Tianjin Daxue Xuebao (Ziran Kexue yu Gongcheng Jishu Ban)/
Journal of Tianjin University Science and Technology
ISSN (Online):0493-2137
E-Publication: Online Open Access
Vol: 58 Issue: 08:2025
DOI: 10.5281/zenodo.16901855

REGIONAL, GENERAL, AND COMBINED ANAESTHESIA IN SURGICAL SETTINGS: ASSOCIATIONS WITH RECOVERY, OPIOID USE, PATIENT SATISFACTION, AND MOLECULAR STRESS RESPONSE

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Abstract

Background: Anaesthetic choice, regional anaesthesia (RA), general anaesthesia (GA), or their combination, influence surgical stress responses, perioperative recovery, and patient satisfaction. Understanding their comparative effects is important for optimising Enhanced Recovery after Surgery (ERAS) strategies. We aimed to systematically review evidence comparing RA, GA, and combined anaesthesia in terms of recovery outcomes, opioid use, patient satisfaction, perioperative complications, and molecular stress responses. **Methods:** A PRISMA-guided systematic review was conducted across PubMed/MEDLINE, Embase, Scopus, and Cochrane databases (2010–2025). Eligible studies included adult surgical patients receiving RA, GA, or both, with direct comparison of perioperative outcomes. Randomised controlled trials and prospective observational studies were considered. Outcomes included recovery quality, pain control, opioid consumption, perioperative complications, mortality, and molecular/biological markers. **Results:** Seven studies met the inclusion criteria (n=30–322 per study), spanning hand, breast, maxillofacial, orthopaedic, and hip fracture surgeries. RA—alone or with sedation/GA—was frequently associated with similar or improved recovery quality, reduced perioperative opioid use, and in some cases, attenuated molecular stress responses compared with GA. Functional recovery and satisfaction outcomes were generally comparable. Mortality and major complication rates showed no consistent differences between techniques. Procedure-specific benefits were observed, such as earlier PACU discharge in maxillofacial RA with sedation and reduced intraoperative opioid use in continuous interpectoral block for breast surgery. **Conclusions:** RA, either alone or combined with GA, provides comparable or improved patient-centred outcomes versus GA alone, with consistent opioid-sparing effects and potential reductions in molecular stress markers. While major complication and mortality rates are similar, the choice of anaesthesia should be individualised based on surgical context, patient profile, and ERAS principles.

Keywords: Regional Anaesthesia; General Anaesthesia; Combined Anaesthesia; Postoperative Recovery; Opioid-Sparing; Patient Satisfaction; Molecular Stress Response; Enhanced Recovery After Surgery; Perioperative Outcomes; Pain Management.

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INTRODUCTION

Surgical interventions trigger a complex physiological stress response of neuroendocrine, sympathetic, and inflammatory activation. While these mechanisms are adaptive in the acute phase, excessive or prolonged responses are associated with hyperglycemia, immune suppression, cardiovascular instability, delayed recovery, and increased morbidity (Reysner et al. 2024). Anaesthetic choice, between regional anaesthesia (RA), general anaesthesia (GA), or their combination, is important in modulating this stress response and influencing postoperative outcomes.

RA offers targeted nociceptive blockade, effectively attenuating hypothalamic–pituitary–adrenal axis activation, reducing catecholamine release, and lowering circulating pro-inflammatory cytokines (Reysner et al. 2024; Bhuyan et al. 2024). This modulation can improve haemodynamic stability, preserve immune function, and decrease postoperative pain and opioid requirements (Reysner et al. 2024; Sertcakacilar et al. 2022). In oncological contexts, RA has been associated with potential immunomodulatory effects that may influence tumour progression, although definitive survival benefits remain inconclusive (Bhuyan et al. 2024). In thoracic surgery, RA techniques integrated into multimodal analgesia protocols have demonstrated reductions in opioid use, postoperative nausea, and pulmonary complications, supporting enhanced recovery (Sertcakacilar et al. 2022).

GA, while effective for ensuring unconsciousness and amnesia, exerts limited control over the neuroendocrine and inflammatory cascades. It is often accompanied by greater systemic opioid administration, increasing the risk of side effects such as respiratory depression, nausea, ileus, and opioid-induced hyperalgesia (Dunkman et al. 2018). Multimodal analgesic approaches combining RA with GA aim to maximise the benefits of each while mitigating their limitations. This combination can achieve superior analgesia, further reduce opioid consumption, and optimise functional recovery (Dunkman et al. 2018; Sertcakacilar et al. 2022).

