

Regional Anaesthesia for Cancer Surgery and Its Impact on Recurrence and Metastasis: What Is the Evidence?

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Abstract

Regional anaesthesia (RA) is thought to potentially affect cancer recurrence and metastasis by reducing the perioperative stress response, supporting immune function, and decreasing the use of opioids and volatile agents. This review examines the mechanistic evidence and clinical results across eight major cancer types. Although RA reliably enhances pain management and perioperative recovery, its impact on cancer outcomes remains uncertain. The most notable reductions in recurrence are observed in bladder and oesophageal cancers, while the effects on breast, colorectal, gastric, and gynaecological cancers are limited. Variability in study methods, confounding variables, and a scarcity of high-quality randomised controlled trials hinder definitive conclusions. Until more solid evidence is available, personalised anaesthetic strategies are essential.

Keywords: Regional Anaesthesia, Cancer Recurrence, Metastasis

Introduction

Cancer surgery can cure localised tumours, yet recurrence and metastasis—responsible for ~90% of cancer deaths—remain major concerns due to perioperative stress and immune suppression [1, 2]. Anaesthetic techniques may influence these outcomes, with regional anaesthesia (RA) potentially preserving anti-tumour immunity by reducing surgical stress and opioid use. RA also provides adequate analgesia and minimises opioid-related side effects [3], blunts neuroendocrine responses⁴, and enables the use of propofol over immunosuppressive inhaled agents [1, 4]. This review examines mechanistic and clinical evidence from the past two decades across eight major cancer types, highlighting limitations and implications of RA in oncologic surgery.

Methodology

A narrative review was performed using PubMed, Google Scholar, and Scopus. The keywords used

included “regional anaesthesia,” “cancer recurrence,” “metastasis,” “oncologic outcomes,” along with relevant cancer-related terms. The review considered systematic reviews, meta-analyses and retrospective cohort studies published in English. Studies, such as editorials, case reports, and letters, were excluded. The literature search included articles published between 2000 and 2024, corresponding roughly to the past two decades of research.

Regional Anaesthesia Techniques in Cancer Surgery

Regional anaesthesia (RA) is increasingly adopted in cancer surgeries to enhance pain management and reduce the surgical stress response. By blocking afferent pain pathways, RA can lessen stress-related immune suppression, decrease opioid use, and support recovery [3]. Various RA techniques are used during surgery, from traditional neuraxial methods to newer peripheral nerve blocks. This overview covers these techniques and the cancer surgeries where they are applied,

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emphasizing their intraoperative pain-relief role. Any influence on tumor recurrence is noted only for context.

Neuraxial Anaesthesia: Epidural Analgesia in Major Cancer Surgeries

Epidural anaesthesia is a cornerstone technique in major cancer surgeries, offering continuous intraoperative and postoperative analgesia. It is commonly used in thoracic (e.g., lung, esophageal) and abdominal (e.g., colorectal, gastric) surgeries, providing bilateral pain relief, blunting the neuroendocrine response, and aiding recovery of pulmonary and gastrointestinal function.^{5–8} In hepatic and gallbladder surgeries, epidurals improve immune markers. Combined with general anaesthesia, they are used in gynecologic cancer surgeries for large abdominal incisions, enhancing pain control and early mobilization, despite no proven survival benefit [9, 10]. Overall, epidural RA using dilute solutions of local anaesthetics reduces opioid use and supports recovery across cancer surgeries.

Spinal anaesthesia (intrathecal block) is commonly used for lower abdominal and pelvic cancer surgeries, providing rapid, dense, short-duration anaesthesia. In urologic procedures like TURBT, it avoids airway instrumentation and offers adequate anaesthesia, with retrospective studies suggesting lower recurrence rates than general anaesthesia [11, 12]. It is also employed in select prostate and gynecologic surgeries, often with sedation. Due to limited duration, it suits shorter procedures or is supplemented with spinal opioids. In gynecologic oncology, combined spinal-epidural techniques offer immediate anaesthesia and extended postoperative pain relief. Spinal blocks typically cover T4–L1 dermatomes, reducing intraoperative opioid needs and enhancing analgesia.

