levels at T1, T2 and T3 in propofol group were all lower than that of sevoflurane ($P < 0.05$). The IL-10 levels in propofol at T1, T2, T3 and T4 was much higher than that of sevoflurane	Propofol causes less inflammatory mediator release and can also modulate the balance of cytokines.	Propofol is a superior anesthetic for lung cancer than sevoflurane.
Tian HT et al,[19] 2017	Lung	Propofol vs Sevoflurane	Retrospective n=62	IL-6, IL-10, S100 calcium-binding protein β (S100β)	ELISA	interleukin-6 (IL-6) and matrix metalloproteinase-9 (MMP-9) in serum of patients after the induced anesthesia in the propofol group were significantly higher than those at t1, while the level of interleukin-10 (IL-10) was lower than that at t1 ($p<0.01$); during t2-t4, the levels of IL-6 and MMP-9 in serum of patients in the propofol group were significantly lower than those in patients in the sevoflurane group, while the level of IL-10 was significantly higher than that in patients in the sevoflurane group ($p<0.05$). Concentration of S100β was significantly higher than that at t1 ($p<0.01$) The concentration of S100β was lower than that of patients in the sevoflurane group($p<0.05$)	Propofol had less inflammatory effects when compared to the sevoflurane group when analyzing IL-6 and S100	Propofol is superior to sevoflurane. Propofol anesthesia can significantly reduce the perioperative inflammatory response in patients receiving lung cancer resection surgery
Yamaguchi A et al,[21] 2021	Lung	Propofol vs Sevoflurane	RCT / 1 N=82	CD4+ and CD8+ T cells, programmed death 1 (PD-1) on CD4+ and CD8+ T cells, and regulatory T cells	Flow Cytometry	In the propofol group, the number of CD8+ T cells was significantly lower after the operation than before [50.4±23.2 to 37.5±12.9 (10^4/mL blood), $P<0.05$]. In the Sevoflurane group, CD8+ T cells did not decrease. In sevo group proportion of regulatory T cells had significantly increased after surgery, compared with before (0.0086%±0.0062% to 0.012%±0.0079%, $P<0.05$)	Propofol decreased the number of CD8+ T cells, while sevoflurane increased the proportion of regulatory T cells in patients after lung surgery; however, propofol and sevoflurane did not increase the proportion of PD-1 on CD4+ and CD8+ T cells after lung surgery	Sevoflurane may contribute to cancer progression through an increase in regulatory T cells.
Sen Y et al,[20] 2019	Lung	Propofol (+paravertebral) vs Sevoflurane	Retrospective N=82	VEGF TGF-β	ELISA	Propofol VEGF (671.49 ‡ 225.92) TGF-B (7.95 + 2.88) Sevo	The expression levels of VEGF and TGF-β in Propofol group were significantly lower than	Propofol is more suitable than sevoflurane in non-

			Cangzhou Central Hospital			VEGF (959.74 ‡283.59) TGF-B (11.23 + 3.09) no significant difference in serum levels of VEGF and TGF-β between the two groups before operation, however the postoperative levels were lower in the propofol group. Serum levels of VEGF and TGF-β at 24 h after operation in SGA group were significantly higher than those before operation (P<0.05)	those in Sevoflurane group 24 h after operation (P<0.05). Low levels of VEGF and TGF-β in Propofol group may reduce the risk of invasion, proliferation and metastasis of residual lung cancer cells and improve the long-term prognosis of NSCLC.	small cell lung cancer.
Chen Y et al,[24] 2015	Colorectal	Propofol vs Sevoflurane	RCT / 1 n=30 Sir Run Run Shaw Hospital	NK cells, $CD3^+$, $CD4^+$ $CD19^+$, and $CD4^+$ /$CD8^+$ ratio	Flow Cytometry	Propofol levels of $CD3^+$, $CD4^+$ and $CD4^+$ /$CD8^+$ ratio ((63.6 ± 12.3)%, (36.0 ± 8.7)%, 1.5 ± 0.6) (t=-2.879, -3.682, -3.340 respectively, at 24h postop returning to baseline when compared to preop (t= 0.858, 0.758, -0.074) P>0.05). In Sevoflurane, NK cells began to recover at 24 h ((22.2 ± 12.6)%) to (t= 2.941, P<0.05), but levels were lower than the baseline (t=-2.249, P<0.05).	Both Propofol and Sevoflurane groups increased $CD3^+$, $CD4^+$ $CD19^+$, and $CD4^+$ /$CD8^+$ ratio levels and suppressed NK cell counts. However, levels returned to preoperative baseline in the Propofol group at 24h whereas levels remained suppressed in the Sevoflurane group.	Propofol may have less or shorter impact on immunity.
Oh CS et al,[6] 2022	Colorectal	Propofol vs Sevoflurane	RCT/ 1 n=153 Konkuk University Medical Center, Seoul, Korea	NK cells, CD39, CD73, type 1, type 17 helper T cells, neutrophils, lymphocytes, monocytes, apoptosis	Flow Cytometry	NK cells differed at 24 h postoperatively (20.4 ± 13.4% vs. 20.8 ± 11.3%, 17.9 ± 12.7% vs. 20.7 ± 11.9%, and 18.6 ± 11.6% vs. 21.3 ± 10.8% before anesthesia and after 1 and 24 h after anesthesia, respectively; difference [95% CI], -0.3 [-4.3 to 3.6], -2.8 [-6.8 to 1.1], and -2.6 [-6.2 to 1.0]; P = 0.863, P = 0.136, and P = 0.151 before anesthesia and after 1 and 24 h, respectively).	Apoptosis rate of cytotoxic T cells at Post 24 h was significantly higher in the sevoflurane groups. However, The author considered this significant difference to be clinically meaningless because the fraction of cytotoxic cells at 1 h postop did not differ.	Propofol-based anesthesia was not superior to sevoflurane in terms of alleviating suppression of immune cells including natural killer cells and T lymphocytes during colorectal cancer surgery.
Tylman M et al,[22] 2011	Colorectal	Propofol (+ remifentanil) vs Sevoflurane (+ fentanyl)	RCT /1 n=50 Sahlgrenska University Hospital	IL-8, IL-17, MPO, ICAM-1, V-CAM and L-selectin	ELISA	Levels of IL-8, MPO, ICAM-1 and L-selectin decreased 1h postop in both groups (P<0.05, P<0.01, respectively). In the Sevoflurane group, V-CAM levels were significantly lower at 30min and 1h postop (P<0.01). At 24 h postop, IL-17 levels were significantly increased only in the Sevoflurane group (P<0.05) and not Propofol.	At 24 h post-surgery, IL-17 levels significantly decreased in patients receiving Propofol but not Sevoflurane anesthesia.	Propofol demonstrated more anti-inflammatory effects than Sevoflurane. Sevoflurane increased pro-inflammatory IL-17 cytokine levels longer.

Kvarnström AL et al,[23] 2012	Colorectal	Propofol (+remifentanil) vs. Sevoflurane (+fentanyl)	RCT /1 N=50	IL-1b, IL-6, IL-8, IL-4, IL-10, C3a, SC5b-9, tumour necrosis factor-a TNF-a	Flow Cytometry	C3a Propofol 185.9 (127.8-228.9) Sevo 197.9 (140.9-303.6). SC5b-9 Propofol 137.9 (74.9-209.3) Sevo 160.9 (97.5 - 209.4). IL-1b Propofol <0.8 (<0.8-1.4) Sevo <0.8 (<0.8-1.9). IL-6 Propofol 505 (129.4-1370.0) Sevo 370 (198.0-810.0). IL-8 Propofol 41.2 (34.2-56.2) Sevo 58.4 (37.6-120.0)	There are no significant differences between the propofol and sevoflurane groups regarding complement activation and the release of cytokines of pro- and anti-inflammatory interleukins.	Both Propofol and Sevoflurane based anesthesia have similar effects
Lim JA et al,[5] 2018	Breast	Propofol vs Sevoflurane	RCT / 1 n=40 Konkuk University Medical Center, Seoul, Korea	NK cell, cytotoxic T lymphocyte counts and apoptosis rates	Flow Cytometry		The breast cancer cell count and rate of apoptosis were not different between the breast cancer and NK cell, and breast cancer and CTL, co-cultures. No difference in the level of inflammatory cytokines including TNF-α, IL-6 and -10 was detected between the groups. None of all variables were different between the groups according to time change.	The effect of propofol-based anaesthesia on cancer cell, NK cell and CTL functions did not differ from that of sevoflurane-based anesthesia in breast cancer surgery.
Oh CS et al,[18] 2018	Breast	Propofol vs Sevoflurane	RCT/1 N=201 Konkuk University Medical Center	NK cells, CD39, CD73, type 1, type 17 helper T cells, neutrophils, lymphocytes, monocytes, apoptosis	Flow Cytometry	The mean frequency of CD 39 expression in the propofol *vs* sevoflurane group (17.1 [interquartile range, 11.6 to 22.2%] *vs.* 17.6 [11.3 to 21.2%],16.7 ± 7.6% *vs.* 16.5 ± 7.9%, and 16.9 [11.6 to 21.9%] *vs.* 17.6 [11.8 to 21.6%] at periop intervals; circulating regulatory T cells did not change significantly over time ($P = 0.680$) and did not differ between the two groups (difference [95% CI], 0.01 [−2.04 to 2.06]; $P = 0.995$). types 1 and 17 helper T cells, natural killer cells, and cytotoxic T cells, were not affected by propofol or sevoflurane	The difference in immunosuppression caused by Propofol and Sevoflurane was statistically insignificant	Minimal changes in immune cells between both propofol and sevoflurane during breast cancer surgery.
Yan T et al,[26] 2018	Breast	Propofol (+remifentanil) vs Sevoflurane	RCT/1 N=80 Cancer Hospital of Chinese Academy of Medical Sciences	VEGF-C TGF-β	ELISA	VEGF-C serum concentrations increased postop from 105 (87–193) pg/ml to174 (111–281) pg/ml in the Sevo group ($P = 0.009$), but remained almost unchanged in the Propofol group with 134 (80–205) pg/ml vs.140(92–250) pg/ml($P = 0.402$). The preoperative to postoperative change for VEGF-C of the Sevo group (50 pg/ml) was significantly higher than that of the Propofol group	Both Propofol based anesthesia and Sevoflurane based anesthesia produced similar effects on the release of TGF-β. However, the Propofol group demonstrated better inhibition of VEGF-C.	Propofol -based anesthesia effectively inhibits the release of VEGF-C induced by breast cancer surgery compared to sevoflurane based anesthesia.

						(12 pg/ml) with a difference of 46 (− 11–113) pg/ml ($P = 0.008$).		
Buckley A et al,[25] 2014	Breast	Propofol (+paravertebral block) vs Sevoflurane (+fentanyl)	RCT /1 n=10	NK cell, NKp30, NKp44, NKp46, 2b4, CD16, NKG2D, cytokine production, NK CD107a expression, HCC1500	Flow Cytometry and ELISA	The sevoflurane group had reduced NK cell activating receptor CD16 [from mean (sem), 82 (2)% to 50 (4)%, P=0.001], IL-10 [from 1700 (80) to 1200 (92) pg ml(-1), P=0.001], and IL-1β [from 68 (12) to 19 (4) pg ml(-1), P=0.01]. Sevoflurane group had an increase in NK cell CD107a [23 (2)% to 37(3)%, P=0.007] and apoptosis of HCC1500 [11 (1)% to 21 (2)%, P=0.0001] compared to Propofol group.	Patients in the propofol group maintained healthy donor NK anti-tumour cell activity compared with serum from women in the sevoflurane group.	Propofol based anesthesia better preserves NK cells than Sevoflurane based anesthesia in women with Breast cancer.
Cho JS et al,[27] 2017	Breast	Propofol (+ketorolac) vs Sevoflurane (fentanyl)	RCT /1 n=50 Severance Hospital, Yonsei University Health	NK cell, IL-2, neutrophil, and lymphocyte counts	ELISA	NK cell counts (%) increased after surgery in the Propofol group postop 15.2 (3.2) to 20.1 (3.5), $P = 0.048$], whereas it decreased in the Sevoflurane group [19.5 (2.8) to 16.4 (1.9), $P = 0.032$]. The change of NKCC over time was significantly different between the groups ($P = 0.04$)	Propofol anesthesia demonstrated a favorable impact on immune function by preserving NKCC compared with sevoflurane.	Propofol anesthesia was superior to Sevoflurane in preserving NK cells in Breast Cancer patients.
Ai L et al,[4] 2020	Gastric	Propofol vs. Sevoflurane	RCT /1 N=36 Jinzhou Medical University.	NK cells, CD3-CD56+, GZMB, apoptosis rate TGF-β1	Flow Cytometry	Postop, NK cells to induce apoptosis in BGC-823 tumor cells in the propofol group (44.1±0.68 vs. 16.5 ± 0.21, $P < 0.05$). mean GZMB expression level in peripheral blood NK cells in the propofol group (65.5± 0.83) was significantly higher than that in the sevoflurane group (50.5 ± 0.49, $P < 0.05$)	In the propofol group, the apoptosis of BGC-823 was significantly stronger than that in the sevoflurane group. Propofol promoted the killing effects of NK cells on tumor cells. Propofol promotes nuclear importation of SMAD4 in NK cells and upregulates GZMB expression	Propofol is superior at inducing NK cell cytotoxicity in patients with gastric cancer than sevoflurane. Propofol enhances the tumor cell killing effects of NK cells.
Liu S et al,[32] 2016	Cervical	Propofol vs Sevoflurane	RCT /1 n=60 Xuzhou Central Hospital	NK cells, $CD3^+$ cells, $CD4^+$ cells, $CD8^+$ cells, $CD4^+/CD8^+$ ratio, and B lymphocytes	Flow Cytometry	CD3 -Propofol (1.73± 0.54) Sevo (1.59 ± 0.53). CD 4+ Propofol (0.96 ± 0.29) Sevo (0.79 + 0.31). CD8 Propofol (0.75 ± 0.30) Sevo (0.84 ± 0.31). NK cells Propofol (0.56 ± 0.27) Sevo (0.53 ± 0.26). B cells Propofol (0.38 ±0.18) Sevo (0.42 ± 0.19)	The cell counts of $CD3^+$, $CD4^+$, NK cells, and the $CD4^+/CD8^+$ ratios were significantly lower in the Sevoflurane group than that in the Propofol group.	Propofol was superior to Sevoflurane in protecting circulating lymphocytes in Cervical cancer patients

Figure 1.2 Anesthesia Modality and Impact on Immune cells and Cancer [1,7,17]

POSITIVE EFFECT

•Propofol

- Antioxidant and anti-inflammatory
- Preserves/ enhances NK cell function
- Increases cytotoxic T-Lymphocytes
- Decrease secretion of proinflammatory cytokines
- Induces NK cell cytotoxicity in patients with colorectal and Gastric cancers
- inhibit cancer cell proliferation, invasion, and migration in gastric cancer
- protects circulating lymphocytes in Cervical cancer
- Inhibits upregulation of HIF1A decreasing cancer cell migration and invasion in lung cancer
- increases cell apoptosis via miR-24/p27 pathway in breast cancer

•Regional/Local Anesthesia

- ecrease surgery-induced neuroendocrine responses via suppression of HPA-axis and SNS
- Preserves cell-mediated immunity associated with less immunosuppression and cancer recurrence
- Block Voltage Gated Sodium Channels (which are significantly expressed and active in breast, lung, and colorectal cancers) suppressing tumor metastasis

•Lidocaine

- Increases NK cells
- Antitumor and antiangiogenic properties
- directly inhibits EGF receptor (target for anticancer drugs)
- Inhibits cancer cell invasion via Calcium modulation and blockage of ectodomain shedding of heparin-binding EGF
- inhibits serum-induced proliferation in tongue cancer cells
- reduces inflammatory tumor necrosis factor-alpha, IL-1, and IL-8 levels
- IV infusion increased survival rates and reduced recurrence in pancreatic and bladder cancer patients

COX-2 Inhibitors

- increases NK cell cytotoxicity
- Promotes cytotoxic T-Lymphocyte immune response
- **Celecoxib** reduces myeloid-derived suppressor cells
- **Ketorolac** is shown to have a 5-fold reduction in breast cancer recurrence

•Fentanyl/Remifentanil*

- Antitumor-like effects in colorectal cancer cells.
- Inhibit tumor growth and cell invasion via downregulation of miR-182 and MMP-9 in colorectal cancer

Beta-Blockers**

- reduces proliferation of liver cancer cells
- preserves NK cell function (with NSAIDs)
- attenuates regulatory T-cell in breast cancer
- reduces risk of breast cancer-related deaths

•Sevoflurane

- Apoptosis/Decreases T-Lymphocytes.
- Increases Breast cancer cell proliferation, migration and invasion
- Decreases NK cells
- increases pro-inflammatory cytokines
- Increases pro-tumorigenic cytokines, hypoxia inducted factor-1a, and matrix metalloproteinases

•Isoflurane

- Attenuates NK cells
- Apoptosis of T-Lymphocytes
- Upregulation of HIF-1α in prostate and renal cancers
- Increase in malignant potential of ovarian cancer cells

Nitrous

- Depression of neutrophil chemotaxis
- Stimulates lung and liver metastasis (not colorectal)
- Inhibition of hematopoietic cell formation for tumor surveillance

Ketamine

- Decreases NK cells.
- Apoptosis of T-Lymphocytes.
- Attenuation of proinflammatory cytokines
- Stimulates lung and liver metastasis.
- Inhibition of dendritic cell maturation/function

•Morphine

- Suppresses NK cells and T cells
- promotes lymphocyte apoptosis
- decreases macrophage function
- promotes tumor neovascularization, angiogenesis, tumor progression and growth

Fentanyl/ Remifentanil*

- Decrease NK cells.
- Associated with higher mortality rates and lower survival rates in Lung cancer

Midazolam

- No effect on cytotoxic T-Lymphocytes
- impairs monocyte and neutrophil function

Dexmedetomine

- Associated with decreased survival rates in patients with Lung cancer
- Dose-dependent increases in tumor cell retention and metastasis in Breast, Lung and colorectal cancers
- Increases cancer cell proliferation and migration, via upregulation of antiapoptotic proteins

Dexamethasone

- increases tumor cell proliferation in solid cancers
- Decreased survival in rectal cancers (increases in Lung cancer)

Oxygen (FiO2 80%)**

- Increase tumor cell proliferation via angiogenesis
- Hyperoxia decreases cancer-free survival rates

•NEGATIVE EFFECT

*NK: natural killer; HIF1a: hypoxia inducted factor-1a; HPA-axis: hypothalamic-pituitary-adrenal axis; SNS: sympathetic nervous system; EGF: epidermal growth factor; IL: interleukin; miR-182: MicroRNA 182; MMP-9: matrix metalloproteinase; *data on perioperative opioids are controversial due to over expression of Mu-Opioid receptors [MOR] **Data on recurrence is undetermined*

Primary Aim

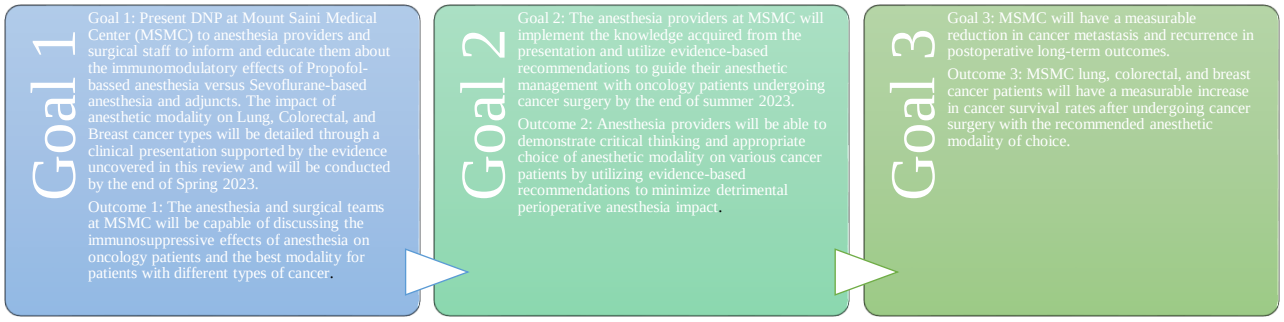
Numerous studies demonstrate the use of general anesthesia with inhaled anesthetics, such as Sevoflurane, correlate with an increase in cancer recurrence among patients undergoing cancer resection surgery.[10,11] Contrarily, more recent research suggests that TIVA with Propofol or supplemental regional anesthesia in this patient population may decrease the need for anesthetics, opioid consumption and improve postoperative cancer outcomes.[26] Anesthesia providers should therefore be fully knowledgeable of the effects of all their anesthetic agents on different types of cancers when caring for oncological patients.

