LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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Cancer and Anesthesia: Old Friends or New Enemies?

Kanser ve Anestezi: Eski Dostlar, Yeni Düşmanlar mı?

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Cancer is the second leading cause of death worldwide after cardiovascular diseases. Despite the development of new therapeutic modalities, mortality related to recurrence and metastasis remains a significant problem.

In recent years, perioperative anesthetic management in oncologic surgery has become a topic of growing debate among oncologic surgeons and anesthesiologists. Beyond surgical resection and the perioperative stress response, factors including anesthetic agents, hypothermia, and blood transfusion may contribute to making the perioperative period a vulnerable window for tumor metastasis (1).

During tumor resection, circulating tumor cells released from the primary tumor may disseminate to distant organs through the bloodstream or lymphatic circulation, thereby contributing to metastatic spread. During tumor resection, cytokines released from immune cells-most notably interleukin-6-initiate an inflammatory cascade that enhances tumor cell motility, invasion, and proliferative potential. Concurrently, activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system increases the release of catecholamines and cortisol, leading to perioperative immunosuppression. Ischemia and tissue hypoxia induced by surgical incision activate physiological defense mechanisms aimed at tissue repair through angiogenesis, mediated by increased expression of hypoxia-inducible factor-1α and vascular endothelial growth factor. Tumor cells may utilize these same mechanisms to enhance proliferation, angiogenesis, and vascular remodeling, ultimately promoting metastatic dissemination. Thus, the triad of inflammation, immunosuppression, and angiogenesis that characterizes the perioperative period forms a fundamental basis of metastatic tumor biology (2).

Studies investigating the relationship between anesthetic technique and oncologic outcomes in cancer surgery have frequently focused on comparing the two principal anesthetic techniques: inhalational anesthesia and propofol-based total intravenous anesthesia, with survival commonly used as the primary endpoint. Until recent years, numerous retrospective and heterogeneous studies suggested that total intravenous techniques might be superior (3). However, the limited number of completed randomized controlled trials (RCTs) have not demonstrated a significant difference in survival outcomes between these approaches, and the results of several ongoing RCTs are still awaited (4).

Another important question is whether adding regional anesthetic techniques to general anesthesia, which are known to attenuate the perioperative stress response, could improve survival outcomes. In vitro studies have demonstrated that regional anesthesia may increase apoptosis and enhance the activity of natural killer (NK) cells involved in the elimination of cancer cells. Regional anesthesia is also known to reduce opioid consumption by providing effective postoperative analgesia (2). This is particularly relevant because opioids may promote tumor growth and dissemination through their effects on the immune system, including decreased neutrophil chemotaxis, reduced NK

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cell cytotoxicity, and suppression of T- and B-cell responses as well as antibody production (3). However, randomized studies have generally demonstrated no survival benefit when regional anesthesia combined with general anesthesia is compared with general anesthesia with opioid-based techniques. In a large prospective study involving more than 34.000 patients investigating the relationship between opioids and breast cancer recurrence, patients were followed for more than eight years, and no association between opioid use and cancer recurrence was found (5).

In the context of oncological outcomes, evidence from in vitro and animal studies does not fully align with results from clinical studies. Experimental models rely on artificially induced cancers and fail to adequately reflect the impact of standard oncologic treatments in humans, such as chemotherapy and radiotherapy.

Similarly, *in vitro* studies evaluating anesthetic agents typically assess the effects of a single agent under highly controlled experimental conditions. However, in clinical practice, anesthesia is performed using a combination of drugs and techniques. Consequently, in clinical studies, it is difficult to isolate and attribute oncological outcomes to any single anesthetic agent.

During the perioperative period, the recommendation best supported by evidence is to avoid unnecessary blood transfusions. Although leukocyte reduction techniques are applied to stored blood products, residual leukocytes, biologically active cytokines, and released pro-inflammatory mediators may promote tumor progression in the setting of transfusion-related immunosuppression. Large meta-analyses have demonstrated that allogeneic blood transfusion is associated with increased complications and reduced survival (2). In this context, the literature recommends focusing on restrictive transfusion strategies, preoperative anemia management, and strategies to reduce perioperative blood loss.

Although current studies indicate that the perioperative period represents a highly sensitive metastatic window influenced by both surgical and anesthetic factors, there is no definitive evidence sufficiently strong to change clinical practice. In the future, pharmacogenetic strategies tailored to tumor type may enable more individualized approaches.

Keywords: Cancer, anesthesia, surgery

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Footnotes

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