Truncal Blocks: Paravertebral Block for Breast and Thoracic Surgery

Paravertebral nerve blocks (PVB) involve injecting local anaesthetic into the paravertebral space to create a unilateral segmental block, commonly used in breast and thoracic cancer surgeries. In breast surgery, PVBs (T2–T6) provide chest wall analgesia, reduce opioid use, and lower chronic post-mastectomy pain, sometimes serving as the primary anaesthetic with sedation. A large randomized controlled trial by Sessler et al. found that paravertebral–propofol anaesthesia was comparable to sevoflurane–opioid general anaesthesia, with no significant difference in breast cancer recurrence [13].

Newer Peripheral Nerve Blocks for Cancer Surgery Analgesia

Pectoral nerve blocks (PECS I and II) and Serratus Anterior Plane blocks (SAP) are ultrasound-guided techniques for breast and lateral thoracic wall surgeries. PECS II anaesthetizes pectoral and intercostal nerves, providing effective pain relief for mastectomies, lumpectomies, and axillary dissections. Serratus blocks target the lateral thoracic nerves for anterolateral chest wall pain relief [14, 15]. Both reduce opioid use and improve comfort when epidural or paravertebral blocks are unsuitable. A trial showed better pain control and less morphine use with PECS blocks during mastectomy [16].

Transversus Abdominis Plane (TAP) and Quadratus Lumborum (QL) blocks are ultrasound-guided peripheral techniques for analgesia in abdominal and pelvic cancer surgeries. TAP blocks anesthetize T6–L1 segmental nerves and are effective in colorectal, gynecologic, and urologic surgeries, reducing morphine use and pain scores, especially in laparoscopic procedures [17]. QL blocks, deposited near the thoracolumbar fascia, offer broader T7–L1 analgesia with some visceral coverage, suitable for ovarian, bladder, prostate, and hepatobiliary surgeries [18, 19]. Both blocks aid early recovery and are preferred when epidurals are contraindicated, though often combined with systemic or neuraxial analgesia for optimal effect.

Erector spinae plane (ESP) block is an ultrasound-guided interfascial block first described by Forero et al. in 2016 [20]. In cancer surgeries (thoracic, breast, abdominal), ESP blocks are increasingly used for postoperative pain relief and lower opioid needs. For example, in breast cancer surgery, an ESP block reduced 24-hour morphine use and pain scores versus general anaesthesia alone [21]. In thoracic (lung cancer) surgery, continuous ESP blocks have nearly halved 48-hour opioid use relative to intercostal nerve blocks while improving pain relief [22], and a propensity-score analysis found ESP blocks yielded lower 24-hour pain scores than thoracic paravertebral blocks, supporting ESP as a safe and effective alternative for oncologic thoracic analgesia [23]. Likewise, in major abdominal cancer surgeries, adding a pre-incisional ESP block to standard analgesia has produced significantly lower postoperative pain scores and opioid consumption, highlighting the ESP block's analgesic benefits and its role in enhancing recovery [24].

Mechanism linking regional anaesthesia and cancer recurrence

Several biological mechanisms have been proposed to explain how regional anaesthesia and analgesia may reduce cancer recurrence or metastasis compared to general anaesthesia (GA) techniques, as outlined in Table 1.

The following sections review the clinical evidence for this

Sr. No	Mechanism	How it Works
1	Reducing Surgical Stress Response and Preserving Immune Function [25-31]	↓ Afferent pain signals & sympathetic outflow
		↓ Catecholamines, cortisol, IL-6, TNF- α
		↓ VEGF and ↓ Tumor Angiogenesis
		↓ Systemic inflammation & ↑ NK cell, T-cell activity
2	Opioid-Sparing and the Link to Cancer [32-37]	↓ Systemic opioid requirement
		↓ EMT and tumor proliferation
		↓ Tumor progression and recurrence
3	Direct Anti-Tumor Effects of Local Anesthetics [38-45]	↓ VGSC blockade on tumor cells
		↓ Cell migration & invasion
		↑ Apoptosis induction
		↓ Viability of micro metastatic tumor cells

Table 1: Proposed Biological Mechanisms

hypothesis across different surgical oncology specialties.

A. Head and Neck Cancer Surgeries

Head and neck cancer surgeries rely on general anaesthesia, with limited use of regional techniques. Cervical epidural or nerve blocks may reduce stress and opioid use, as seen in a small trial [47], but evidence on recurrence or survival remains scarce [48, 49]. While RA aids pain control, its impact on oncologic outcomes is unproven, warranting further research.