Currently, there is insufficient understanding of the perioperative influence anesthetic modalities have on cancer patients' immune systems. Furthermore, a lack of large randomized controlled trials perpetuates controversy over anesthesia's long-term postoperative effects, including effects on survival and cancer recurrence rates. As research in anesthesia evolves in surgical oncology, emerging data exploring various components better reflect the extent of immunomodulation anesthetic agents have on cancer patients.

This study aims to educate anesthesia providers on the perioperative effects of Propofol-based anesthesia compared to Sevoflurane-based anesthesia on cancer patients diagnosed with lung, colorectal, or breast cancer undergoing cancer surgery. The findings synthesized in this study are compelling and fill a gap in the literature; thus, education on these results would contribute to optimal decision-making for anesthesia providers. The study seeks to explain and disseminate information and evidence validating the effects of anesthetic agents on oncology patients to enhance patient outcomes. The doctorate in nursing practice (DNP) action plan and quality improvement (QI) project aims to illustrate a clear understanding of the

immunosuppressive consequences of anesthetic modalities on cancer patients and provide evidence-based recommendations developed through this review.

Figure 1.3 S.M.A.R.T. Goals



Goal 1: Present DNP at Mount Saini Medical Center (MSMC) to anesthesia providers and surgical staff to inform and educate them about the immunomodulatory effects of Propofol-based anesthesia versus Sevoflurane-based anesthesia and adjuncts. The impact of anesthetic modality on Lung, Colorectal, and Breast cancer types will be detailed through a clinical presentation supported by the evidence uncovered in this review and will be conducted by the end of Spring 2023. Outcome 1: The anesthesia and surgical teams at MSMC will be capable of discussing the immunosuppressive effects of anesthesia on oncology patients and the best modality for patients with different types of cancer.

Goal 2: The anesthesia providers at MSMC will implement the knowledge acquired from the presentation and utilize evidence-based recommendations to guide their anesthetic management with oncology patients undergoing cancer surgery by the end of summer 2023. Outcome 2: Anesthesia providers will be able to demonstrate critical thinking and appropriate choice of anesthetic modality on various cancer patients by utilizing evidence-based recommendations to minimize detrimental perioperative anesthesia impact.

Goal 3: MSMC will have a measurable reduction in cancer metastasis and recurrence in postoperative long-term outcomes. Outcome 3: MSMC lung, colorectal, and breast cancer patients will have a measurable increase in cancer survival rates after undergoing cancer surgery with the recommended anesthetic modality of choice.

Figure 1.4 S.W.O.T. Analysis

METHODOLOGY FOR PROPOSAL

Setting and Participants

The setting for the proposed DNP will be conducted in a teaching hospital in Miami Beach, Florida. The involved participants in the study include patients with primary lung, colorectal, or breast cancer, surgical oncology staff, anesthesiologists, certified registered nurse anesthesiologist, student registered nurse anesthesiologists, preoperative and post-anesthesia care units.

Description of Approach and Project Procedures

An education module is to be disseminated to all staff involved in order to educate anesthesia providers on the perioperative effects of Propofol-based anesthesia compared to Sevoflurane-based anesthesia on cancer patients diagnosed with primary lung, colorectal, or breast cancer undergoing cancer surgery. In addition, providing information guiding best practices and evidence-based recommendations should aid optimal decision-making for anesthesia providers.

Participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. There are no known alternatives available to the participant other than not taking part in this project. However, if the participant would like to receive the educational material, it will be provided to them at no cost.

The educational intervention will be conveyed by a 10-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. Once results are collected, and data synthesized, a statistical

analysis of findings will reveal correlations. All collected material will be kept confidential, stored in a password encrypted digital cloud, and accessible to the investigators of this study.

Protection of Human Subjects

Standard patient safety and practices should be maintained at all times and is of utmost priority. Protection of study participants should not be delineated or compromised at any point. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

Confidentiality

The records of this project will be kept private and protected to the fullest extent provided by law. If any report is issued or private investigators decide to publish, there will not be any information that will make it possible to identify the participant. Records will be stored securely, and only the project team will have access to the records.

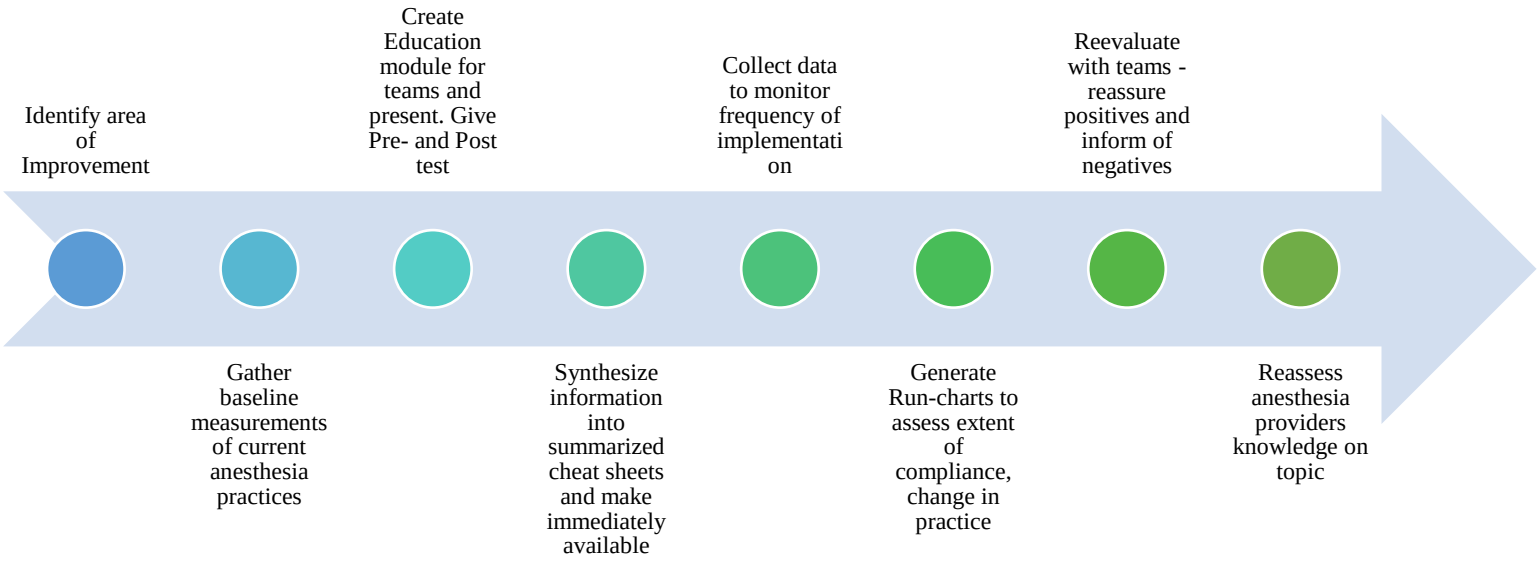
Data Collection, Management and Analysis

If an education module is considered, to assess learning or influence in change of anesthesia care, anesthesia providers will be given a set of questions to answer prior to the education module and then again after. Once results are collected, and data synthesized, a statistical analysis of findings can reveal correlations.

Quality Improvement project outcomes are best scrutinized utilizing a run chart.[31] The run chart tool allows for real-time evidence to demonstrate if evidence-based recommendations from the module are being implemented in actual time. It allows researchers to document the

frequency at which interventions occur (y-axis) in a given time frame (x-axis).[31] The amount of frequency should increase over time until it is standard practice at the facility, theoretically, this will be reflected with a direct correlation in enhanced cancer patient outcomes. If frequency decreases overtime, the level of effect exerted by the quality improvement recommendations diminish.[31] Input of findings and variables will undergo chi-squared test and *t* test. Independent researchers will examine study validity and reliability. Final outcomes will be presented with visual tables for enhanced interpretation to strengthen the study.

Figure 1.5 Timeline



Summary and Research Limitations of the Review of Literature

Variations in anesthetic practice in the surgical setting is a problem and clarity on the relationship of Sevoflurane-based anesthesia and Propofol-based anesthesia can improve cancer patient outcomes. Thus, the study aimed to analyze existing research and compartmentalize results to come to a better understanding. The author created subgroup analysis for each cancer type which compared the same anesthetic agents, virtually eliminating heterogeneity. The clinical characteristics of the 15 included RCTs are illustrated in the attached Table 1.1 *Immunomodulation Effects of Propofol vs Sevoflurane based Anesthesia by Cancer Type (most common).* Of the included RCTs, 2 were for comparative analysis, and 13 were on the three deadliest cancers. The table included, 5 RCTs on Breast cancer, 4 RCTs on Lung cancer, and 4 RCTs on Colorectal cancer. All the studies examined the immunomodulating effects of using Propofol-based anesthesia versus Sevoflurane-based anesthesia in the deadliest cancers.

All studies were RCTs that satisfied the criteria outlined by the John Hopkins Nursing Evidence-Based Practice tool for Level 1 research classification. All included articles consisted of experimental studies yielding quantitative data, which underwent ELISA or flow cytometry analysis, and extrapolated conclusive results for clinical implementation. Standardization of multiple variables enhance power, validity, and reliability. Thus, allowing for standardization across the independent examinations of individual cancers to provide an answer to the clinical question posed for investigation was a strength of the study.

Conclusions about cancer should not be generalized, the subgroup analysis on the cancer type and intervention performed enhanced external validity; strengthening the study. After research scrutiny, it was determined all articles were high-quality in their own respective as both

stand-alone and combined research. After subgroup analysis, the research presented sufficiently powered the article's PICOT.

However, in order to accurately reflect an oncology population, a small sample, ranging from (n=10) to (n=201), is critically low according to current recommendations. A study weakness since it may introduce bias. In addition, poor uniformity among reporting of additional choices of agents, the timing of blood samples drawn, type of immune cells tested and methodology to test across all studies contributed to variance in results. Arguably controversial, the author believes that the heterogeneity of immune cells analyzed enhanced credibility, because although immune cells varied, study findings resulted in invariable conclusions reinforcing the thesis with multiple aspects.

The variance among type of surgery and patient prognosis prior to surgery may threaten internal validity. However, in the authors addendum, information about anesthetic agents' impact on cancer metastasis, cancer stages, recurrence and mortality were provided. Therefore, strengthening the study's external validity by incorporating statistical outcomes to verify consequential application. Internal validity was enhanced by providing clear results detailing which patients benefited from interventions. The study's objective and design were congruent. Sufficient standardized RCTs and post-hoc analysis consistently demonstrated clinical significance of outcome applicability.

QI Study Limitations

QI study limitations include a small sample size and one hospital site of implementation. A small sample size is unable to reflect the oncology population accurately and reduces the generalizability of the result findings. An insufficient sample size also creates a lack of statistical power, unable to back significant correlations of study findings. A non-response bias is also

introduced due to participant involvement being fully volunteer-based and optional. Participants were also not blinded to researchers conducting the QI, possibly contributing to response bias. Implementation of the study at a single hospital site introduces sampling bias, limiting the external validity of the study.

In order to address these limitations, a more extensive QI study must be conducted with an adequate sample size at multiple hospital sites. Participation should be required, and a double-blind approach should be taken. Conducting a priori power analysis to determine a numerical sample size minimum to identify a meaningful or significant impact may be beneficial to assess if the study is being underpowered. Statistical power may also be enhanced by increasing the number of data points collected perioperatively from surgical oncology patients, serving as an alternative to increasing sample size.

