

## Relationship between Anesthesia and Tumor: Can the Anesthesia affect the Prognosis of the Tumor?

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### Abstract

Nowadays, cancer is still one of the most common reasons of death in the world. Surgery as the main treatment for some potentially treatable solid tumors. However, tumor metastasis is the most important cause of death in patients with these tumors. Clinical studies have found that surgery is an influence factor on tumor metastasis. In the perioperative period, the small residual lesions can be killed by the immune system, while it may also escape from the immune attack and then becoming the source of tumor metastasis and recurrence. Anesthesia covers the whole perioperative period, the effect on the patient's immune function mainly in the perioperative period. In recent years, the potential impact of anesthesia and some factors on the long-term prognosis of patients after resection of tumor has been paid more and more attention.

**Keywords:** Cancer; Cancer recurrence; General anesthesia; Anesthesia drugs; Immunosuppression

### Intravenous Anesthetics

The literature has showed propofol can inhibit tumor cell invasion, proliferation and metastasis (mice showed that propofol play an anti-metastasis role in tumor) [1-10]. Propofol can also make cancer cell apoptosis in non-small cell lung cancer, colon cancer and ovarian [11]. The adhesion of propofol conjugates are inhibited the breast cancer cell migration and promoting apoptosis of cancer cells [12]. The present research showed that propofol may has less impact on the tumor metastasis mechanism and it had no obvious effect on the activity of NK cells but enhance the function of T cells in immune suppression effect during anesthesia. Propofol was found to inhibit hypoxia inducible factor in prostate cancer, so as to reduce stress damage during anesthesia [13,14]. Other studies have indicated that propofol can inhibit the function of neutrophils, monocytes and macrophages in the innate immune response, as well as the inhibition of B lymphocytes in critically ill patients [15,16]. The study also showed that propofol can increase the ratio of Th1/Th2 in PBMCs, it maintain the cell-mediated immune effect, which is beneficial for patients with immune dysfunction.

In a rat experimental, thiopentone and ketamine can promote the growth of implanted tumor cells and inhibit the activity of NK cells. However, propofol has played the protective effect. Ketamine mostly used in pediatric anesthesia, *in vitro* studies have found that ketamine can suppress neutrophil adhesion molecules on the surface and the production of oxygen free radicals, inhibit monocytes catalysis and through the mitochondrial pathway induced apoptosis of T lymphocytes [17,18]. Research about midazolam on tumor prognosis is not many, and that have no reference significance here.

### Opioid Drugs

During the perioperative period, opioid drugs can affect the activity of NK cells and macrophages, inhibit the production of immune factors, so as to play a role in inhibiting immune defense function and promoting tumor recurrence and migration [19,20]. Opioids also play a role in the treatment of chronic pain. Opioid antagonist naloxone can inhibit NK cytotoxicity, lymphocyte proliferation, reduces the INF- $\gamma$  that caused by lower abdominal surgery which means cell immunosuppression and opioid peptides and their receptors are closely related. Studies have showed that fentanyl inhibits the immune func-

tion of the body by inhibiting the activity of NK cells and be related to the dose [21]. Morphine can inhibit the apoptosis of breast cancer cells [22,23]. In a study showed that morphine and tramadol can inhibit T lymphocyte proliferation, but morphine showed persistent inhibition effect [24]. Morphine did not affect the activity of NK cells, and tramadol can increase inhibit the activity of NK cells [25]. Rats founded that tramadol can inhibit blocking surgical tumor metastasis and enhanced NK cell activity. However, comparative studies have suggested that certain opioids may be less immunoactive with less potential adverse effects on cancer immunosurveillance [26].

### Inhaled Anesthetics

Inhalation anesthesia drugs (halothane, enflurane, isoflurane, sevoflurane) can inhibit the NK cells activity and reduced adhesion of neutrophils to endothelial cells and inhibition of lymphocyte proliferation [27]. Reducing the adhesion of neutrophils to endothelial cells and inhibiting the proliferation of lymphocytes. At the same time, inhaled anesthetics can inhibit the release of cytokines from peripheral blood mononuclear cells (PBMC), thereby inhibiting the inflammatory reaction [28]. The research showed that isoflurane can reduce the phagocytosis of human alveolar macrophages so as to play the anti-inflammation effect [29]. The reversible inhibition of cell activity enhanced cytotoxicity of NK cells was induced *in vitro* [30]. Nitrous oxide is also considered for promoted the postoperative tumor metastasis, while there is also the opposite view [31]. *In vitro*, sevoflurane can affect the NK cells which is to release active cytokines such as IL-1B and TNF- $\alpha$ . Isoflurane can increase the malignant potential of ovarian cancer cells by up regulate cell cycle, promoting cell proliferation and angiogenesis [32]. Another study showed that sevoflurane is better in