B. Breast Cancer Surgeries

Research on anaesthetic management in breast cancer surgery investigates whether regional anaesthesia (RA) improves oncologic outcomes. Early retrospective studies, such as Exadaktylos et al. [50] suggested reduced recurrence with RA, but larger trials failed to confirm this. A major RCT by Sessler et al. (2019) involving over 2,100 women found no significant difference in recurrence between those receiving a paravertebral block with propofol and those given sevoflurane with opioids [13]. A 2022 sub-study in ER-negative patients showed a non-significant trend toward reduced early recurrence with RA [51], while a 2021 Taiwanese study reported lower locoregional recurrence with paravertebral block and propofol [52]. In contrast, a study conducted by Huang YH et al found no difference between RA and propofol [53]. Lu et al. (2021) observed better 5-year disease-free survival with epidural anaesthesia in node-negative patients, though confounding limits its reliability [54]. A 2023 review found no clear RA benefit, though lidocaine showed potential [55]. A 2024 meta-

analysis by Xie et al. showed a slight recurrence reduction with RA across 24,000 patients, mostly in prostate cancer, not breast cancer [56]. Thus, RA improves pain management but shows limited oncologic benefit in breast cancer surgery.

C. Gastrointestinal Cancer Surgeries

1. Colorectal Surgery:

A 2022 Danish study of over 11,000 patients undergoing curative colorectal cancer resection found no association between epidural analgesia and recurrence or mortality [57]. Similarly, Wu et al. (2021) reported no significant difference between epidural and intravenous analgesia in 1,282 rectal cancer patients [58]. Gottschalk et al. (2010) also observed no benefit of epidural analgesia in reducing recurrence in 669 colorectal cancer patients [6]. Gupta et al. (2011) found reduced mortality in rectal but not colonic cancer with epidural use [5]. While epidurals improve perioperative pain, stress response, and gastrointestinal recovery, most studies do not support a long-term oncologic benefit.

2. Gastric Cancer:

Retrospective studies show inconsistent results. Wang et al. [7] suggested a survival benefit with epidurals in patients under 65, but not in older patients—conversely, Cummings et al. [8] and Shin et al. [59] reported no significant effect of epidural analgesia on recurrence or survival. Meta-analyses remain inconclusive due to heterogeneity and methodological variability.

3. Esophageal Cancer:

Hiller et al. (2014) found longer epidural use (>36 hours)

linked to improved recurrence-free and overall survival [60]. Heinrich et al. (2021) reported better short-term outcomes but no significant difference in 3-year survival [61]. A review by Pérez-González et al. (2018) concluded that current evidence is insufficient to confirm survival benefits [62].

D. Urological Cancer Surgeries

1. Bladder Cancer Surgeries:

A 2023 systematic review by Wang et al. [11] of 8 retrospective studies found spinal anaesthesia associated with lower recurrence in bladder cancer compared to general anaesthesia (GA). Jang et al. (2016) [12] reported higher 5-year survival in TURBT patients under RA (96.3%) vs. GA (87.5%), though not statistically significant. Meta-analyses suggest RA, particularly spinal anaesthesia, may reduce recurrence in non-muscle-invasive bladder cancer (NMIBC), but no apparent effect on progression or overall survival is established.

2. Prostate Cancer:

Initial retrospective studies, like Biki et al. (2008) [63], hinted at a reduction in recurrence with RA. However, subsequent studies by Tsui et al. [64], Ehdaie et al. [65], Wuethrich et al. [66], and Forget et al. [67] found no significant differences in recurrence or survival. A 2015 meta-analysis by Lee et al. [68] confirmed no oncologic benefit with RA during radical prostatectomy, but noted a significantly lower mortality risk. Overall, while early data were promising, current evidence does not support RA's impact on prostate cancer outcomes.

E. Thoracic Cancer Surgeries

A 2021 RCT by Xu et al. [69] with 400 patients undergoing VATS for lung cancer, compared epidural-general anaesthesia versus general anaesthesia with opioids. After 32 months, no significant difference in survival. Du et al. (2021)[70] studied over 1,700 elderly patients undergoing major surgeries, mostly for cancer, and found no significant survival differences. To conclude, TEA helps reduce postoperative pain, improve pulmonary function, and aid early recovery, but doesn't seem to affect cancer recurrence or metastasis.