RESULTS

Table 2.1 Participant Background

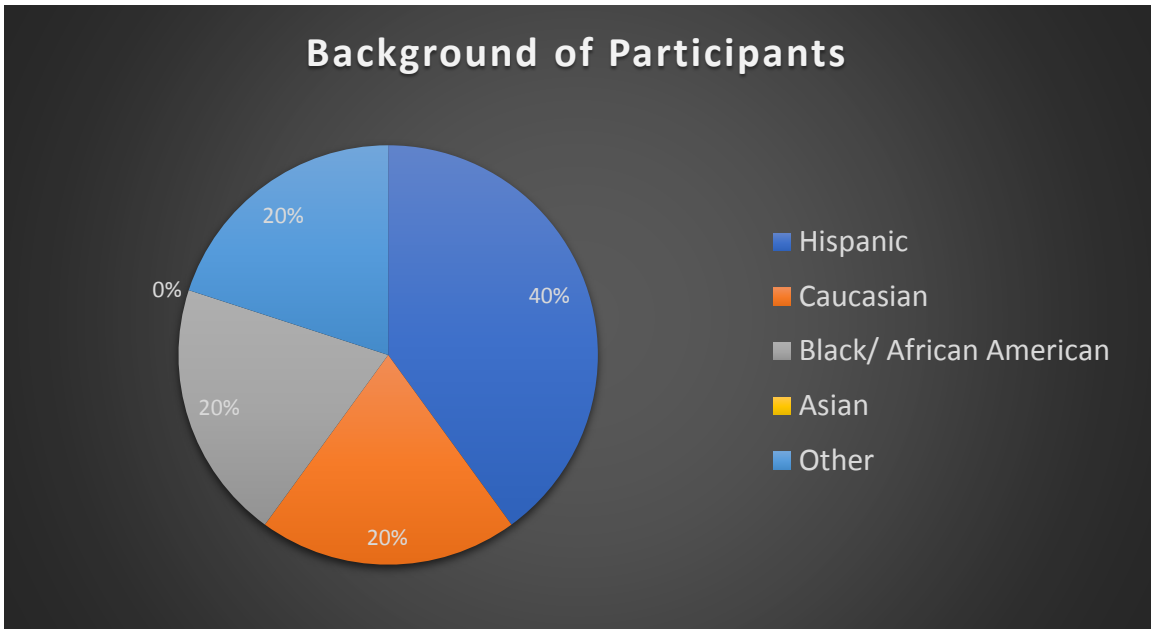


Table 2.2 Participant Demographics

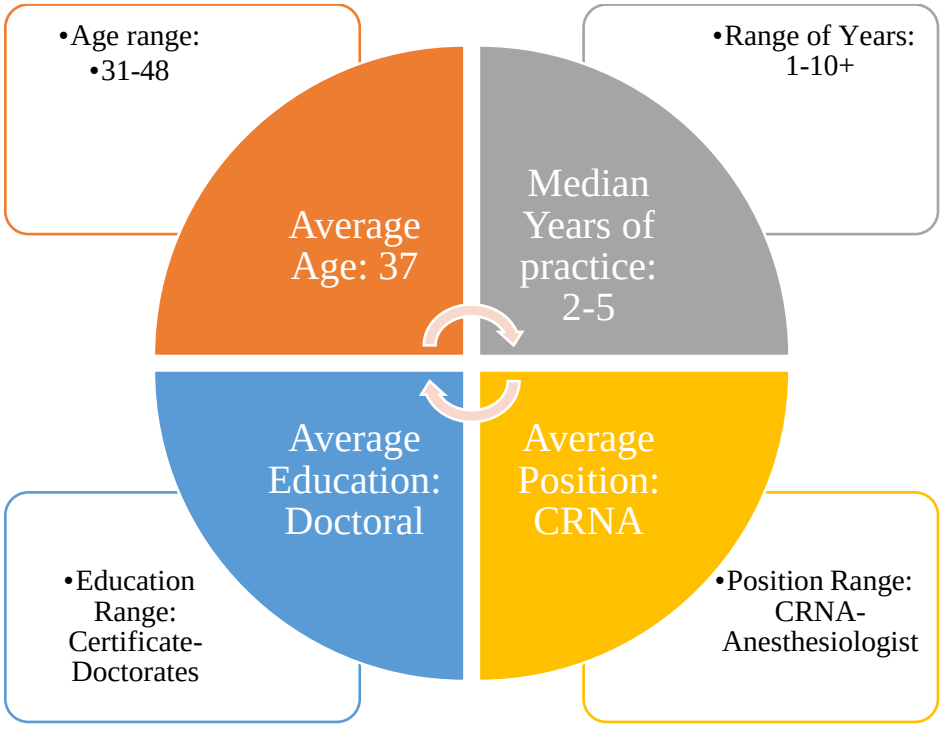
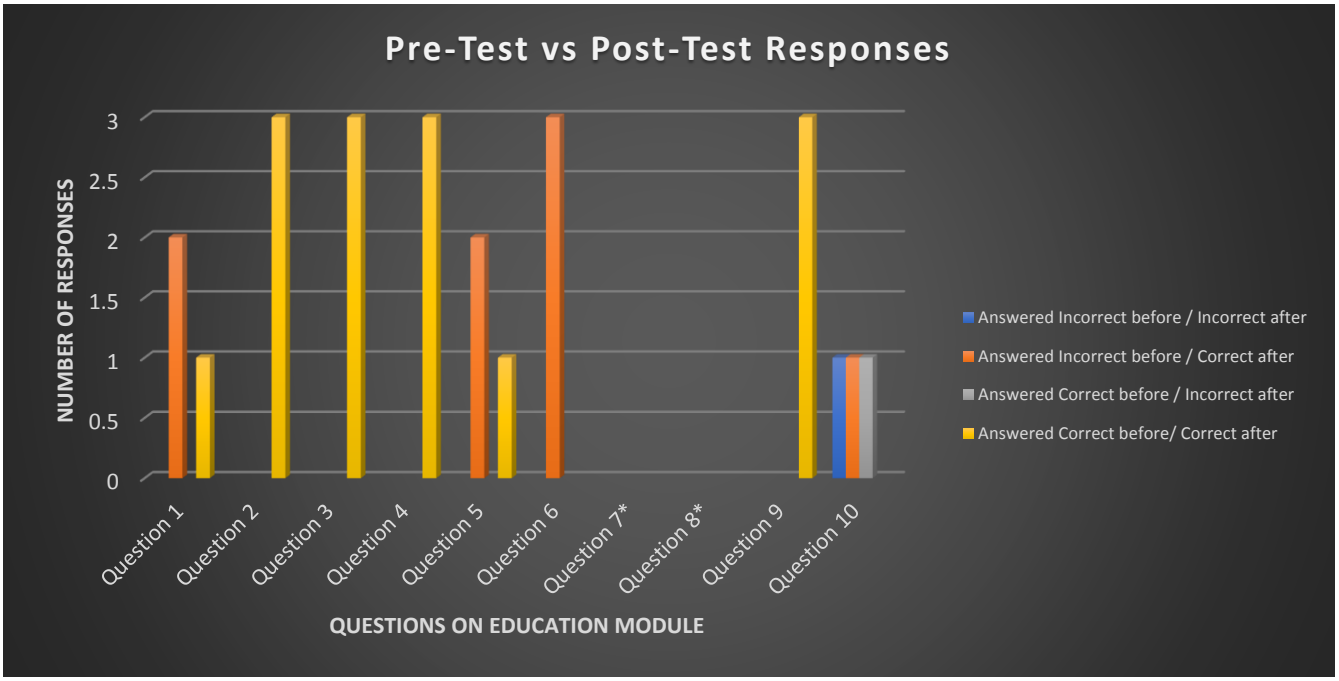


Table 2.3 Pre-Test vs Post-Test Responses



**Questions 7 and 8 were omitted in this chart and further analyzed in the following charts*

Participants were asked in question 7 "*How likely are you to utilize Sevoflurane with Cancer patients?*" and in question 8 "*How likely are you to utilize Propofol TIVA with Cancer patients?*" Both questions gave participants five answer options ranging from "*Extremely Unlikely*" to "*Extremely Likely*" The purpose of this question before and after the education module was to determine if the information provided swayed anesthesia providers to change way they administered anesthesia to cancer patients. The two questions would not only indicate learning had occurred, but positive change has effectively taken place. The following chart depicts participant responses.

Table 2.4 Question 7 Pre-Test Responses

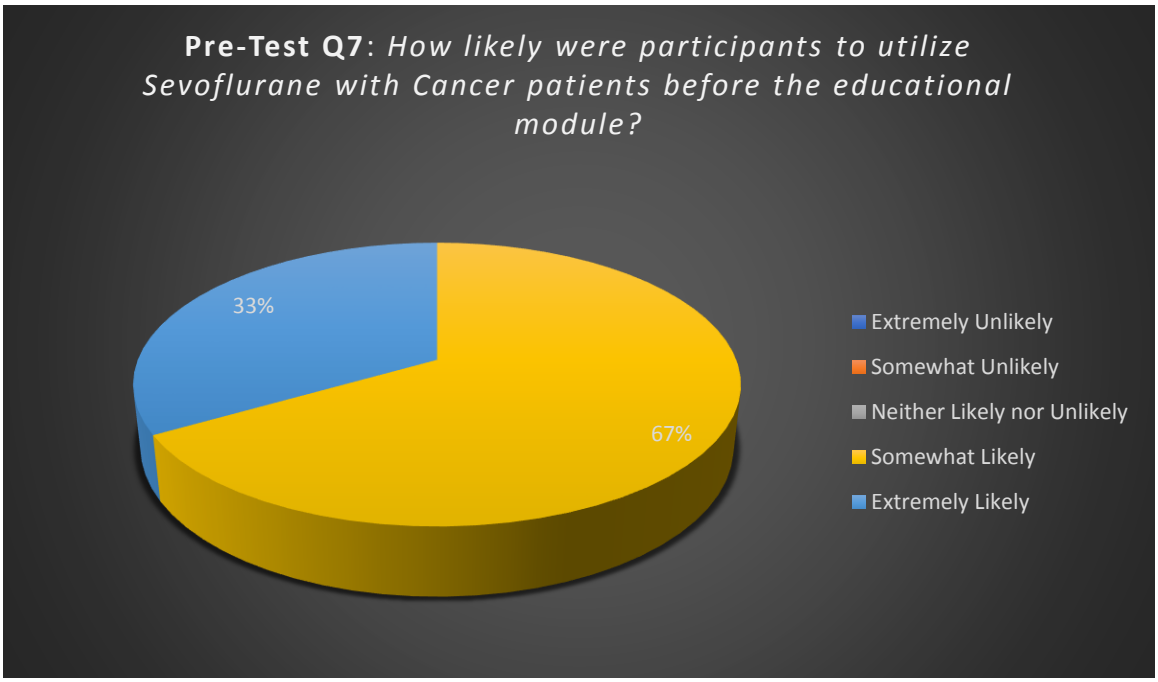


Table 2.5 Question 7 Post-Test Responses

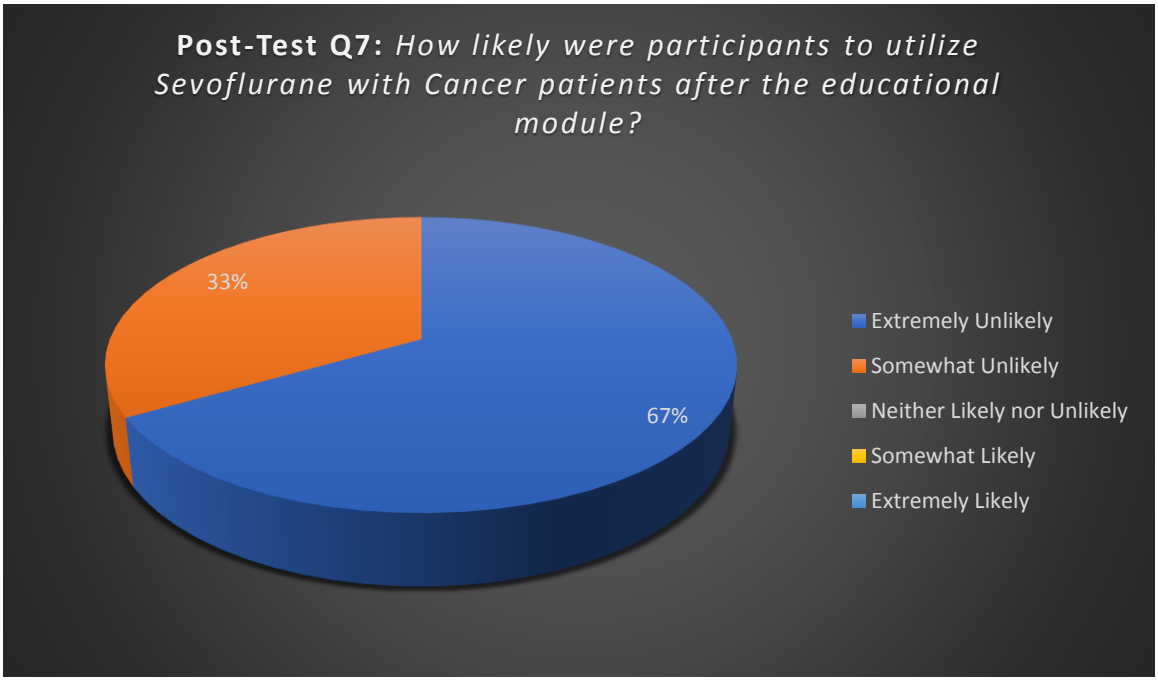


Table 2.6 Question 8 Pre-Test Responses

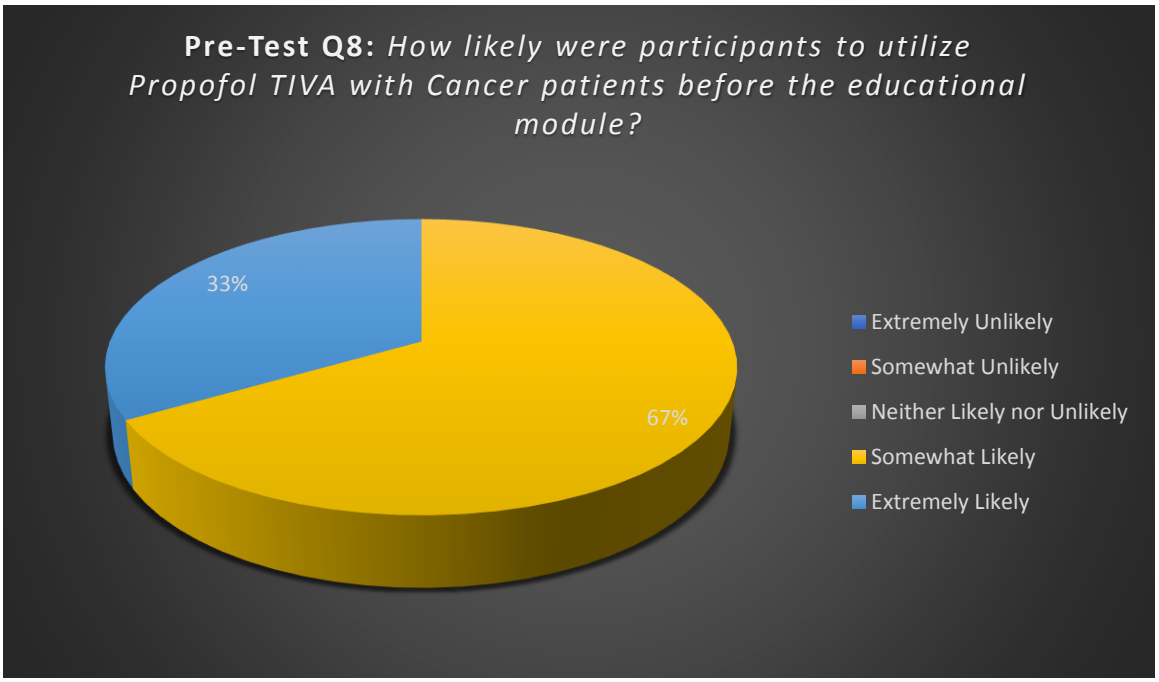
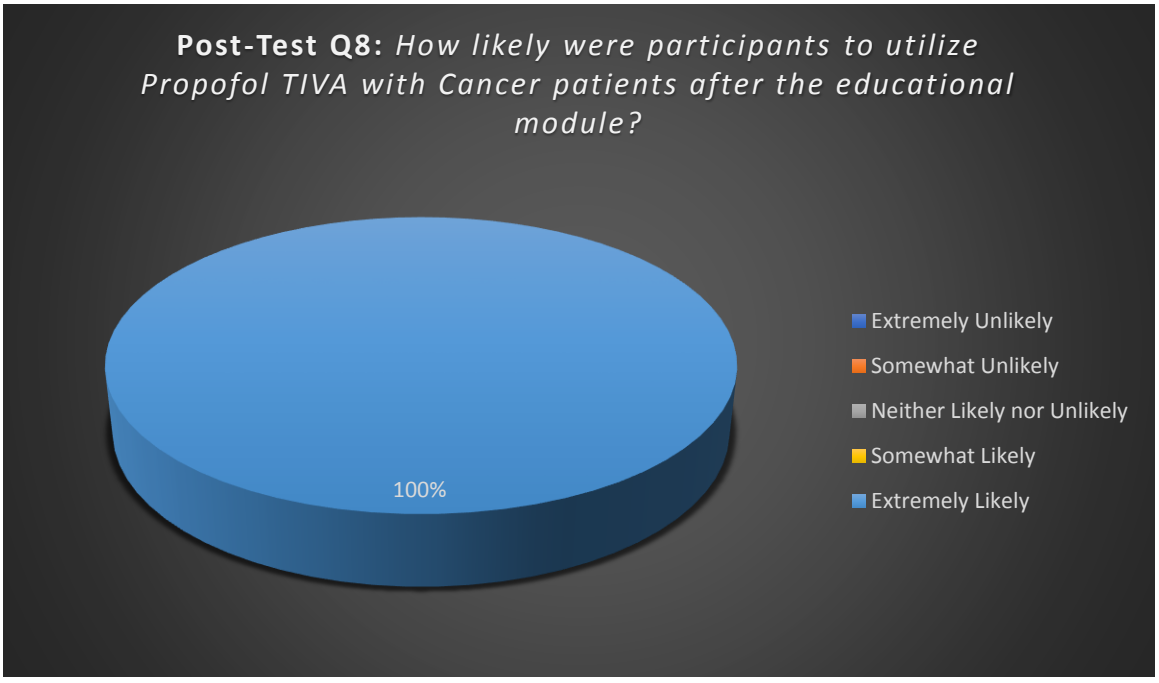


Table 2.7 Question 8 Post-Test Responses



Although correlation does not equal causation, the study findings are strongly suggestive that learning has occurred and positive change in mindset on anesthetic practice has effectively taken place. This is evident by the change in responses. In question 7 when participants were asked "*How likely are you to utilize Sevoflurane with Cancer patients?*" 67% of participants responded they were 'Somewhat likely' and 33% said 'Extremely likely.' After the educational module, when asked the same question in regard to using Sevoflurane, 67% of participants responded 'Extremely unlikely' and 33% said 'Somewhat unlikely.' Prior to the educational module participants were also asked "*How likely are you to utilize Propofol TIVA with Cancer patients?*" and 67% replied 'Somewhat like' and 33% said 'Extremely likely' After the educational module, 100% of participants responded they were 'Extremely likely.'

The study results after the educational module for question 7 "*How likely are you to utilize Sevoflurane with Cancer patients?*" reflects participant understanding of the harmful effects of Sevoflurane on cancer patients. The change in participant responses on question 8 "*How likely are you to utilize Propofol TIVA with Cancer patients?*" indicates participant understanding of the lesser immunomodulatory effects of Propofol on the oncology population.

CONCLUSION

The goal of the QI study was to educate anesthesia providers on the harmful effects of anesthesia modalities on cancer patients and provide evidence-based recommendations to improve clinical decision-making and patient outcomes. The findings generated positive outcomes, anesthesia provider knowledge on the harmful effects of anesthesia modalities on cancer patients was enhanced, inclination to utilize Propofol TIVA on patients with deadly cancers was increased, and overall enriched clinical decision-making. Ultimately, the Quality Improvement was able to answer to the research question.

REFERENCES

1. Kim R. Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. *J Transl Med*. 2018;16(1):8. Published 2018 Jan 18. doi:10.1186/s12967-018-1389-7
2. Hovaguimian F, Braun J, Z'graggen BR, et al. Anesthesia and Circulating Tumor Cells in Primary Breast Cancer Patients: A Randomized Controlled Trial. *Anesthesiology*. 2020;133(3):548-558. doi:10.1097/ALN.0000000000003409
3. Fang P, Zhou J, Xia Z, Lu Y, Liu X. Effects of Propofol *Versus* Sevoflurane on Postoperative Breast Cancer Prognosis: A Narrative Review. *Front Oncol*. 2022;11:793093. Published 2022 Jan 20. doi:10.3389/fonc.2021.793093
4. Ai L, Wang H. Effects of propofol and sevoflurane on tumor killing activity of peripheral blood natural killer cells in patients with gastric cancer. *J Int Med Res*. 2020;48(3):300060520904861. doi:10.1177/0300060520904861
5. Lim JA, Oh CS, Yoon TG, et al. The effect of propofol and sevoflurane on cancer cell, natural killer cell, and cytotoxic T lymphocyte function in patients undergoing breast cancer surgery: an in vitro analysis. *BMC Cancer*. 2018;18(1):159. Published 2018 Feb 7. doi:10.1186/s12885-018-4064-8
6. Oh CS, Park HJ, Piao L, et al. Expression Profiles of Immune Cells after Propofol or Sevoflurane Anesthesia for Colorectal Cancer Surgery: A Prospective Double-blind Randomized Trial. *Anesthesiology*. 2022;136(3):448-458. doi:10.1097/ALN.0000000000004119

7. Enlund M, Berglund A, Andreasson K, Cicek C, Enlund A, Bergkvist L. The choice of anaesthetic--sevoflurane or propofol--and outcome from cancer surgery: a retrospective analysis. *Ups J Med Sci*. 2014;119(3):251-261. doi:10.3109/03009734.2014.922649
8. Hurtado C, Bendure J, Bennetts P. Anesthetic and Analgesic Influence on Cancer Recurrence and Metastasis. *AANA J*. 2021;89(3):221-226.
9. Ren J, Wang J, Chen J, et al. The outcome of intravenous and inhalation anesthesia after pancreatic cancer resection: a retrospective study. *BMC Anesthesiol*. 2022;22(1):169. Published 2022 May 30. doi:10.1186/s12871-022-01703-8
10. Huang YH, Wu ZF, Lee MS, et al. Propofol-based total intravenous anesthesia is associated with better survival than desflurane anesthesia in glioblastoma surgery. *PLoS One*. 2021;16(8):e0255627. Published 2021 Aug 5. doi:10.1371/journal.pone.0255627
11. Tseng WC, Lee MS, Lin YC, et al. Propofol-Based Total Intravenous Anesthesia is Associated with Better Survival than Desflurane Anesthesia in Epithelial Ovarian Cancer Surgery: A Retrospective Cohort Study. *Front Pharmacol*. 2021;12:685265. Published 2021 Sep 24. doi:10.3389/fphar.2021.685265
12. Goic A. El Juramento Hipocrático [The Hippocratic Oath]. *Rev Med Chil*. 1998;126(10):1151-1152.
13. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: An overview [published online ahead of print, 2021 Apr 5]. *Int J Cancer*. 2021;10.1002/ijc.33588. doi:10.1002/ijc.33588
14. Alkabban FM, Ferguson T. Breast Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; August 7, 2021.

