

Editorial

CANCER SURGERY: HOW MUCH AN ANESTHESIOLOGIST CAN INFLUENCE CANCER RECURRENCE?

Cancer has been among the major contributors to significant death and disability across the globe for several decades.¹ Life of the affected individual will be changed forever after the diagnosis of cancer as they are subjected to a wide range of investigations, multimodal therapy for cancer, adverse effects related to cancer therapy and follow-up. The main modalities of treatment for cancer include surgery, chemotherapy, radiotherapy, or a combination of them. The best that can be hoped for by the patient is a curative therapy that does not contribute to functional limitation and not to have any recurrence subsequently.



The best and the most curative form of therapy for solid tumors is surgical excision under anesthesia.² Patients who need to undergo cancer surgery will have to endure a variety of problems in the perioperative period. For these patients, the perioperative phase is the most critical period in determining the risk of cancer recurrence. Strange as it may sound, surgery invariably abets cancer recurrence though not deliberately due to its inability to radically eliminate each cancer cell at the surgical site, facilitating seeding of the cancer cells into lymphatics and bloodstream during resection, stimulating the hypothalamo-pituitary-adrenal axis and releasing the inflammatory mediators with resultant suppression of host immune responses, and by promoting the release of mediators that enhance the invasiveness and motility of cancer cells.¹⁻⁴

The fate of these remnant cancer cells following surgery is determined largely by the resilience of the cancer cells *vs* that of the host immune system. The remnant cancer cells may either be completely eliminated by the host's immune system or may remain dormant escaping the immunosurveillance awaiting favorable environment. Various factors that are essential ingredients of perioperative patient care may influence the host immune status adversely and/or contribute to creation of a micro-environment favorable to cancer cell growth and proliferation.¹⁻⁴ Therefore, though the anesthesiologist's role in the perioperative care of every patient is important, this becomes very crucial, specifically for cancer patients.

A multitude of problems afflict cancer patients during their perioperative care. Psychological issues, such as anxiety, stress, and depression augment the pathological impact already caused by the invading cancer cells. Further, both nutrition and exercise ability are affected preoperatively. All these suppress host immune system. Hyperglycemia, hypothermia, blood transfusion, and use of statins in the perioperative period have been implicated in contributing to immunosuppression and buildup of favorable microenvironment for cancer cells. The adverse impact of these factors may be countered by immune-enhancing nutrition supplementation, improving effort tolerance, psychological counseling, use of cyclooxygenase-2 inhibitors for analgesia, and β -blockers to suppress sympathetic surge.¹⁻¹⁰

Several decades of research data (largely based on animal studies, *in vitro* and *in vivo* experiments on cancer cells, retrospective and observational human studies) have raised considerable suspicion regarding pro-tumor effects of volatile anesthetic agents.¹⁻⁴ The intravenous induction agents, specifically propofol, have shown promising antitumor effects. Moreover, suppression of neuroendocrine response to surgery is better alleviated by a total intravenous anesthesia regimen based on propofol compared with volatile anesthetic-based anesthesia.¹⁻¹⁰ However, opioids, especially morphine and nondepolarizing neuromuscular blockers, specifically atracurium, have been implicated for their possible protumor effects.^{1-4,11,12} Use of regional anesthesia either as solo technique or in combination with general anesthesia can completely suppress the neuroendocrine response while avoiding or limiting the use of the general anesthesia drugs implicated in abetting cancer spread.¹³⁻¹⁵

However, the evidence from these studies is inferior as it suffers from several drawbacks, such as poor quality of research, presence of several confounders, presence of bias, inadequate follow-up, absence of control groups, inability to isolate the effects of a particular drug or technique, etc. Hence, at best, their data can be used to serve as a starting point for conducting good quality randomized controlled trials (RCTs) on humans.

Lack of quality RCTs and difficulty in formulating such studies (considering the heterogeneity of the cancer, wide range of patient comorbidities, variety of anesthesia techniques, and medications with resultant

impracticability of finding a suitable cohort for long-term follow-up) have made it extremely difficult to obtain reliable data that can stratify the technique and drugs suitable for different cancer cohorts. While future may hold the key to unraveling these mysteries, at this juncture, the best that can be advocated is to opt for a comprehensive perioperative management plan that relies on the triad of ensuring maximal patient comfort, providing optimal surgical conditions, and assisting in enhanced recovery. Anesthesiologist is a key player in ensuring that each patient undergoing cancer surgery can get the best perioperative management including providing chronic pain relief for those suffering from the long-term effects of cancer.

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