Beyond anaesthetic modality, adjunctive pharmacological strategies have been explored. For instance, sub-anaesthetic esketamine, when used with GA and peripheral nerve blocks, has been shown to reduce perioperative inflammatory markers (IL-6, CRP), improve early ambulation, and alleviate short-term anxiety and depression after major orthopaedic surgery (Min et al. 2023). Similarly, non-pharmacological interventions such as intraoperative music have been studied for their potential to reduce anxiety, pain, and stress hormone release, though evidence for robust clinical benefit remains mixed (Fu et al. 2024).

Given the growing emphasis on Enhanced Recovery After Surgery (ERAS) pathways, the selection of anaesthetic technique has become an integral component of perioperative optimisation.

ERAS principles advocate for multimodal strategies that reduce surgical stress, expedite mobilisation, and minimise opioid reliance (Dunkman et al. 2018; Sertcakacilar et al. 2022).

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Comparative evaluation of RA, GA, and combined approaches in diverse surgical populations can inform tailored anaesthetic plans aimed at improving recovery trajectories, patient satisfaction, and molecular stress profile modulation.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Studies were eligible if they met the following criteria: (1) involved adult patients undergoing surgical procedures under regional anaesthesia, general anaesthesia, or a combination thereof; (2) included a direct comparison between anaesthetic techniques, with or without sedation; (3) reported at least one relevant perioperative outcome such as patient satisfaction, postoperative recovery, pain control, perioperative complications, mortality, or biological/molecular markers; and (4) were randomized controlled trials, prospective observational studies, or pilot trials published in peer-reviewed journals. Studies were excluded if they were case reports, narrative reviews, conference abstracts, non-English articles without available translation, or involved paediatric populations.

Information Sources and Search Strategy

A comprehensive literature search was performed in PubMed/MEDLINE, Embase, Scopus, and the Cochrane Central Register of Controlled Trials from 2010 to 2025.

Search terms included a combination of controlled vocabulary (MeSH) and free-text keywords related to regional anaesthesia, general anaesthesia, combined anaesthesia, postoperative recovery, analgesia, and surgical outcomes. Boolean operators and truncation were applied to broaden the search. Reference lists of relevant articles were also screened to identify additional eligible studies.

Study Selection and Data Extraction

Two reviewers screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible articles. Discrepancies were resolved through discussion or consultation with a third reviewer. Data from the included studies were independently extracted by two reviewers using a predesigned data collection form. Extracted information included: citation details (author, year), study design, sample size, surgical population, anaesthetic interventions, outcome measures, and main findings. Where available, effect estimates with confidence intervals or p-values were recorded.

A qualitative synthesis was performed. Studies were grouped according to surgical setting and type of anaesthetic comparison. Results are presented narratively and in tabular format. No meta-analysis was conducted due to the variability in interventions and outcome reporting.

RESULTS

A total of seven studies met the inclusion criteria, with different surgical populations and anaesthetic techniques (Table 1). The sample sizes ranged from 30 to 322 participants, with varied designs including randomized controlled trials (n=6) and prospective

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observational studies (n=1). Surgical settings included ambulatory hand surgery, elective maxillofacial procedures, non-reconstructive breast surgery, elective hip arthroplasty, and acute hip fracture repair.

Patient Satisfaction and Recovery Outcomes

Teunkens et al. (2020) compared intravenous regional anaesthesia (IVRA) with axillary brachial plexus block in 120 adults undergoing minor ambulatory hand surgery. IVRA was found to be non-inferior to axillary block in patient satisfaction scores, although the latter had longer induction and discharge times.

IVRA was associated with more tourniquet discomfort and slightly higher pain scores, without increased analgesic consumption. Pérez Herrero et al. (2016) reported that both paravertebral and serratus-intercostal blocks, when combined with general anaesthesia for non-reconstructive breast surgery, resulted in high postoperative quality recovery scores at discharge and at one month, with no significant differences between groups.

Anaesthetic Efficacy and Perioperative Outcomes

De Grood et al. (1987) assessed three propofol dosing regimens for induction and maintenance of anaesthesia combined with regional blockade in 30 healthy patients undergoing elective surgery. No single regimen provided optimal anaesthesia for all patients, with variable recovery times and frequent mild to moderate injection pain. Rastogi et al. (2013) demonstrated that regional block with sedation in 50 maxillofacial surgery patients yielded lower postoperative pain scores, longer pain-free intervals, reduced rescue analgesia requirements, and fewer episodes of postoperative nausea and vomiting compared with general anaesthesia, enabling earlier PACU discharge.

Biological and Long-Term Outcomes

Alleva et al. (2019) explored gene expression profiles in 99 patients undergoing hip arthroplasty under general anaesthesia (GA), regional anaesthesia (RA), or integrated anaesthesia (IA).