15. Siddiqui F, Vaqar S, Siddiqui AH. Lung Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; May 5, 2022.
16. Lotfollahzadeh S, Recio-Boiles A, Cagir B. Colon Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 10, 2022.
17. Anesthesia and cancer recurrence. Uptodate.com. Updated December 2022. Accessed January 2023. https://www.uptodate.com/contents/anesthesia-and-cancer-recurrence#H1040624967
18. Hu XL, Tang HH, Zhou ZG, Yin F, Liu WJ. The effect of sevoflurane inhalation anesthesia only and propofol total intravenous anesthesia on perioperative cytokine balance in lung cancer patients. *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi*. 2011;27(6):659-661.
19. Tian HT, Duan XH, Yang YF, Wang Y, Bai QL, Zhang X. Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection. *Eur Rev Med Pharmacol Sci*. 2017;21(23):5515-5522. doi:10.26355/eurrev_201712_13943
20. Sen Y, Xiyang H, Yu H. Effect of thoracic paraspinal block-propofol intravenous general anesthesia on VEGF and TGF-β in patients receiving radical resection of lung cancer. *Medicine (Baltimore)*. 2019;98(47):e18088. doi:10.1097/MD.0000000000018088
21. Yamaguchi A, Kawagoe I, Inoue S, et al. Propofol decreases CD8+ T cells and sevoflurane increases regulatory T cells after lung cancer resection: a randomized controlled trial. *J Thorac Dis*. 2021;13(9):5430-5438. doi:10.21037/jtd-21-878
22. Tylman M, Sarbinowski R, Bengtson JP, Kvarnström A, Bengtsson A. Inflammatory response in patients undergoing colorectal cancer surgery: the effect of two different anesthetic techniques. *Minerva Anestesiol*. 2011;77(3):275-282.

23. Kvarnström AL, Sarbinowski RT, Bengtson JP, Jacobsson LM, Bengtsson AL. Complement activation and interleukin response in major abdominal surgery. *Scand J Immunol*. 2012;75(5):510-516. doi:10.1111/j.1365-3083.2012.02672.x

24. Chen Y, Liang M, Zhu Y, Zhou D. *Zhonghua Yi Xue Za Zhi*. The effect of propofol and sevoflurane on the perioperative immunity in patients under laparoscopic radical resection of colorectal cancer 2015;95(42):3440-3444.

25. Buckley A, McQuaid S, Johnson P, Buggy DJ. Effect of anaesthetic technique on the natural killer cell anti-tumour activity of serum from women undergoing breast cancer surgery: a pilot study. *Br J Anaesth*. 2014;113 Suppl 1:i56-i62. doi:10.1093/bja/aeu200

26. Yan T, Zhang GH, Wang BN, Sun L, Zheng H. Effects of propofol/remifentanil-based total intravenous anesthesia versus sevoflurane-based inhalational anesthesia on the release of VEGF-C and TGF-β and prognosis after breast cancer surgery: a prospective, randomized and controlled study. *BMC Anesthesiol*. 2018;18(1):131. Published 2018 Sep 22. doi:10.1186/s12871-018-0588-3

27. Cho JS, Lee MH, Kim SI, et al. The Effects of Perioperative Anesthesia and Analgesia on Immune Function in Patients Undergoing Breast Cancer Resection: A Prospective Randomized Study. *Int J Med Sci*. 2017;14(10):970-976. Published 2017 Aug 18. doi:10.7150/ijms.20064

28. Lee ZX, Ng KT, Ang E, et al. Effect of perioperative regional anesthesia on cancer recurrence: A meta-analysis of randomized controlled trials. *Int J Surg*. 2020;82:192-199. doi:10.1016/j.ijsu.2020.08.034

29. Wigmore TJ, Mohammed K, Jhanji S. Long-term Survival for Patients Undergoing Volatile versus IV Anesthesia for Cancer Surgery: A Retrospective Analysis. *Anesthesiology*. 2016;124(1):69-79. doi:10.1097/ALN.0000000000000936 [chart]
30. Awards, Accreditations, and Points of Distinction. Mount Sinai Medical Center. Updated 2021. Accessed December 11, 2022. https://www.msmc.com/about-msmc/awards-accreditations-and-points-of-distinction/
31. McQuillan RF, Silver SA, Harel Z, et al. How to Measure and Interpret Quality Improvement Data. *Clin J Am Soc Nephrol*. 2016;11(5):908-914. doi:10.2215/CJN.11511015
32. Liu S, Gu X, Zhu L, et al. Effects of propofol and sevoflurane on perioperative immune response in patients undergoing laparoscopic radical hysterectomy for cervical cancer. *Medicine (Baltimore)*. 2016;95(49):e5479. doi:10.1097/MD.0000000000005479

APPENDIX

Appendix A: Recruitment Letter

Nicole Wertheim College of Nursing & Health Sciences

Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers:
A Quality Improvement Educational Module

Dear Miami Beach Anesthesia Associate /ALUMNI Perioperative Providers:

My name is Tatiana Amaya, and I am a student from the Anesthesiology Nursing Program Department of Nurse Anesthesiology at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to increase health care providers' awareness on the harmful effects of anesthesia modalities on the oncology population and provide evidence-based recommendations to improve clinical decision-making and patient outcomes. You are eligible to take part in this project because you are a part of the Miami Beach Anesthesia Associate / ALUMNI perioperative provider.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. Next, you will complete a pre-test questionnaire, which is expected to take approximately 5 minutes. You will then be asked to view an approximately 15 minutes long educational presentation online. After going through the educational module, you will be asked to complete the post-test questionnaire, which is expected to take approximately 5 minutes. *No compensation will be provided.*

Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate or have any questions about the study, please email or contact me at Tatiana Amaya (407) 463-5913 / TAmay002@fiu.edu

Thank you very much.

Sincerely,

Tatiana Amaya MSN, RN, CCRN-CSC-CMC
(407) 463-5913
TAmay002@fiu.edu

Appendix B: QI Project IRB Exemption

FIU | Research & Economic Development
FLORIDA INTERNATIONAL UNIVERSITY

MEMORANDUM

To: Dr. Jorge Valdes

CC: Tatiana Amaya

From: Carrie Bassols, BA, IRB Coordinator CeB

Date: March 7, 2023

Proposal Title: "Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers: A Quality Improvement Educational Module"

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #:	IRB-23-0101	**IRB Exemption Date:**	03/07/23
TOPAZ Reference #:	112803		

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
1) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

Appendix C: QI Project Consent

FIU | FLORIDA INTERNATIONAL UNIVERSITY

CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT

Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers: A quality improvement educational Module

SUMMARY INFORMATION
Things you should know about this study:

- **Purpose:** Educational module to increase providers awareness of the perioperative immunosuppressive impact of Propofol and Sevoflurane based anesthesia in deadly cancer types and preferred modalities for the administration of anesthesia.
- **Procedures**: If the participant chooses to participate, they will be asked to complete a pretest, watch a voice PowerPoint, and then a post test
- **Duration:** This will take about a total of 20 minutes total. (5 minute pre-test, 10 min PowerPoint and 5 post test)
- **Risks**: There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.
- **Benefits:** The main benefit to you from this research is increase the participants knowledge on the harmful effects of anesthesia modalities on the oncology population and provide evidence-based recommendations to improve clinical decision-making and patient outcomes.
- **Alternatives:** There are no known alternatives available to the participant other than not taking part in this quality improvement project.
- **Participation:** Taking part in this quality improvement project is voluntary.

Please carefully read the entire document before agreeing to participate.

NUMBER OF STUDY PARTICIPANTS:

If the participant decides to be in this study, they will be one of 10-20 people in this research study.

PURPOSE OF THE PROJECT

The participant is being asked to be in a quality improvement project. The goal of this project is to increase providers' knowledge on the harmful effects of anesthesia modalities on deadly cancers and provide evidence-based recommendations to anesthesia personnel to improve clinical decision-making and patient outcomes. If you decide to participate, you will be 1 of 10-20 participants

DURATION OF THE PROJECT
The participation will require about 20 minutes

PROCEDURES
If the participant agrees to be in the project, PI will ask you to do the following things:
1. Complete an online 10 question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided
2. Review the educational PowerPoint Module lasting 15 minutes via Qualtrics, an Online survey product for which the URL link is provided.
3. Complete the online 10 question post-test survey via Qualtrics, an Online survey product for which the URL link is provided.

RISKS AND/OR DISCOMFORTS
The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

BENEFITS
The following benefits may be associated with participation in this project: A paradigm shift in the anesthetic management of oncology patients could signify an overall reduction in cancer recurrence rates, tumor metastasis, and mortality rates, particularly in deadly cancers. An increased participants knowledge on the harmful effects of anesthesia modalities and evidence-based recommendations for these cancer patients will improve clinical decision-making and patient outcomes. The overall objective of the program is to increase the providers' knowledge based on the current literature.

ALTERNATIVES
There are no known alternatives available to the participant other than not taking part in this project. However, if the participant would like to receive the educational material, it will be provided to them at no cost.

CONFIDENTIALITY
The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, PI might publish, it will not include any information that will make it possible to identify the participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this quality improvement project is voluntary.

COMPENSATION & COSTS
There is no cost or payment to the participant for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW

The participation in this project is voluntary. The participant is free to participate in the project or withdraw the consent at any time during the project. The participant's withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove the participant without their consent at such time that they feel it is in their best interest.

RESEARCHER CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Tatiana Amaya at (407) 463-5913 / TAmay002@fiu.edu and Dr. Valdes at (305) 302-8348 / jvalde@fiu.edu.

IRB CONTACT INFORMATION

If the participant would like to talk with someone about their rights pertaining to being a subject in this project or about ethical issues with this project, the participant may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

Appendix D: QI Project Letter of Support

Miami Beach Anesthesiology Associates, Inc.

Mount Sinai Medical Center • Division of Anesthesia

February 2, 2023

Jorge A. Valdes, DNP, CRNA, APRN, FAANA
Clinical Associate Professor
Department of Nurse Anesthesiology
Florida International University

Dr. Valdes,

Thank you for inviting Miami Beach Anesthesiology Associates to participate in the Doctor of Nursing Practice (DNP) project conducted by Tatiana Amaya entitled "Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers: Quality Improvement Educational Module" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthesiology at Florida International University. I have granted the student permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This proposed quality improvement project seeks to utilize the latest literature to increase providers awareness on the harmful effects of anesthesia modalities on the oncology population and provide evidence-based recommendations to improve clinical decision-making and patient outcomes.

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password encrypted digital cloud, and only be accessible to the investigators of this study: Tatiana Amaya and Dr. Jorge Valdes, CRNA, FAANA.

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Tatiana Amaya will behave professionally, follow standards of care, and not impede hospital performance. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

Respectfully,

Jampierre (J.P.) Mato, DNP, CRNA, APRN
Executive CRNA Director
SRNA Coordinator/Supervisor
Electronic Mail: Jampierre@bellsouth.net
Mobile Phone: 954-668-6080

4300 Alton Road, Suite 2454, Miami Beach, FL 33140
Office (305) 674-2742 • Facsimile (305) 674-9723

Appendix E: QI Project Pre-test and Post-test Survey

Pretest and Posttest Questionnaire:

Immunomodulation of Propofol versus Sevoflurane based Anesthesia on Deadly Cancers:

A Quality Improvement Educational Module

INTRODUCTION

The primary aim of this QI project is to increase providers' awareness of the harmful effects of anesthesia modalities on the oncology population and provide evidence-based recommendations to improve clinical decision-making and patient outcomes

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format and are meant to measure knowledge on the immunomodulation effects of anesthesia modalities on cancer patients

PERSONAL INFORMATION

1. **Gender:** Male Female Other_____
2. **Ages 25 and above: _____**
3. **Ethnicity:** Hispanic Caucasian African American Asian Other_____
4. **Position/Title:** CRNA Anesthesiologist Resident Anesthesiologist Assistant
5. **Level of Education:** Certificate Bachelors Masters DNP PhD
6. How many years have you been a perioperative provider?

   Over 10 5-10 years 2-5 years 1-2 years

QUESTIONNAIRE

1. **Which of the following are the most common cancers? Select 3:**
    a. Pancreatic
    b. Colorectal
    c. Lung
    d. Skin
    e. Gastric
    f. Ovarian
    g. Breast
2. **Inhibition of immune response by anesthesia may contribute to proliferation of circulating tumor cells and have pro-tumorigenic consequences.**
    a. True
    b. False
3. **Which of the following anesthesia management options is recommended for a patient with Breast cancer?**
    a. Propofol TIVA, low dose sevoflurane, and morphine
    b. Propofol TIVA, paravertebral block, and ketorolac
    c. Sevoflurane, nitrous, and midazolam
    d. Isoflurane, ketamine, and fentanyl
4. **Which of the following anesthesia management options is recommended for a patient with Lung cancer?**
    a. Propofol TIVA, ketamine, and morphine
    b. Sevoflurane, nitrous, and celecoxib

c. Propofol TIVA, lidocaine, paravertebral block

d. Isoflurane, midazolam and fentanyl

5. **Which of the following anesthesia management options is recommended for a patient with Colorectal cancer?**

    a. Sevoflurane, ketamine, and fentanyl

    b. Propofol TIVA, paravertebral block, and morphine

    c. Propofol TIVA, remifentanil, and ketorolac

    d. Isoflurane, nitrous, and midazolam

6. **All of the following anesthesia management options should be generally avoided in cancer patients, except?**

    a. Nitrous

    b. Ketamine

    c. Halothane

    d. Morphine

    e. Ketorolac

7. **How likely are you to utilize Sevoflurane with Cancer patients?**

    a. Most likely

    b. Somewhat likely

    c. Somewhat unlikely

    d. Most unlikely

8. **How likely are you to utilize Propofol TIVA with Cancer patients?**

    a. Most likely

    b. Somewhat likely

c. Somewhat unlikely

d. Most unlikely

9. Regional and Local anesthesia are contraindicated for cancer patients because they induce tumor metastasis

a. True

b. False

10. Which of the following anesthesia modalities cause depression of neutrophil chemotaxis, stimulates lung and liver cancer metastasis and inhibits hematopoietic cell formation for tumor surveillance?