F. Gynecological Cancer Surgeries

1. Ovarian Cancer:

A Retrospective study in 2023 comparing perioperative epidural analgesia (EA) to GA in ovarian cancer patients found no significant survival benefit from epidural analgesia [10]. Lacassie et al. (2013) [9] analyzed 80 women with advanced ovarian cancer in Chile, finding no significant

difference in recurrence or survival between the EA and non-EA groups. To conclude, despite promising mechanistic rationale, the current body of evidence does not support a definitive oncologic benefit from the use of RA in gynecologic cancer surgeries.

G. Hepatocellular, Pancreatic, and Gallbladder Cancer Surgeries

1. Hepatocellular Carcinoma (HCC):

The impact of regional anaesthesia on HCC recurrence remains inconclusive. Lai et al. found that patients under GA for small HCCs had a lower recurrence risk than those under epidural anaesthesia, indicating GA might be advantageous in some cases [71]. An extensive study from Sun Yat-Sen University reported higher recurrence and mortality with epidural morphine analgesia post-resection versus intravenous fentanyl, questioning epidural analgesia's oncologic benefit [72]. Despite conflicting outcomes, Sun et al. showed that combined epidural and general anaesthesia can reduce perioperative immunosuppression by maintaining T-cell and interferon- γ responses, potentially improving oncologic control [73].

2. Pancreatic Cancer:

Lin et al [74] and Alexander et al. [75] found no significant difference in recurrence or survival between patients who received epidural anaesthesia and those who did not receive it. Overall, regional anaesthesia may benefit immune preservation and pain relief, but doesn't appear to improve long-term outcomes.

3. Gallbladder Cancer:

Zhu et al. compared GA with combined epidural-general anaesthesia in gallbladder cancer surgery. The combined group had better intraoperative stability and higher postoperative T-cell counts, indicating immune preservation [76]. Despite these immune benefits, survival rates showed no significant differences, implying that improved perioperative immunity may not impact long-term outcomes. To conclude, the impact of regional anaesthesia on recurrence in HCC, pancreatic, and gallbladder cancers is unclear.

Ongoing Prospective Trials:

Currently, no prospective trials studying the effect of regional anaesthesia on cancer recurrence are registered in the clinical trials database. Several trials are currently in the recruitment phase (NCT05494502, NCT06082141), primarily investigating the impact of regional nerve blocks on pain in patients undergoing breast cancer surgery.

Limitations

Much of the evidence that links regional anaesthesia to decreased recurrence rates for cancer is from observational studies, which can be influenced by other factors, including patient selection, the tumor's stage at diagnosis, and perioperative treatment factors such as type of postoperative pain management and use of adjuvants. Due to the heterogeneity of studies included in meta-analyses, there are limitations related to the sample size and follow-up variability of RCTs. Furthermore, due to publication bias and variations in how recurrence was defined, it is difficult to accurately interpret the results of the data. Although RA has been shown to improve recovery and provide better pain control, the ability to consistently show a benefit of RA on cancer outcomes has been lacking.

Future perspectives

Regional anaesthesia will continue to influence post-operative recovery, and while it is believed to offer benefits during this period, many questions remain about how regional anaesthesia affects metastasis or cancer recurrence. Currently, there are no large-scale, ongoing studies on this topic. Therefore, due to limited data, its role in impacting

oncologic outcomes should be carefully considered. Future research should investigate how biomarkers can guide regional anaesthesia (RA) treatment, the effects of RA on the immune system (immunological profiling), and establish criteria for patient selection to identify those who may benefit more from RA based on their individual circumstances. Until then, RA's primary value will be in providing effective pain relief and maintaining immune function during the perioperative period.

Conclusion

Regional anaesthesia (RA) can improve perioperative recovery, but its direct impact on cancer outcomes remains unclear. While RA may support immune function, evidence of increased disease-free survival is inconclusive across various types of cancer. Some early signs of benefit in bladder and esophageal cancers exist, but findings are inconsistent. Variability in study designs and confounding factors hinders definitive conclusions about RA reducing cancer recurrence. More high-quality trials are needed, with personalized anaesthetic approaches. Prospective studies with biomarkers are essential to determine if RA can lower recurrence rates and enhance long-term survival.

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