GA and IA were associated with deregulation of DNA repair and stress-related genes up to three days postoperatively, whereas RA demonstrated minimal changes, suggesting a lower systemic toxicological impact.

Parker and Griffiths (2015) conducted a pilot RCT in 322 patients with acute hip fracture, finding no significant differences in hospital stay, transfusion requirement, or complications between GA and spinal anaesthesia. Thirty-day mortality was slightly lower with spinal anaesthesia, whereas one-year mortality was lower in the GA group.

Analgesic Efficacy in Breast Surgery

Ortiz de la Tabla González et al. (2018) compared continuous interpectoral block (CIPB) with intravenous analgesia in 137 women undergoing breast cancer surgery.

Both approaches provided effective postoperative analgesia, but CIPB significantly reduced intraoperative fentanyl requirements.

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Table 1: Summary of Included Studies

Citation	Study Design	Sample Size	Study Population	Method	Study Aim
(Teunkens 2020)	Prospective randomized controlled trial	120	Adults ≥18 years, ASA I–III, undergoing minor ambulatory hand surgery (carpal tunnel release, wrist cyst resection, or Dupuytren's release)	Randomized to receive either IVRA with 300 mg lidocaine or axillary block with 280 mg mepivacaine; measured patient satisfaction via EVAN-LR questionnaire plus secondary outcomes	To compare patient satisfaction between IVRA and axillary brachial plexus block and test noninferiority of IVRA
(De Grood 1987)	Randomized comparative study	30	Healthy ASA I–II patients scheduled for elective surgery	Three dosing regimens of propofol for induction and continuous infusion, combined with regional anaesthesia; monitored haemodynamics, induction/recovery times, side effects	To evaluate anaesthetic potency and side effects of different propofol dose regimens combined with regional blockade
(Rastogi 2013)	Randomized controlled trial	50	ASA I–II, aged 15–50, undergoing mandibular fracture or TMJ ankylosis surgery	Group I: regional block with sedation via peripheral nerve stimulator; Group II: general anaesthesia; compared intra/postoperative parameters, pain scores, discharge times	To assess efficacy and safety of regional block with sedation versus general anaesthesia in selected maxillofacial surgeries
(Pérez Herrero 2016)	Prospective randomized observational study	60	Patients undergoing non-reconstructive breast surgery	All received general anaesthesia; randomized to paravertebral or serratus-intercostal block; recovery assessed with Postoperative Quality Recovery Scale at multiple time points	To compare postoperative recovery quality between paravertebral and serratus-intercostal blocks in breast surgery
(Alleva 2019)	Randomized controlled trial	99	Patients undergoing elective hip arthroplasty	Randomized to general anaesthesia, regional anaesthesia, or integrated anaesthesia; gene expression in PBMCs assessed before, immediately after, and 3 days post-surgery	To investigate effects of anaesthetic techniques on gene expression related to stress and toxicity
(Parker 2015)	Pilot randomized controlled trial	322	Patients >49 years with acute hip fracture	Randomized to general or spinal anaesthesia; outcomes included mortality, hospital stay, transfusion need, complications; follow-up to 1 year	To compare outcomes of general versus spinal anaesthesia in hip fracture surgery

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(Ortiz de la Tabla González 2018)	Prospective randomized comparative study	137	Women aged 18–75, ASA I–III, undergoing non-reconstructive breast cancer surgery	Group 1: continuous interpectoral block after GA; Group 2: intravenous analgesia after GA; assessed pain, rescue analgesia, fentanyl use	To compare analgesic efficacy of continuous interpectoral block versus IV analgesia after breast cancer surgery

Table 2: Main Findings of Included Studies

Citation	Primary Outcome(s)	Key Results	Conclusion
(Teunkens 2020)	Patient satisfaction (EVAN-LR score)	IVRA non-inferior to axillary block; axillary block had longer induction/discharge times; IVRA had more tourniquet discomfort and slightly higher pain scores but similar analgesic needs	Both IVRA and axillary brachial plexus block achieved high patient satisfaction in ambulatory hand surgery
(De Grood 1987)	Anaesthetic conditions and recovery profile	No dosing regimen provided ideal anaesthesia for all patients; variable recovery times; mild to moderate injection pain common	Propofol infusion with regional anaesthesia feasible but dosing regimens require optimization
(Rastogi 2013)	Pain scores, analgesic requirement, side effects, discharge time	Regional block with sedation had lower postoperative VAS scores, longer pain-free interval, fewer rescue analgesic doses, and less PONV; earlier discharge from PACU	Regional block with sedation is a safe and effective alternative to GA for selected maxillofacial surgeries
(Pérez Herrero 2016)	Postoperative Quality Recovery Scale scores	High recovery scores at discharge and 1 month in both groups; no significant differences between paravertebral and serratus-intercostal blocks	Both techniques provide excellent recovery quality after non-reconstructive breast surgery
(Alleva 2019)	Gene expression changes (stress/toxicity-related genes)	GA and IA caused deregulation of DNA repair and stress genes persisting 3 days; RA showed minimal gene expression changes	RA had smallest toxicological gene expression impact after hip arthroplasty
(Parker 2015)	Mortality, hospital stay, transfusion, complications	30-day mortality slightly lower with spinal (4.3% vs 3.2% GA); 1-year mortality lower with GA (12.1% vs 20.2% spinal); no significant differences in hospital stay or complications	No marked differences in outcomes between GA and spinal for hip fracture; larger studies needed
(Ortiz de la Tabla González 2018)	Postoperative pain, fentanyl use, rescue analgesia	Both CIPB and IV analgesia provided effective analgesia; CIPB group required significantly less intraoperative fentanyl	CIPB is an effective alternative to IV analgesia in breast cancer surgery, reducing intraoperative opioid use