a. Lidocaine

b. Midazolam

c. Halothane

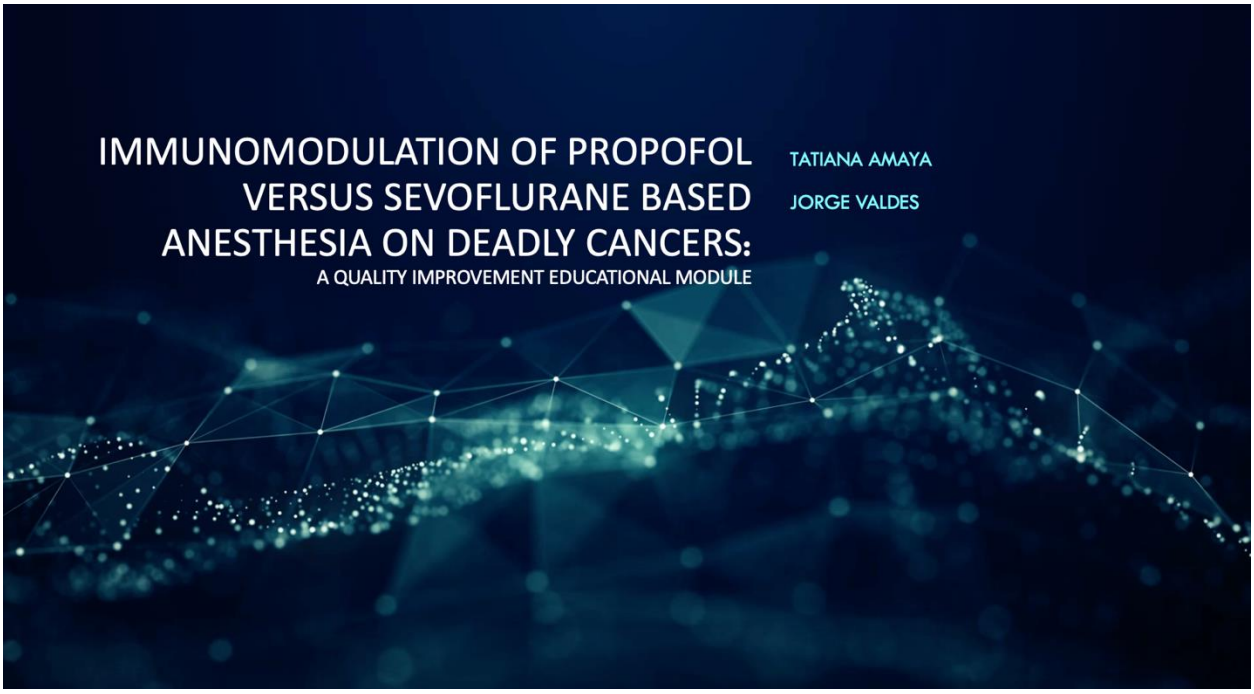
d. Nitrous

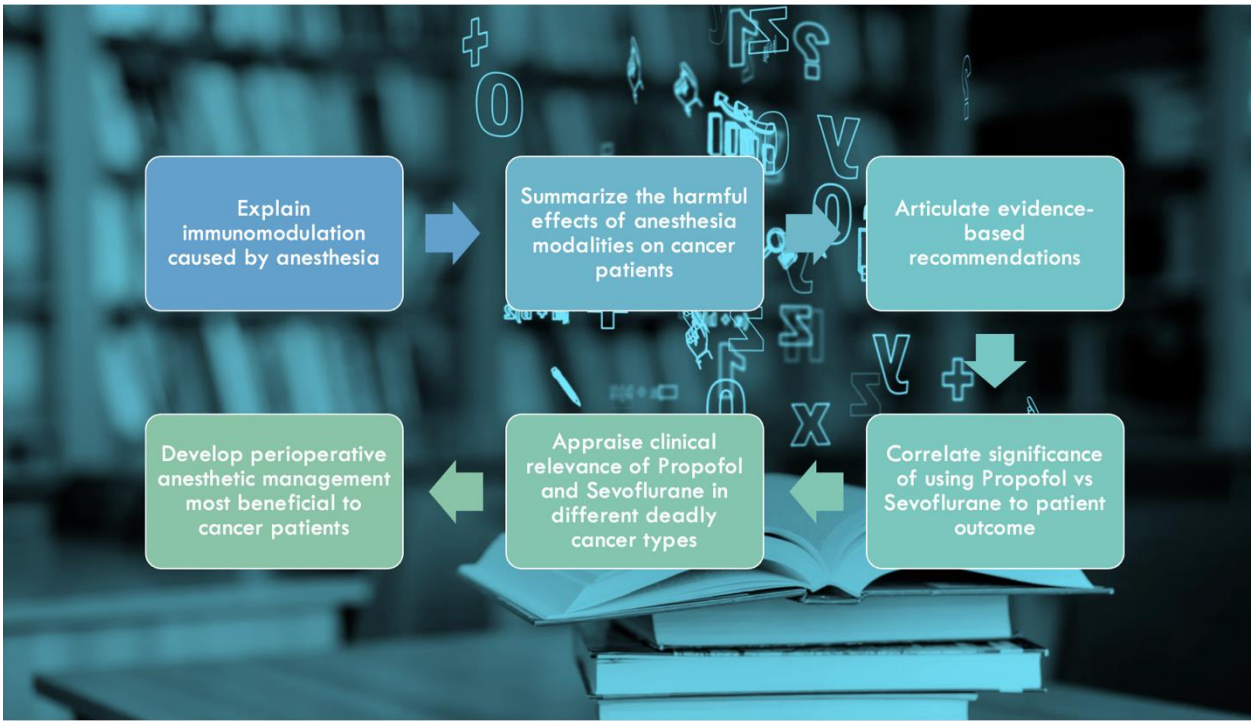
e. Sevoflurane

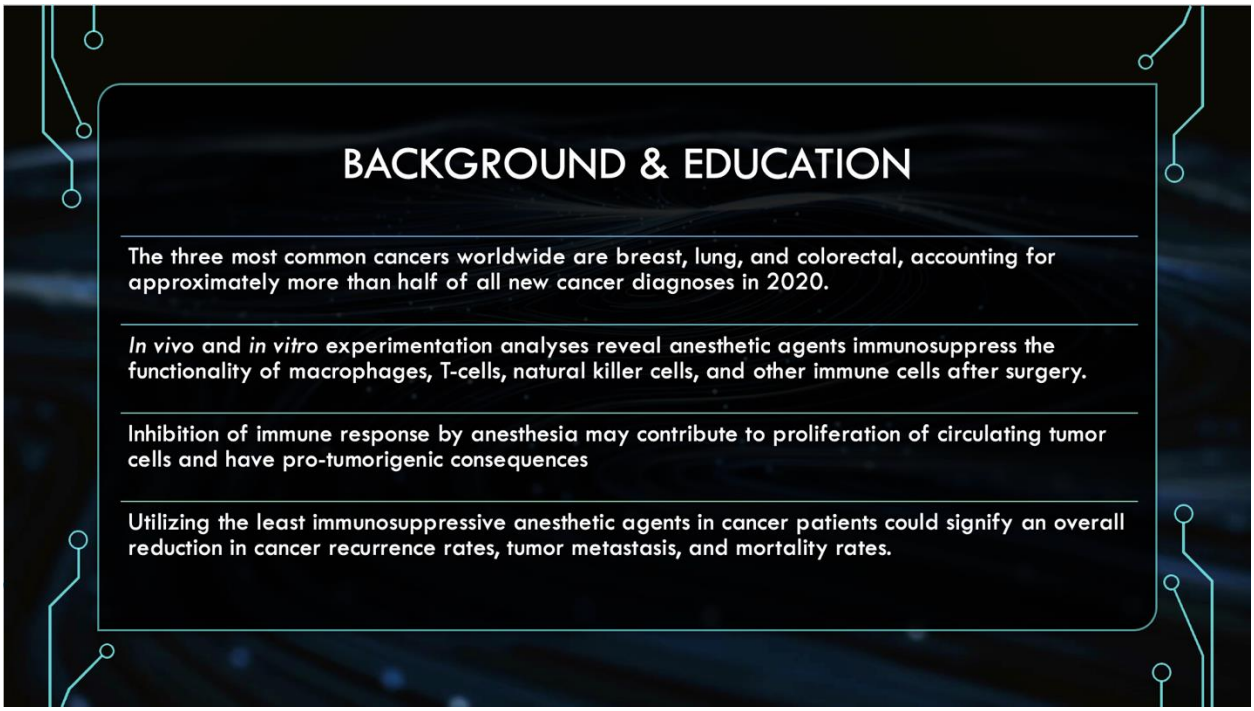
f. Isoflurane

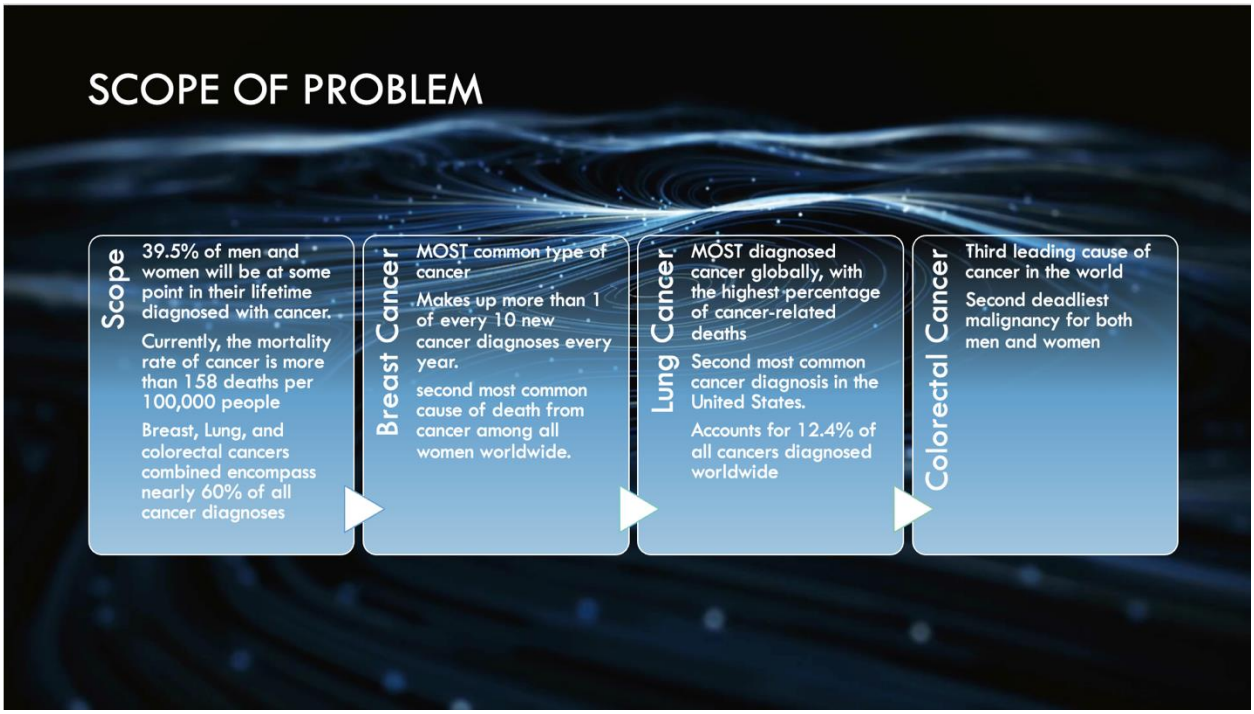
ANSWER KEY: *1)BCG, 2)A 3)B 4)C 5)C 6)E 7)_ 8)_ 9)B 10)D*

Appendix F: QI Project Educational Module

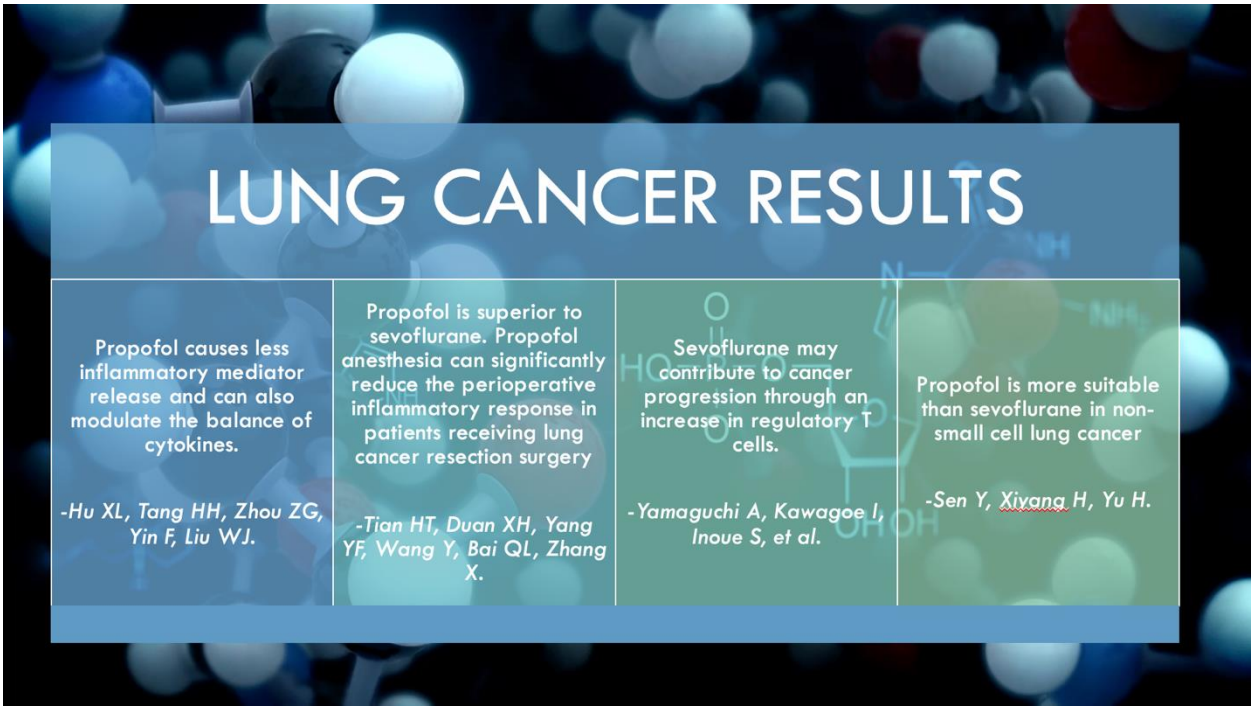


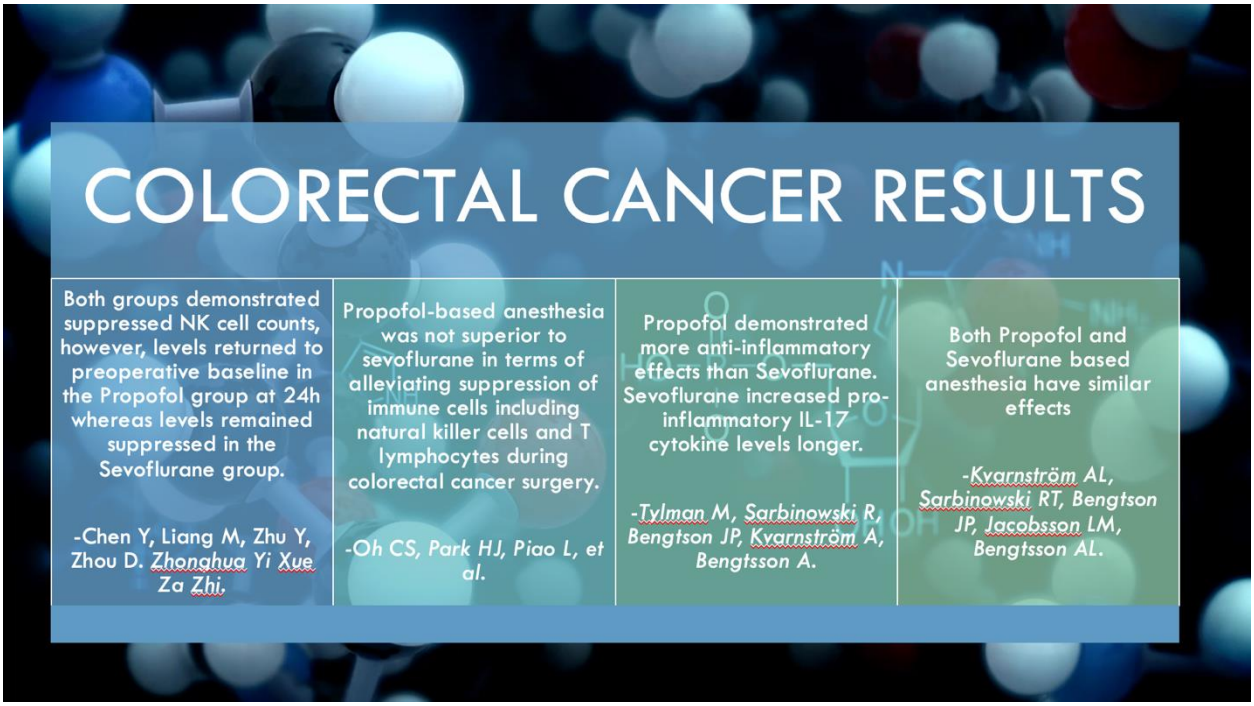


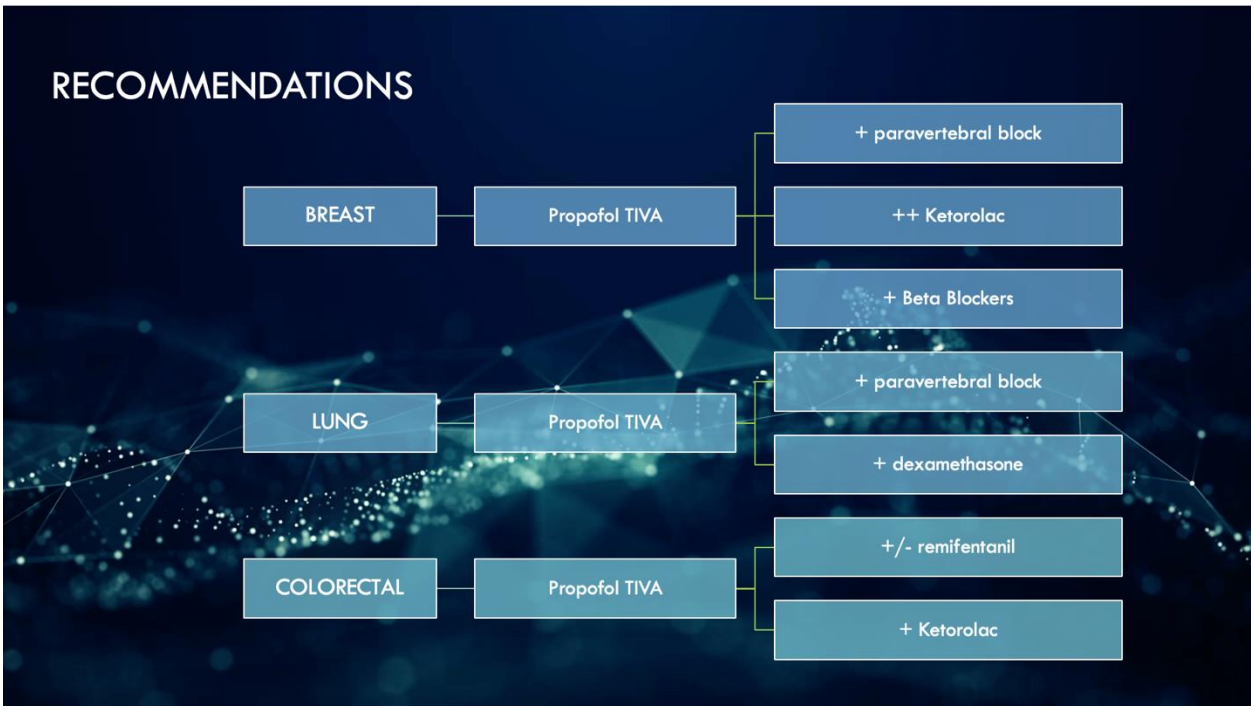

BACKGROUND & EDUCATION
The three most common cancers worldwide are breast, lung, and colorectal, accounting for approximately more than half of all new cancer diagnoses in 2020.
In vivo and *in vitro* experimentation analyses reveal anesthetic agents immunosuppress the functionality of macrophages, T-cells, natural killer cells, and other immune cells after surgery.
Inhibition of immune response by anesthesia may contribute to proliferation of circulating tumor cells and have pro-tumorigenic consequences
Utilizing the least immunosuppressive anesthetic agents in cancer patients could signify an overall reduction in cancer recurrence rates, tumor metastasis, and mortality rates.