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regulation of hepatocellular carcinoma in patients with peri-operative plasma inflammatory factors of information than isoflurane, so as to improve the prognosis of patients with tumor [33]. For a surgery for colorectal cancer study showed that sevoflurane compared with propofol total intravenous anesthesia to colorectal cancer five years survival rate of 4.7% and 5.6% growth [34]. Another study showed that patients with sevoflurane anesthesia and propofol anesthesia compared to reduce apoptosis of breast cancer cells in the breast cancer surgery [35]. Comparison of the propofol and isoflurane on the surgically induced that immune response effects of Th1/Th2 ratio in isoflurane group was found to decline markedly than propofol group [36-38]. It is indicating that compared with isoflurane, propofol is better to reduce the surgery stress which reduces the immune inhibition [39]. Patients with sevoflurane anesthesia can reduce the pro-inflammatory cytokines and matrix metalloproteinases [40]. Another clinical data showed that volatile anesthetics have exacerbated the effect of perioperative immunosuppression, but propofol have the opposite effect.

## Local Anesthetics

Lidocaine has the membrane stabilizing effect [41]. The clinical concentrations can directly inhibit EGF receptors, and the proliferation of tumor cells, it can also reduce the invasive ability of tumor cells [42]. In vitro experiments found that ropivacaine can inhibit the growth of tumor cells.

## Other Drugs

Dexmedetomidine can improve the patients undergoing radical operation for colon cancer cell immune function; reduce the probability of micro metastasis in blood circulation [43]. Another research showed patients with cellular immune transient suppression in breast cancer after radical surgery during general anesthesia, continuous intravenous infusion of dexmedetomidine can effectively inhibit perioperative stress and reduce the inhibition of cellular immune function after operation [44]. Juan has demonstrated that intraoperative dexamethasone administration to NSCLC patients was not associated with a significant impact on recurrence-free survival and overall survival [45]. De Oliveira shows that there were no evidence for an association between perioperative systemic dexamethasone administration and ovarian cancer recurrence after primary cytoreductive surgery. Kervoelen insisted dexamethasone is widely used in the treatment of multiple myeloma by its cytotoxic effect, while its cytotoxic effect has also reported, and at last they suggested that the effect of dexamethasone should be re-evaluated within molecular subgroups of myeloma patients to improve its efficacy and reduce its adverse effects [46,47].

## Selection of Anesthetic Techniques

At present, the advantages of combined anesthesia are obviously, and its usage is gradually increasing in the clinical [48]. Studies have shown that general anesthesia combined with epidural anesthesia can significantly reduce the short-term recurrence and metastasis rate of breast cancer, and improve the survival rate of patients with short-term recurrence free metastasis [49]. Compared with simple general anesthesia, combined anesthesia, epidural or spinal anesthesia can reduce the postoperative immune suppression. Some studies point out that local anesthesia and regional anesthesia can reduce tumor metastasis and recurrence [50-52]. While another recent analysis showed that regional block anesthesia cannot improve the overall survival rate of patients with cancer. A study of anesthesia for colon cancer surgery shows that propofol intravenous anesthesia and thoracic epidural anesthesia compared with general anesthesia with sevoflurane could

influence the colon cancer cells, from the colorectal cancer patients serum inhibited cell proliferation invasion and induced apoptosis effect than sevoflurane anesthesia [53-55]. The mechanism maybe that the anesthesia will affect serum micro environment which affects the transfer of tumor cell biology and cancer cells, but this result is due to anti-inflammatory and antitumor properties by the propofol and epidural anesthesia or lidocaine and ropivacaine induced anti-inflammatory, anti-cytotoxic and anti-proliferative effects are not sure.

## Conclusion

There are various factors affect the immune function of the patients during perioperative period and it cannot be considered a single factor to the prognosis of the tumor. The prognosis of the tumor is longer follow-up time, the influence factors are too many, the evaluation standard is detailed, which requires us to invest more research in order to accurate experimental results. As an anesthesiologist, it is necessary for us to according to the immune status of the patients during perioperative period to select appropriate anesthesia methods and drugs, in order to maximize the long-term prognosis of patients with surgical procedures.

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