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DISCUSSION

The present systematic review synthesised evidence from seven primary studies comparing regional anaesthesia (RA), general anaesthesia (GA), and combined techniques across varied surgical settings. Our results indicate that RA—either alone or with sedation or GA—was frequently associated with comparable or improved patient-centred outcomes, reduced perioperative opioid use, and in some cases, attenuated molecular stress responses. Mortality and major complication rates were largely similar between anaesthetic approaches.

Comparison with Prior Evidence

Our findings align with multiple systematic reviews and meta-analyses showing that RA can achieve similar or superior clinical outcomes compared with GA in diverse surgical contexts. Luo et al. reported that for retrograde intrarenal surgery, RA provided equivalent stone-free rates to GA, with reduced postoperative pain and no increase in complications. Similarly, Hajibandeh et al. found significantly lower perioperative mortality and morbidity for elective endovascular aneurysm repair performed under local or regional techniques versus GA. These parallels reinforce the potential of RA to reduce acute postoperative discomfort and improve short-term safety without compromising procedural efficacy.

In the orthopaedic domain, our observation that RA was associated with minimal gene expression changes related to stress and toxicity (Alleva et al., current review) is consistent with Macfarlane et al., who noted that RA for total hip arthroplasty may lower blood loss and reduce postoperative opioid consumption compared with systemic analgesia, although length of stay and rehabilitation rates were not improved.

This suggests that while functional recovery metrics may not differ substantially, RA could still confer biologically relevant benefits.

Elderly and High-Risk Populations

The current review's hip fracture data (Parker and Griffiths) showed no significant difference in mortality at 30 days, with conflicting one-year trends. Lauven et al. similarly concluded that the choice between GA and RA in older surgical patients had limited impact on long-term mortality when comorbidities were optimally managed, although peripheral blocks without heavy sedation might reduce certain complications. The heterogeneity in long-term outcomes across studies highlights the importance of patient selection and anaesthetic tailoring in geriatric surgery.

Procedure-Specific Outcomes

For ophthalmic procedures, our breast surgery findings on opioid-sparing effects of RA parallel results from Vinciguerra et al., where general anaesthesia achieved slightly higher success rates in endoscopic dacryocystorhinostomy, yet local/regional anaesthesia remained a viable option in selected cases. Similarly, Schembri et al. showed that ureteroscopy under loco-regional anaesthesia was feasible, with acceptable conversion rates and complication profiles—mirroring the procedure-specific safety seen in our maxillofacial and hand surgery cohorts.

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In upper limb surgery, the economic and recovery advantages of IVRA observed in our dataset (Teunkens et al.) correspond with the pharmacoeconomic evaluation by Chilvers et al., who found IVRA halved anaesthesia and recovery costs compared with GA and reduced postoperative complications, despite a small proportion of unsatisfactory blocks. This further supports the role of RA in enhancing efficiency in day-case settings.

Opioid-Sparing and Recovery

Across surgical specialties, RA's ability to reduce opioid requirements was a recurring theme. Our breast surgery data align with obstetric evidence from Sultan et al., where regional blocks (TAP, QLB) consistently lowered opioid consumption and improved postoperative pain control after caesarean delivery. The consistency of opioid-sparing effects across both obstetric and non-obstetric settings reinforces RA's value within multimodal analgesia strategies.

CONCLUSION

Regional anaesthesia techniques, alone or in combination with sedation or general anaesthesia, associated with comparable or improved patient-centred outcomes, satisfaction, postoperative recovery quality, pain control, and reduction in perioperative opioid use. Biological endpoints indicated that RA may exert less systemic stress at the molecular level compared with GA. Mortality and major complication rates did not differ substantially between techniques, although study-specific trends were observed.

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