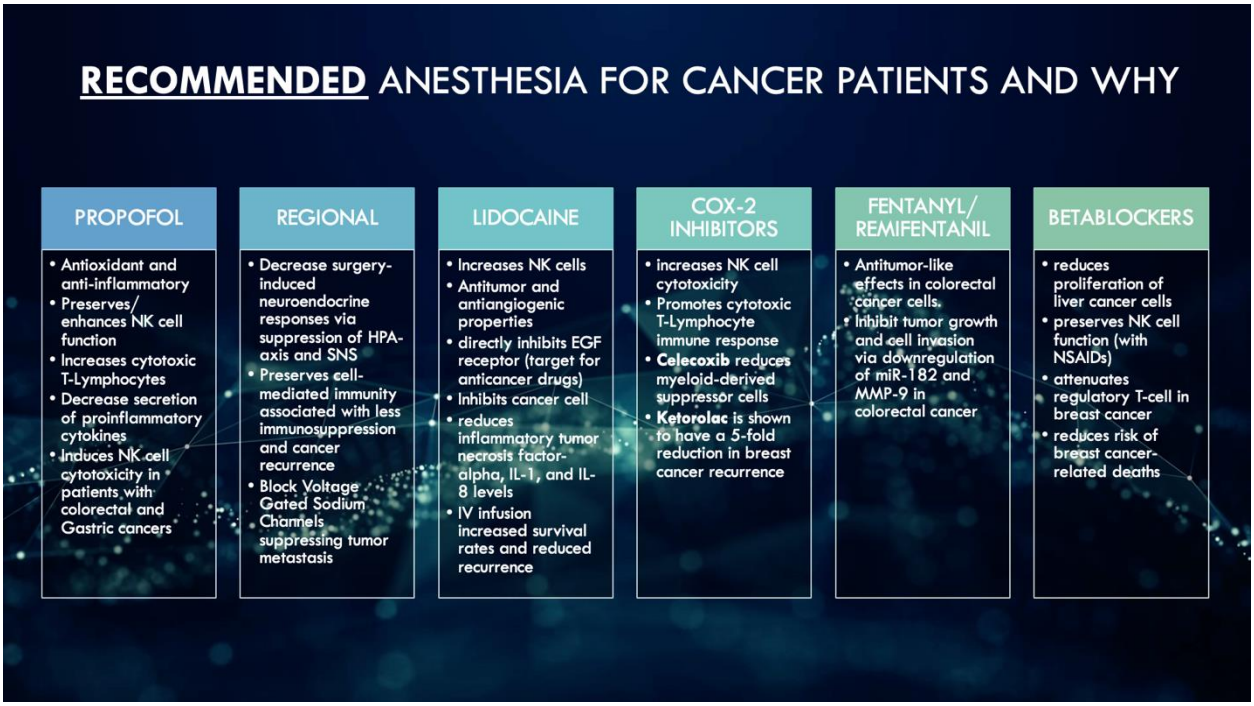

SCOPE OF PROBLEM
Scope
39.5% of men and women will be at some point in their lifetime diagnosed with cancer.
Currently, the mortality rate of cancer is more than 158 deaths per 100,000 people
Breast, Lung, and colorectal cancers combined encompass nearly 60% of all cancer diagnoses
Breast Cancer
MOST common type of cancer
Makes up more than 1 of every 10 new cancer diagnoses every year.
second most common cause of death from cancer among all women worldwide.
Lung Cancer
MOST diagnosed cancer globally, with the highest percentage of cancer-related deaths
Second most common cancer diagnosis in the United States.
Accounts for 12.4% of all cancers diagnosed worldwide
Colorectal Cancer
Third leading cause of cancer in the world
Second deadliest malignancy for both men and women

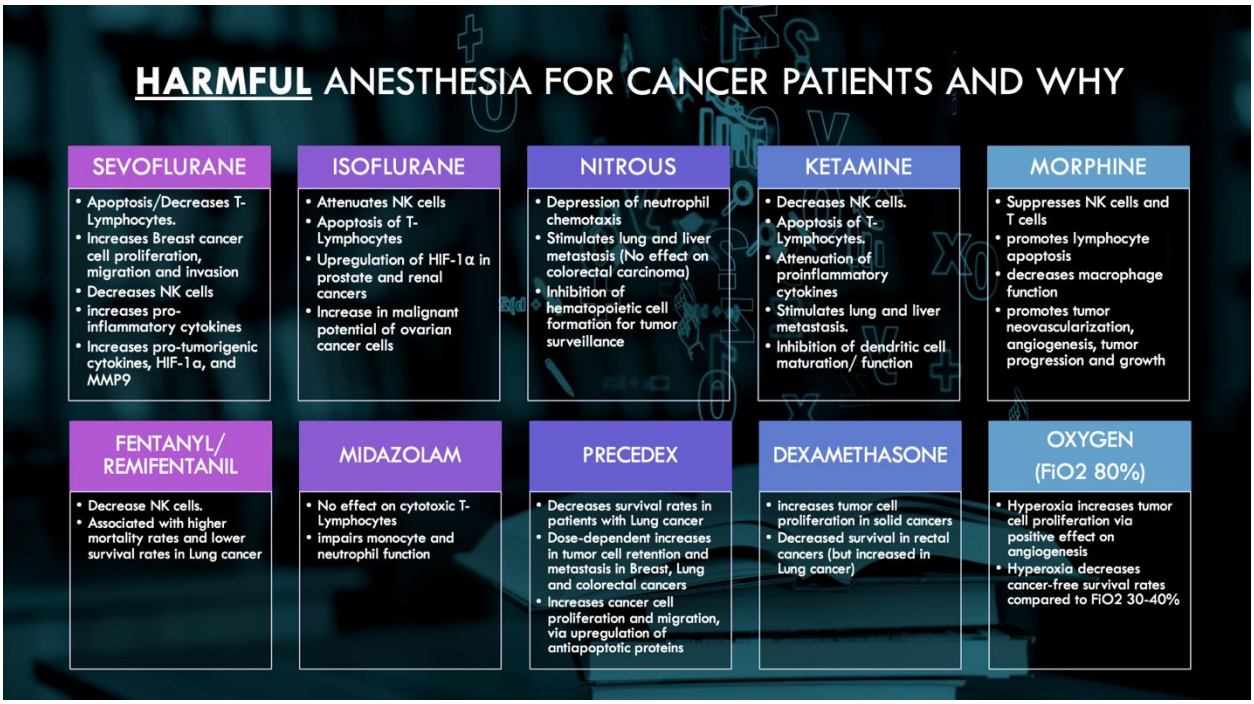

BREAST CANCER RESULTS
The effect of propofol-based anesthesia on cancer cell, NK cell and CTL functions did not differ from that of sevoflurane-based anesthesia in breast cancer surgery.
-Lim JA, Oh CS, Yoon TG, et al.
Minimal changes in immune cells between both propofol and sevoflurane during breast cancer surgery. The difference in immunosuppression caused by Propofol and Sevoflurane was statistically insignificant
-Oh CS, Lee J, Yoon TG, et al.
Propofol-based anesthesia effectively inhibits the release of VEGF-C induced by breast cancer surgery compared to sevoflurane-based anesthesia.
-Yan T, Zhang GH, Wang BN, Sun L, Zheng H.
Patients in the propofol group maintained healthy donor NK anti-tumour cell activity compared with serum from women in the sevoflurane group.
-Buckley A, McQuaid S, Johnson P, Buggy DJ.
Propofol anesthesia demonstrated a favorable impact on immune function by preserving NKCC compared with sevoflurane.
-Cho JS, Lee MH, Kim SI, et al.

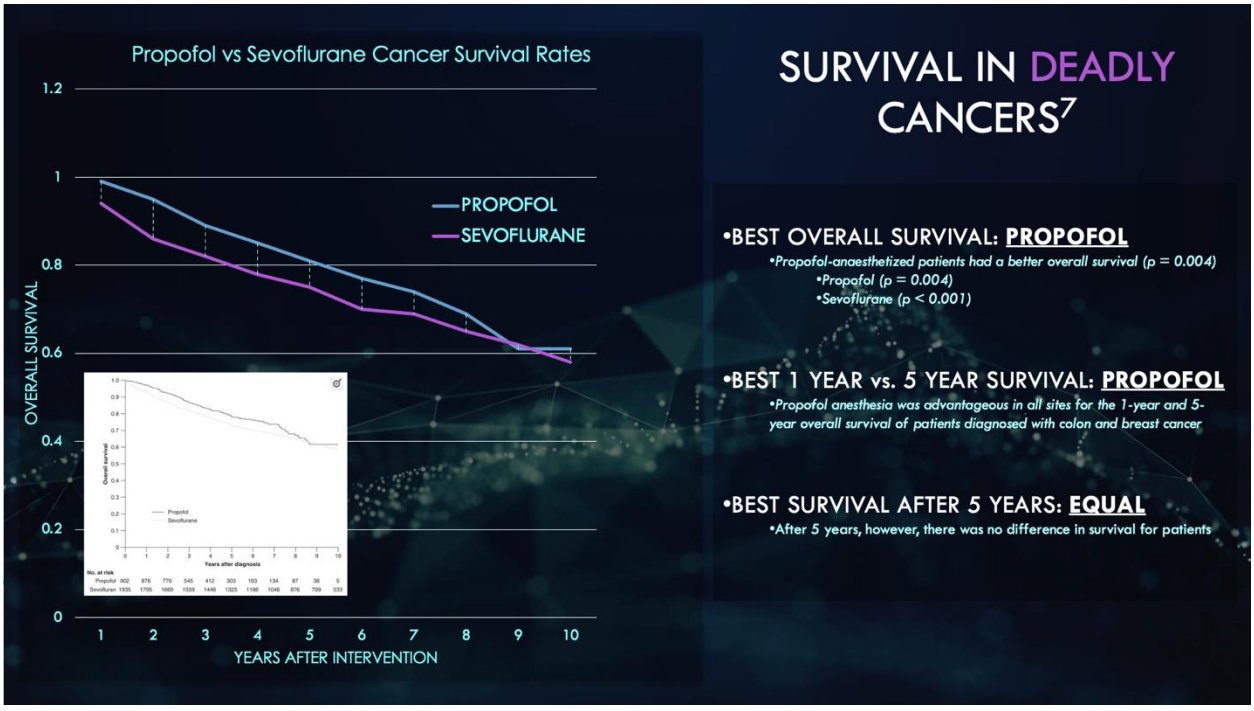

LUNG CANCER RESULTS
Propofol causes less inflammatory mediator release and can also modulate the balance of cytokines.
-Hu XL, Tang HH, Zhou ZG, Yin F, Liu WJ.
Propofol is superior to sevoflurane. Propofol anesthesia can significantly reduce the perioperative inflammatory response in patients receiving lung cancer resection surgery
-Tian HT, Duan XH, Yang YF, Wang Y, Bai QL, Zhang X.
Sevoflurane may contribute to cancer progression through an increase in regulatory T cells.
-Yamaguchi A, Kawagoe I, Inoue S, et al.
Propofol is more suitable than sevoflurane in non-small cell lung cancer
-Sen Y, Xiyang H, Yu H.

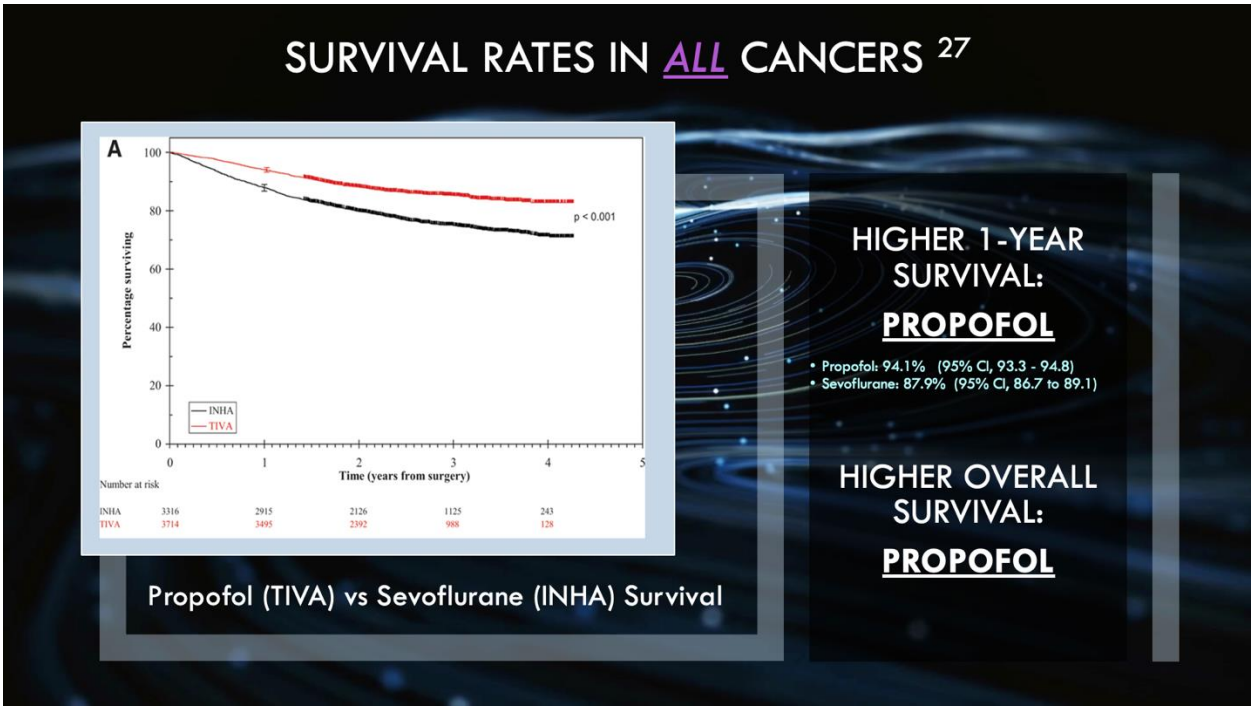

COLORECTAL CANCER RESULTS
Both groups demonstrated suppressed NK cell counts, however, levels returned to preoperative baseline in the Propofol group at 24h whereas levels remained suppressed in the Sevoflurane group.
-Chen Y, Liang M, Zhu Y, Zhou D. Zhonghua Yi Xue Za Zhi.
Propofol-based anesthesia was not superior to sevoflurane in terms of alleviating suppression of immune cells including natural killer cells and T lymphocytes during colorectal cancer surgery.
-Oh CS, Park HJ, Piao L, et al.
Propofol demonstrated more anti-inflammatory effects than Sevoflurane. Sevoflurane increased pro-inflammatory IL-17 cytokine levels longer.
-Tylman M, Sarbinowski R, Bengtson JP, Kvarnström A, Bengtsson A.
Both Propofol and Sevoflurane based anesthesia have similar effects
-Kvarnström AL, Sarbinowski RT, Bengtson JP, Jacobsson LM, Bengtsson AL.


RECOMMENDATIONS
BREAST
Propofol TIVA
+ paravertebral block
++ Ketorolac
+ Beta Blockers
LUNG
Propofol TIVA
+ paravertebral block
+ dexamethasone
COLORECTAL
Propofol TIVA
+/- remifentanil
+ Ketorolac

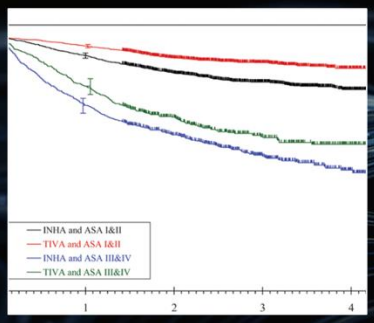

RECOMMENDED ANESTHESIA FOR CANCER PATIENTS AND WHY
PROPOFOL
• Antioxidant and anti-inflammatory
• Preserves/ enhances NK cell function
• Increases cytotoxic T-Lymphocytes
• Decrease secretion of proinflammatory cytokines
• Induces NK cell cytotoxicity in patients with colorectal and Gastric cancers
REGIONAL
• Decrease surgery-induced neuroendocrine responses via suppression of HPA-axis and SNS
• Preserves cell-mediated immunity associated with less immunosuppression and cancer recurrence
• Block Voltage Gated Sodium Channels suppressing tumor metastasis
LIDOCAINE
• Increases NK cells
• Antitumor and antiangiogenic properties
• directly inhibits EGF receptor (target for anticancer drugs)
• Inhibits cancer cell
• reduces inflammatory tumor necrosis factor-alpha, IL-1, and IL-8 levels
• IV infusion increased survival rates and reduced recurrence
COX-2 INHIBITORS
• increases NK cell cytotoxicity
• Promotes cytotoxic T-Lymphocyte immune response
• Celecoxib reduces myeloid-derived suppressor cells
• Ketorolac is shown to have a 5-fold reduction in breast cancer recurrence
FENTANYL/ REMIFENTANIL
• Antitumor-like effects in colorectal cancer cells.
• Inhibit tumor growth and cell invasion via downregulation of miR-182 and MMP-9 in colorectal cancer
BETABLOCKERS
• reduces proliferation of liver cancer cells
• preserves NK cell function (with NSAIDs)
• attenuates regulatory T-cell in breast cancer
• reduces risk of breast cancer-related deaths


HARMFUL ANESTHESIA FOR CANCER PATIENTS AND WHY
SEVOFLURANE
• Apoptosis/Decreases T-Lymphocytes.
• Increases Breast cancer cell proliferation, migration and invasion
• Decreases NK cells
• increases pro-inflammatory cytokines
• Increases pro-tumorigenic cytokines, HIF-1a, and MMP9
ISOFLURANE
• Attenuates NK cells
• Apoptosis of T-Lymphocytes
• Upregulation of HIF-1α in prostate and renal cancers
• Increase in malignant potential of ovarian cancer cells
NITROUS
• Depression of neutrophil chemotaxis
• Stimulates lung and liver metastasis (No effect on colorectal carcinoma)
• Inhibition of hematopoietic cell formation for tumor surveillance
KETAMINE
• Decreases NK cells.
• Apoptosis of T-Lymphocytes.
• Attenuation of proinflammatory cytokines
• Stimulates lung and liver metastasis.
• Inhibition of dendritic cell maturation/ function
MORPHINE
• Suppresses NK cells and T cells
• promotes lymphocyte apoptosis
• decreases macrophage function
• promotes tumor neovascularization, angiogenesis, tumor progression and growth
FENTANYL/ REMIFENTANIL
• Decrease NK cells.
• Associated with higher mortality rates and lower survival rates in Lung cancer
MIDAZOLAM
• No effect on cytotoxic T-Lymphocytes
• impairs monocyte and neutrophil function
PRECEDEX
• Decreases survival rates in patients with Lung cancer
• Dose-dependent increases in tumor cell retention and metastasis in Breast, Lung and colorectal cancers
• Increases cancer cell proliferation and migration, via upregulation of antiapoptotic proteins
DEXAMETHASONE
• increases tumor cell proliferation in solid cancers
• Decreased survival in rectal cancers (but increased in Lung cancer)
OXYGEN (FiO2 80%)
• Hyperoxia increases tumor cell proliferation via positive effect on angiogenesis
• Hyperoxia decreases cancer-free survival rates compared to FiO2 30-40%

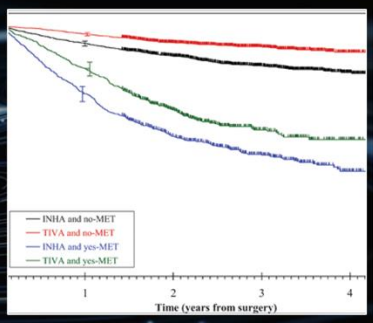

Propofol vs Sevoflurane Cancer Survival Rates
PROPOFOL
SEVOFLURANE
OVERALL SURVIVAL
YEARS AFTER INTERVENTION
SURVIVAL IN DEADLY CANCERS7
•BEST OVERALL SURVIVAL: PROPOFOL
•Propofol-anaesthetized patients had a better overall survival (p = 0.004)
•Propofol (p = 0.004)
•Sevoflurane (p < 0.001)
•BEST 1 YEAR vs. 5 YEAR SURVIVAL: PROPOFOL
•Propofol anesthesia was advantageous in all sites for the 1-year and 5-year overall survival of patients diagnosed with colon and breast cancer
•BEST SURVIVAL AFTER 5 YEARS: EQUAL
•After 5 years, however, there was no difference in survival for patients


SURVIVAL RATES IN ALL CANCERS 27
A
Percentage surviving
Time (years from surgery)
p < 0.001
INHA
TIVA
Number at risk
INHA 3316 2915 2126 1125 243
TIVA 3714 3495 2392 988 128
Propofol (TIVA) vs Sevoflurane (INHA) Survival
HIGHER 1-YEAR SURVIVAL:
PROPOFOL
• Propofol: 94.1% (95% CI, 93.3 - 94.8)
• Sevoflurane: 87.9% (95% CI, 86.7 to 89.1)
HIGHER OVERALL SURVIVAL:
PROPOFOL

SURVIVAL RATES IN *ALL* CANCER PATIENTS [27]



Propofol TIVA vs INHA ASA 1-2
Propofol TIVA vs INHA ASA 3-4



Propofol TIVA vs INHA Non-Metastatic Cancer
Propofol TIVA vs INHA Metastatic Cancer

HIGHER SURVIVAL IN ASA 1-4:
PROPOFOL

HIGHER SURVIVAL WITH OR WITHOUT METASTASIS:
PROPOFOL

MORTALITY[27]

HIGHER MORTALITY:
SEVOFLURANE/ ISOFLURANE

- *Mortality after cancer surgery was approximately 50% greater in patients who received inhaled volatile general anesthesia (Sevoflurane or Isoflurane) than Propofol TIVA*

Sevoflurane/ Isoflurane: 24%
- (796 / 3,316)

Propofol: 13.6%
- (504 / 3,714)

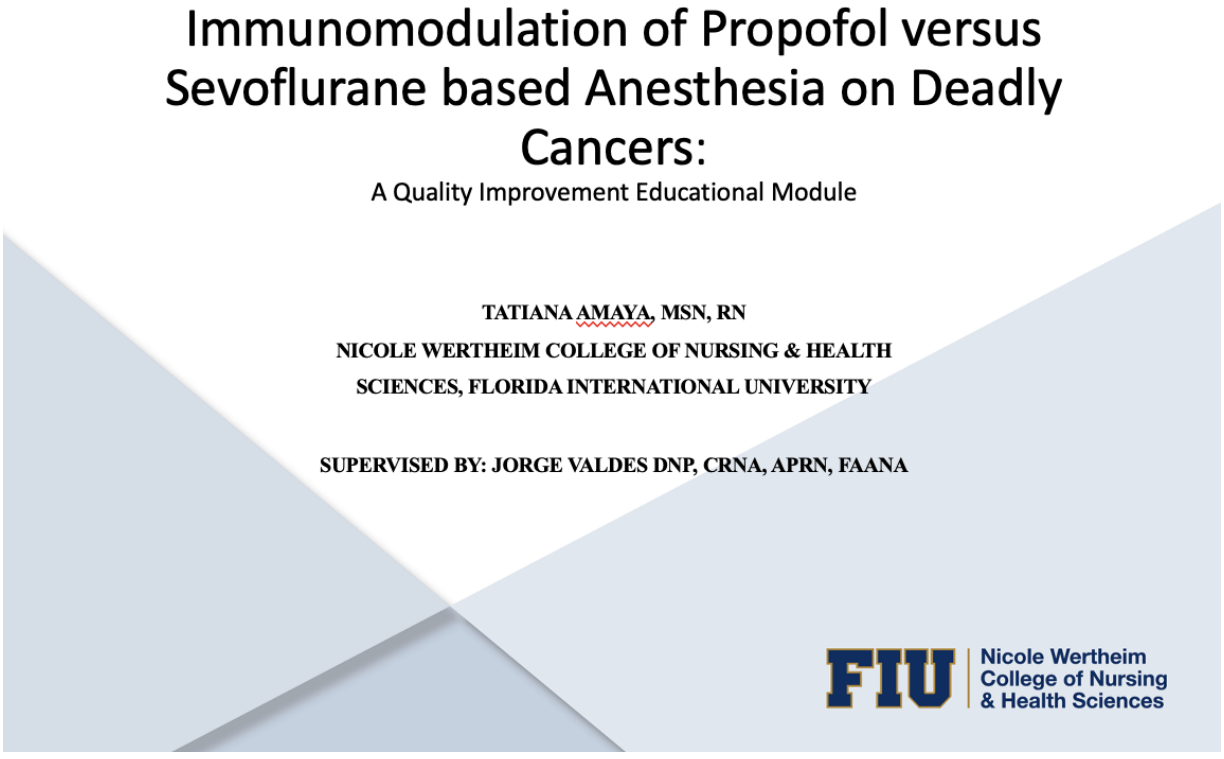
Med Res. 2020;48(3):300060520904861

5. Lim JA, Oh CS, Yoon TG, et al. The effect of propofol and sevoflurane on cancer cell, natural killer cell, and cytotoxic T lymphocyte function in patients undergoing breast cancer surgery: an in vitro analysis. *BMC Cancer*. 2018;18(1):159. Published 2018 Feb 7. doi:10.1186/s12885-018-4064-8

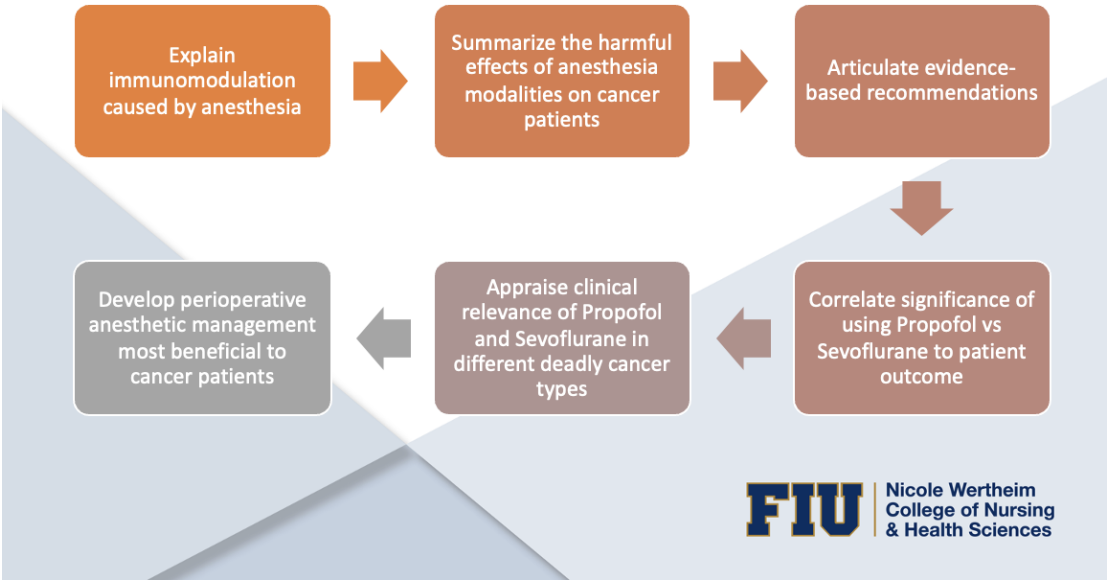
REFERENCES

6. Oh CS, Park HJ, Piao L, et al. Expression Profiles of Immune Cells after Propofol or Sevoflurane Anesthesia for Colorectal Cancer Surgery: A Prospective Double-blind Randomized Trial. *Anesthesiology*. 2022;136(3):448-458. doi:10.1097/ALN.0000000000004119
7. Enlund M, Berglund A, Andreasson K, Cicek C, Enlund A, Bergkvist L. The choice of anaesthetic--sevoflurane or propofol--and outcome from cancer surgery: a retrospective analysis. *Ups J Med Sci*. 2014;119(3):251-261. doi:10.3109/03009734.2014.922649
8. Hurtado C, Bendure J, Bennetts P. Anesthetic and Analgesic Influence on Cancer Recurrence and Metastasis. *AANA J*. 2021;89(3):221-226.
9. Ren J, Wang J, Chen J, et al. The outcome of intravenous and inhalation anesthesia after pancreatic cancer resection: a retrospective study. *BMC Anesthesiol*. 2022;22(1):169. Published 2022 May 30. doi:10.1186/s12871-022-01703-8
10. Huang YH, Wu ZF, Lee MS, et al. Propofol-based total intravenous anesthesia is associated with better survival than desflurane anesthesia in glioblastoma surgery. *PLoS One*. 2021;16(8):e0255627. Published 2021 Aug 5. doi:10.1371/journal.pone.0255627
11. Tseng WC, Lee MS, Lin YC, et al. Propofol-Based Total Intravenous Anesthesia is Associated with Better Survival than Desflurane Anesthesia in Epithelial Ovarian Cancer Surgery: A Retrospective Cohort Study. *Front Pharmacol*. 2021;12:685265. Published 2021 Sep 24. doi:10.3389/fphar.2021.685265
12. Goic A. El Juramento Hipocrático [The Hippocratic Oath]. *Rev Med Chil*. 1998;126(10):1151-1152.
13. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: An overview [published online ahead of print, 2021 Apr 5]. *Int J Cancer*. 2021;10.1002/ijc.33588. doi:10.1002/ijc.33588
14. Alkabban FM, Ferguson T. Breast Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; August 7, 2021.
15. Siddiqui F, Vaqar S, Siddiqui AH. Lung Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; May 5, 2022.
16. Lotfollahzadeh S, Recio-Boiles A, Cagir B. Colon Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 10, 2022.
17. Tohme S, Simmons RL, Tsung A. Surgery for Cancer: A Trigger for Metastases. *Cancer Res*. 2017;77(7):1548-1552. doi:10.1158/0008-5472.CAN-16-1536

Appendix G: QI Project Dissemination



OBJECTIVES



Background & Education

The three most common cancers worldwide are breast, lung, and colorectal, accounting for approximately more than half of all new cancer diagnoses in 2020.

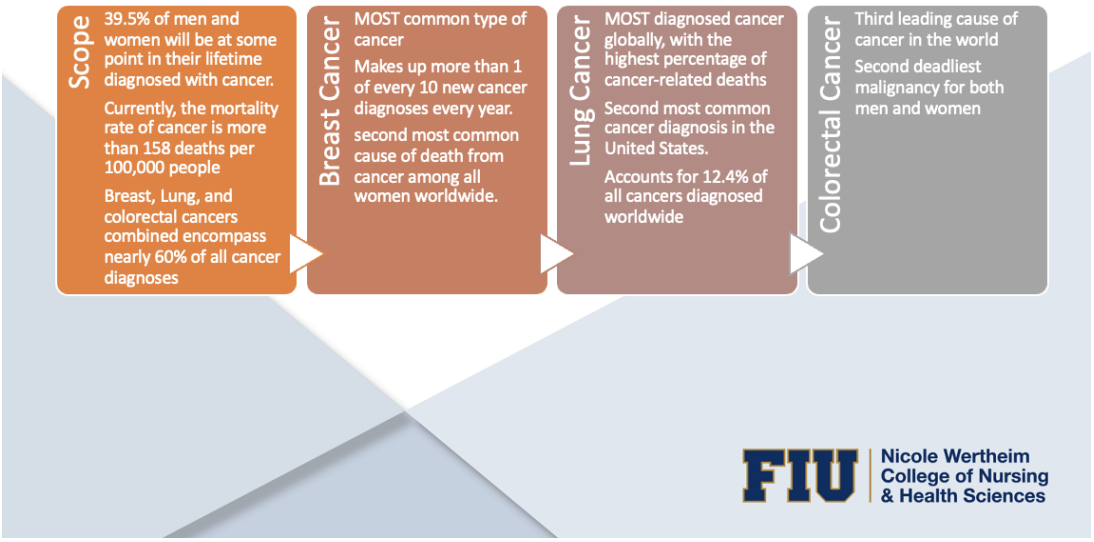
In vivo and *in vitro* experimentation analyses reveal anesthetic agents immunosuppress the functionality of macrophages, T-cells, natural killer cells, and other immune cells after surgery.

Inhibition of immune response by anesthesia may contribute to proliferation of circulating tumor cells and have pro-tumorigenic consequences

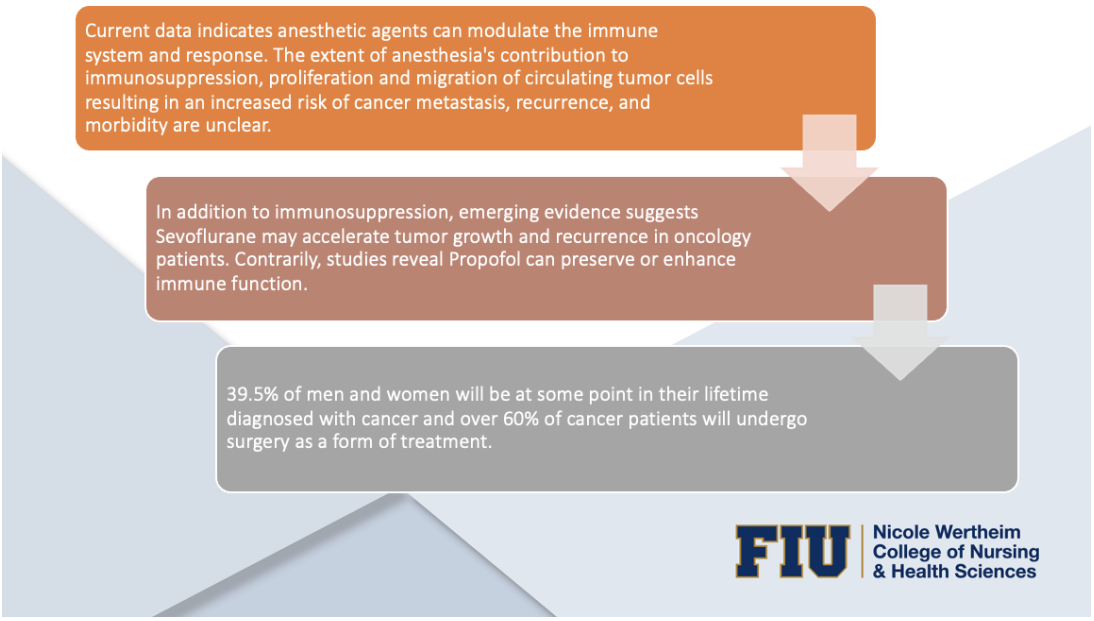
Utilizing the least immunosuppressive anesthetic agents in cancer patients could signify an overall reduction in cancer recurrence rates, tumor metastasis, and mortality rates.

FIU Nicole Wertheim College of Nursing & Health Sciences

SCOPE OF PROBLEM



DNP Project Purpose



DNP Project Purpose

There are currently no standard recommendations for the anesthesia management of these patients. The three most common cancers worldwide responsible for the most deaths are breast, lung, and colorectal, thus comparative studies in these cancers were reviewed to provide guidance for perioperative anesthetic management.

This study aims to educate anesthesia providers on the harmful effects of anesthesia modalities on cancer patients and provide evidence-based recommendations to improve clinical decision-making and patient outcomes.

FIU Nicole Wertheim College of Nursing & Health Sciences

In oncology patients undergoing cancer surgery, how does using Propofol-based anesthesia compared to Sevoflurane-based anesthesia affect immunosuppression in oncology patients within the perioperative period?

PICO

- Population (P): Oncology patients undergoing cancer surgery
- Intervention (I): Propofol-based anesthesia
- Comparison (C): Sevoflurane-based anesthesia
- Outcome (O): Affect immunosuppression
- Time (T): Perioperative period

FIU Nicole Wertheim College of Nursing & Health Sciences

Quality Improvement Methods

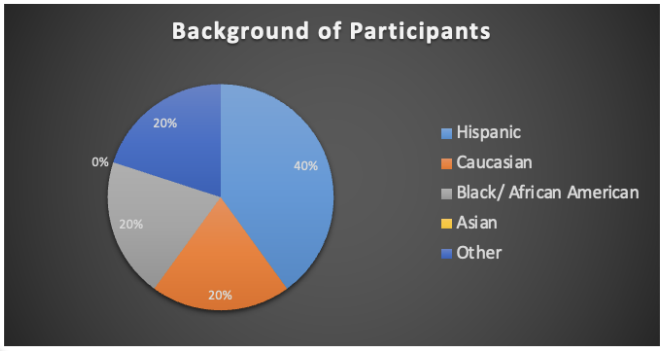
IRB APPROVAL REQUESTED AND GRANTED FROM FIU AND ALUMNI

ANONYMOUS LINK SENT TO PROVIDERS VIA EMAIL WITH LINK TO QUALTRICS CONTAINING PRE AND POST QUESTIONNAIRES AND THE EDUCATIONAL MODULE.

A VOICEOVER POWERPOINT WAS USED TO PRESENT THE EDUCATIONAL MODULE.

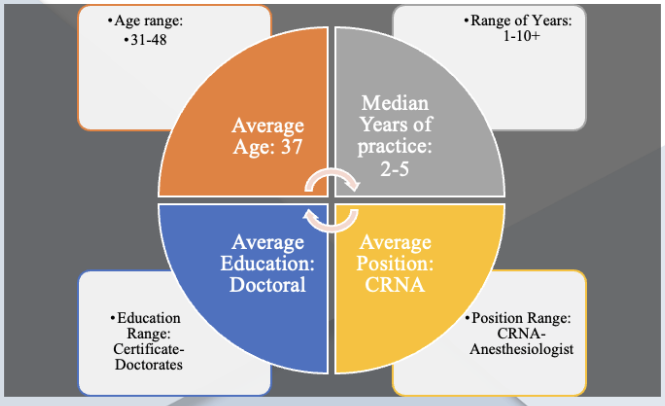
DATA GENERATED VIA QUALTRICS QUESTIONNAIRES WERE EXPORTED INTO EXCEL SPREADSHEET FOR COMPARISON BETWEEN THE PRE AND POST-TESTS.

FIU | Nicole Wertheim College of Nursing & Health Sciences

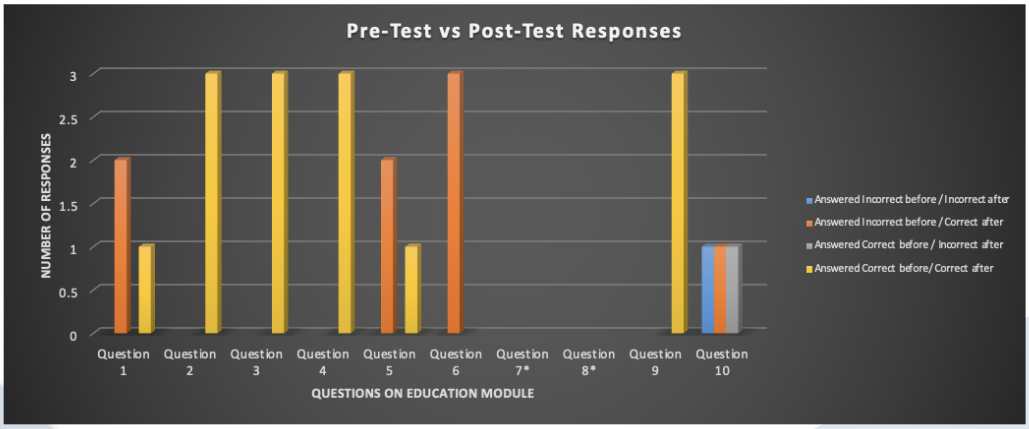


Results

Participant background and demographics as per participant responses.



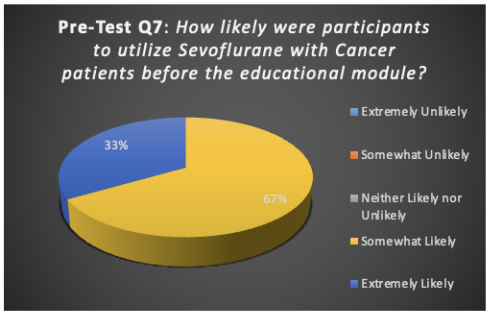
FIU | Nicole Wertheim College of Nursing & Health Sciences

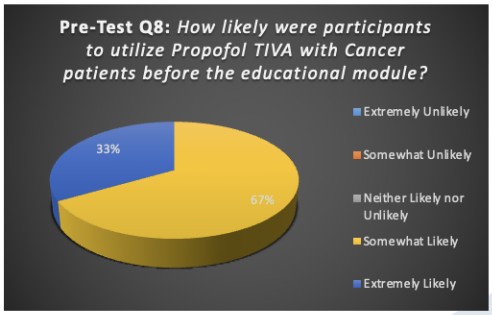


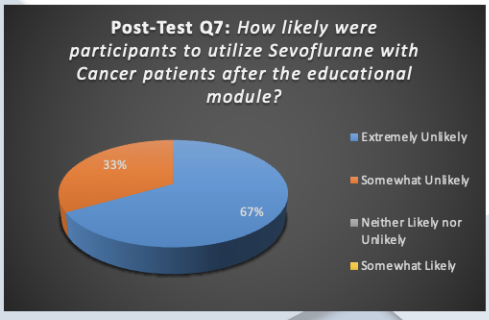
Participants were asked in question 7 "*How likely are you to utilize Sevoflurane with Cancer patients?*" and in question 8 "*How likely are you to utilize Propofol TIVA with Cancer patients?*" Both questions gave participants five answer options ranging from "*Extremely Unlikely*" to "*Extremely Likely*"

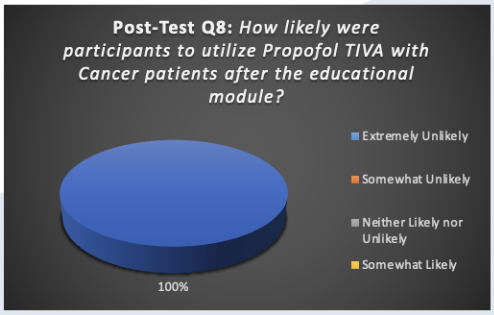
The purpose of this question before and after the education module was to determine if the information provided swayed anesthesia providers to change wav they administered anesthesia to cancer patients. The two questions would not only indicate learning had occurred, but positive change has effectively taken place. The following charts depicts participant responses.

FIU Nicole Wertheim College of Nursing & Health Sciences









FIU Nicole Wertheim College of Nursing & Health Sciences

DISCUSSION

Although correlation does not equal causation, the study findings are strongly suggestive that learning has occurred and positive change in mindset on anesthetic practice has effectively taken place. This is evident by the change in responses.

In question 7 when participants were asked "How likely are you to utilize Sevoflurane with Cancer patients?" 67% of participants responded they were 'Somewhat likely' and 33% said 'Extremely likely.'

After the educational module, when asked the same question in regard to using Sevoflurane, 67% of participants responded, 'Extremely unlikely' and 33% said 'Somewhat unlikely.'

Prior to the educational module participants were also asked in question 8 "How likely are you to utilize Propofol TIVA with Cancer patients?" and 67% replied 'Somewhat like' and 33% said 'Extremely likely'

After the educational module, 100% of participants responded they were 'Extremely likely.'

The study results after the educational module for question 7 "How likely are you to utilize Sevoflurane with Cancer patients?" reflects participant understanding of the harmful effects of Sevoflurane on cancer patients.

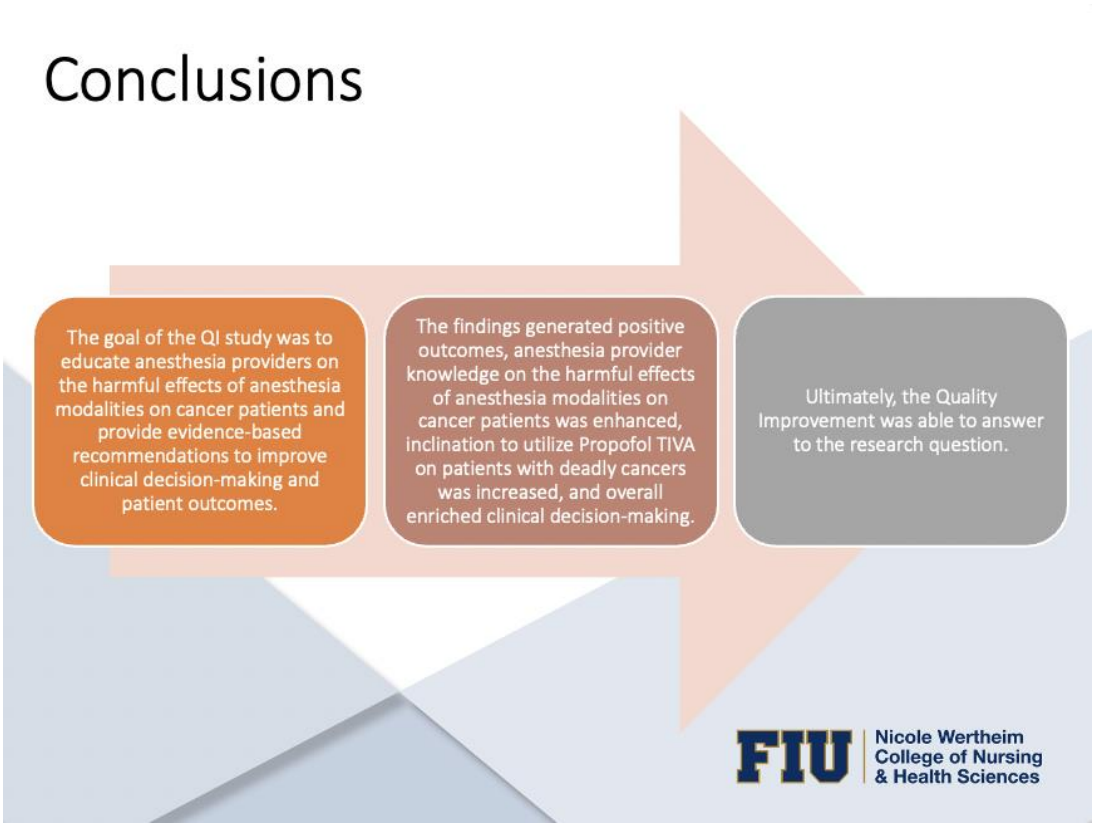
The change in participant responses on question 8 "How likely are you to utilize Propofol TIVA with Cancer patients?" indicates participant understanding of the lesser immunomodulative effects of Propofol on the oncology population.

FIU Nicole Wertheim College of Nursing & Health Sciences

DISCUSSION

- QI study limitations include small sample size and one hospital site of implementation.
- A small sample size is unable to accurately reflect the oncology population and reduces generalizability of result findings. An insufficient sample size also creates a lack of statistical power unable to back significant correlations of study findings.
- A non-response bias is also introduced due to participant involvement being fully volunteer-based and not mandatory.
- Participants were also not blinded to researchers conducting the QI, possibly contributing to response bias.
- Implementation of the study at a single hospital site introduces sampling bias limiting the external validity of the study.
- In order to address these limitations, a larger QI study must be conducted with an adequate sample size at multiple hospital sites. Participation should be required and a double-blind approach should be taken.

FIU Nicole Wertheim College of Nursing & Health Sciences


Conclusions
The goal of the QI study was to educate anesthesia providers on the harmful effects of anesthesia modalities on cancer patients and provide evidence-based recommendations to improve clinical decision-making and patient outcomes.
The findings generated positive outcomes, anesthesia provider knowledge on the harmful effects of anesthesia modalities on cancer patients was enhanced, inclination to utilize Propofol TIVA on patients with deadly cancers was increased, and overall enriched clinical decision-making.
Ultimately, the Quality Improvement was able to answer to the research question.
FIU
Nicole Wertheim College of Nursing & Health Sciences


Thank you,
Jorge Valdes
Study Participants
FIU
Nicole Wertheim College of Nursing & Health Sciences

REFERENCES

1. Kim R. Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. *J Transl Med*. 2018;16(1):8. Published 2018 Jan 18. doi:10.1186/s12967-018-1389-7
2. Hovaguimian F, Braun J, Z'graggen BR, et al. Anesthesia and Circulating Tumor Cells in Primary Breast Cancer Patients: A Randomized Controlled Trial. *Anesthesiology*. 2020;133(3):548-558. doi:10.1097/ALN.0000000000003409
3. Fang P, Zhou J, Xia Z, Lu Y, Liu X. Effects of Propofol *Versus* Sevoflurane on Postoperative Breast Cancer Prognosis: A Narrative Review. *Front Oncol*. 2022;11:793093. Published 2022 Jan 20. doi:10.3389/fonc.2021.793093
4. Ai L, Wang H. Effects of propofol and sevoflurane on tumor killing activity of peripheral blood natural killer cells in patients with gastric cancer. *J Int Med Res*. 2020;48(3):300060520904861. doi:10.1177/0300060520904861
5. Lim JA, Oh CS, Yoon TG, et al. The effect of propofol and sevoflurane on cancer cell, natural killer cell, and cytotoxic T lymphocyte function in patients undergoing breast cancer surgery: an in vitro analysis. *BMC Cancer*. 2018;18(1):159. Published 2018 Feb 7. doi:10.1186/s12885-018-4064-8
6. Oh CS, Park HJ, Piao L, et al. Expression Profiles of Immune Cells after Propofol or Sevoflurane Anesthesia for Colorectal Cancer Surgery: A Prospective Double-blind Randomized Trial. *Anesthesiology*. 2022;136(3):448-458. doi:10.1097/ALN.0000000000004119
7. Enlund M, Berglund A, Andreasson K, Cicek C, Enlund A, Bergkvist L. The choice of anaesthetic--sevoflurane or propofol--and outcome from cancer surgery: a retrospective analysis. *Ups J Med Sci*. 2014;119(3):251-261. doi:10.3109/03009734.2014.922649
8. Hurtado C, Bendure J, Bennetts P. Anesthetic and Analgesic Influence on Cancer Recurrence and Metastasis. *AANA J*. 2021;89(3):221-226.
9. Ren J, Wang J, Chen J, et al. The outcome of intravenous and inhalation anesthesia after pancreatic cancer resection: a retrospective study. *BMC Anesthesiol*. 2022;22(1):169. Published 2022 May 30. doi:10.1186/s12871-022-01703-8
10. Huang YH, Wu ZF, Lee MS, et al. Propofol-based total intravenous anesthesia is associated with better survival than desflurane anesthesia in glioblastoma surgery. *PLoS One*. 2021;16(8):e0255627. Published 2021 Aug 5. doi:10.1371/journal.pone.0255627
11. Tseng WC, Lee MS, Lin YC, et al. Propofol-Based Total Intravenous Anesthesia is Associated with Better Survival than Desflurane Anesthesia in Epithelial Ovarian Cancer Surgery: A Retrospective Cohort Study. *Front Pharmacol*. 2021;12:685265. Published 2021 Sep 24. doi:10.3389/fphar.2021.685265
12. Goic A. El Juramento Hipocrático [The Hippocratic Oath]. *Rev Med Chil*. 1998;126(10):1151-1152.
13. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: An overview [published online ahead of print, 2021 Apr 5]. *Int J Cancer*. 2021;10.1002/ijc.33588. doi:10.1002/ijc.33588
14. Alkabban FM, Ferguson T. Breast Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; August 7, 2021.
15. Siddiqui F, Vaqar S, Siddiqui AH. Lung Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; May 5, 2022.
16. Lotfollahzadeh S, Recio-Boiles A, Cagir B. Colon Cancer. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 10, 2022.

FIU | Nicole Wertheim College of Nursing & Health Sciences

REFERENCES

17. Anesthesia and cancer recurrence. Uptodate.com. Updated December 2022. Accessed January 2023. https://www.uptodate.com/contents/anesthesia-and-cancer-recurrence#H1040624967
18. Hu XL, Tang HH, Zhou ZG, Yin F, Liu WJ. The effect of sevoflurane inhalation anesthesia only and propofol total intravenous anesthesia on perioperative cytokine balance in lung cancer patients. *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi*. 2011;27(6):659-661.
19. Tian HT, Duan XH, Yang YF, Wang Y, Bai QL, Zhang X. Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection. *Eur Rev Med Pharmacol Sci*. 2017;21(23):5515-5522. doi:10.26355/eurrev_201712_13943
20. Sen Y, Xiyang H, Yu H. Effect of thoracic paraspinal block-propofol intravenous general anesthesia on VEGF and TGF-β in patients receiving radical resection of lung cancer. *Medicine (Baltimore)*. 2019;98(47):e18088. doi:10.1097/MD.0000000000018088
21. Yamaguchi A, Kawagoe I, Inoue S, et al. Propofol decreases CD8+ T cells and sevoflurane increases regulatory T cells after lung cancer resection: a randomized controlled trial. *J Thorac Dis*. 2021;13(9):5430-5438. doi:10.21037/jtd-21-878
22. Tylman M, Sarbinowski R, Bengtson JP, Kvarnström A, Bengtsson A. Inflammatory response in patients undergoing colorectal cancer surgery: the effect of two different anesthetic techniques. *Minerva Anestesiol*. 2011;77(3):275-282.
23. Kvarnström AL, Sarbinowski RT, Bengtson JP, Jacobsson LM, Bengtsson AL. Complement activation and interleukin response in major abdominal surgery. *Scand J Immunol*. 2012;75(5):510-516. doi:10.1111/j.1365-3083.2012.02672.x
24. Chen Y, Liang M, Zhu Y, Zhou D. *Zhonghua Yi Xue Za Zhi*. The effect of propofol and sevoflurane on the perioperative immunity in patients under laparoscopic radical resection of colorectal cancer 2015;95(42):3440-3444.
25. Buckley A, McQuaid S, Johnson P, Buggy DJ. Effect of anaesthetic technique on the natural killer cell anti-tumour activity of serum from women undergoing breast cancer surgery: a pilot study. *Br J Anaesth*. 2014;113 Suppl 1:i56-i62. doi:10.1093/bja/aeu200
26. Yan T, Zhang GH, Wang BN, Sun L, Zheng H. Effects of propofol/remifentanil-based total intravenous anesthesia versus sevoflurane-based inhalational anesthesia on the release of VEGF-C and TGF-β and prognosis after breast cancer surgery: a prospective, randomized and controlled study. *BMC Anesthesiol*. 2018;18(1):131. Published 2018 Sep 22. doi:10.1186/s12871-018-0588-3
27. Cho JS, Lee MH, Kim SI, et al. The Effects of Perioperative Anesthesia and Analgesia on Immune Function in Patients Undergoing Breast Cancer Resection: A Prospective Randomized Study. *Int J Med Sci*. 2017;14(10):970-976. Published 2017 Aug 18. doi:10.7150/ijms.20064
28. Lee ZX, Ng KT, Ang E, et al. Effect of perioperative regional anesthesia on cancer recurrence: A meta-analysis of randomized controlled trials. *Int J Surg*. 2020;82:192-199. doi:10.1016/j.ijsu.2020.08.034
29. Wigmore TJ, Mohammed K, Jhanji S. Long-term Survival for Patients Undergoing Volatile versus IV Anesthesia for Cancer Surgery: A Retrospective Analysis. *Anesthesiology*. 2016;124(1):69-79. doi:10.1097/ALN.0000000000000936 [chart]
30. Awards, Accreditations, and Points of Distinction. Mount Sinai Medical Center. Updated 2021. Accessed December 11, 2022. https://www.msmc.com/about-msmc/awards-accreditations-and-points-of-distinction/
31. McQuillan RF, Silver SA, Harel Z, et al. How to Measure and Interpret Quality Improvement Data. *Clin J Am Soc Nephrol*. 2016;11(5):908-914. doi:10.2215/CJN.11511015

FIU | Nicole Wertheim College of Nursing & Health Sciences