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ORIGINAL RESEARCH

Regional Anesthesia vs Opioid Therapy for Postoperative Pain Management in Cardiac Surgery: A Systematic Review

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ABSTRACT

Background : Postoperative pain after cardiac surgery can persist for extended periods, with up to 43% of patients experiencing pain three months post-surgery, and is associated with inadequate management and intense acute postoperative pain. Peripheral sensitization due to tissue injury and central sensitization within the central nervous system contributes to heightened pain sensitivity post-surgery. While opioids are effective, concerns over their adverse effects and potential for misuse prompt a shift towards multimodal analgesia, including regional anesthesia. Despite its advantages, there has been no comprehensive review comparing regional anesthesia and opioids in cardiac surgery. This study aims to systematically review randomized controlled trials to compare the effectiveness of these pain management strategies. context and purpose of the study.

Methods: The literature search was performed across four databases. This study focuses on the postoperative pain scale. Regional block intervention relieves pain in cardiac surgery patients by administering local anesthetics near nerves, which minimizes reliance on systemic opioids and their associated side effects. This approach enhances patient comfort, accelerates recovery, and reduces the risk of opioid dependence. Quality was assessed using the Cochrane Risk of Bias Tool 2. A total of ten articles were included in this systematic review.

Result : The analysis of pain scale data from eight studies revealed significant reductions in postoperative pain with regional block interventions compared to controls. Opioid consumption was notably reduced, indicating a decreased reliance on opioids. The length of time to extubation varied, with the intervention group showing a shorter duration compared to the controls. Adverse effects, including diaphoresis and nausea, were reported, but further research is needed to investigate these effects thoroughly.

Conclusion: Regional anesthesia has proven effective in reducing postoperative pain and minimizing both the dose and duration of opioid use.

Keywords: Analgesia**;** Cardiac surgery; Opioids; Postoperative pain ; Regional anesthesia.

INTRODUCTION

Postoperative pain following cardiac surgery is common and can last for extended periods.[1] According to the International Association for the Study of Pain, up to 43% of patients still experience pain three months after cardiac surgery. It was a multifaceted phenomenon, leading to functional disabilities that prevent patients from returning to work and normal life. Inadequate management and more intense acute postoperative pain are linked to a higher incidence and severity of chronic postoperative pain. Despite the tremendous occurrence of postoperative pain in cardiac surgery patients, there are still no established standards or guidelines for addressing this issue.[2–4]

Postoperative pain often begins with peripheral sensitization, which occurs due to tissue injury during surgery. Surgical trauma activates nociceptors—pain receptors—leading to increased sensitivity at the site of injury. This process is regulated by the production of inflammatory mediators, which decrease the pain threshold and increase pain perception.[5,6] In addition to peripheral mechanisms, central sensitization occurs when nociceptive signals are amplified in the central nervous system (CNS), specifically in the dorsal part of the spinal cord. Following surgery, there is an increase in excitatory neurotransmitters and a decrease in inhibitory signals, leading to heightened pain sensitivity. Central sensitization is linked to conditions like referred pain and secondary hyperalgesia, in which pain is felt in places unaffected by the surgical operation.[5,7,8]

Opioids have traditionally been the cornerstone of postoperative pain management, providing effective relief for acute pain following surgical procedures. However, the increasing reliance on these medications has raised significant concerns due to their associated adverse effects and the potential for misuse. Common adverse consequences of opioids include constipation, nausea, vomiting, drowsiness, and respiratory depression, concurrently delayed post-surgery recovery, increased duration of stay, and expenses to the health care system, while decreasing patient satisfaction. Additionally, the risk of developing opioid tolerance and dependence poses a serious challenge, as patients may require escalating doses to obtain the same degree of pain alleviation. Consequently, there is a growing emphasis on multimodal analgesia approaches that incorporate non-opioid medicines and regional anesthetic procedures to improve pain control while minimizing the hazards associated with opioid use.[9–11]

The use of regional anesthesia or local anesthetic infusions has been shown to reduce persistent postoperative pain in breast cancer surgery, cesarean section, and thoracotomy. By targeting specific nerve pathways, regional techniques provide localized pain relief, which is essential given the multifactorial nature of pain experienced by patients following surgeries such as valve surgery and coronary artery bypass grafting (CABG). The mechanisms through which regional anesthesia decreases postoperative pain include targeted analgesia, prevention of central sensitization, and reduced reliance on systemic opioids. These mechanisms not only enhance patient comfort but also contribute to improved recovery outcomes, including shorter ICU stays and faster extubation times.[12]

These strategies and standards have focused on patient satisfaction and pain control while minimizing the need for opioids. Despite the increasing adoption of regional anesthesia techniques in clinical practice, however, there has not been a comprehensive systematic review comparing the effectiveness of regional anesthesia and opioid therapy specifically in the context of cardiac surgery.[13,14] Therefore, we conducted a systemic review with evidence based solely on randomized controlled trials. This systematic research sought to determine the impact of regional anesthetic on postoperative pain after cardiac surgery when compared to opioids.

METHODS

This systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.

Eligibility Criteria

To enhance specificity, specific inclusion and exclusion criteria were established prior to conducting the literature search for this systematic review. The inclusion criteria encompass randomized controlled trials that have been published in the past decade up to July 2024. The PICOS framework is used to structure the inclusion criteria, including 1) Population: adult patient aged above 18 years old undergoes cardiac surgery; 2) Intervention: regional block; 3) Comparison: patients treated with opioid; 4) Outcome: postoperative pain using pain scale and; 5) Study design: Randomized Controlled Trial (RCT). As part of the intervention, the patients received regional block in the form of Bilateral erector spinae plane Block (ESP), serratus anterior plane block (SAPB), parasternal block, paravertebral block, pecto-intercostal fascia block (PIFB), and intercostal cryo nerve block. Exclusion criteria include 1) Full-text articles inaccessible; 2) Studies conducted in languages other than English; 3) Retracted studies.

Search Strategy

Five autonomous researchers (AAA, ACC, AFA, PMD, and RRA) searched the literature from July to August 2024. Multiple databases, such as PubMed, ScienceDirect, Cochrane Journal, and Google Scholar, were utilized. The search used keywords including ("Regional Anesthesia" OR "Block") AND ("Postoperative pain management" OR "pain management") AND ("Cardiac surgery" OR "Cardiac") AND ("Opioid"). The identification and screening process were documented using the PRISMA Flowchart (Figure 1).

Data Extraction and Analysis

Three authors (AAA, ACC, and PMD) independently extracted the chosen studies into a Google Sheet, and then all authors evaluated the studies' accuracy and suitability. The other authors, AFA, overseeing the process, then subsequently reviewed and documented the findings. Disagreements that emerged during the writing process were resolved through discussions.

Risk of Bias Assessment

RRA utilized the Cochrane Risk of Bias Tool 2 for Randomized Controlled Trials to assess bias risk in the chosen studies, with the process overseen by the other authors. This tool examines five areas: randomization process, deviations from intended interventions, incomplete outcome data, outcome measurement, and selection of reported results. The studies were then classified into three quality categories: low, moderate, and high risk of bias.

Intervention of Interest

Regional block intervention is a highly effective approach for alleviating pain in patients following cardiac surgery. This method involves injecting local anesthetics near specific nerves to interrupt pain signals before they reach the brain, thereby providing focused pain relief. Utilizing regional blocks can significantly decrease the reliance on systemic opioids, which can lead to various side effects, including respiratory depression, nausea, and constipation. By reducing opioid consumption, patients can enjoy a smoother and faster recovery, with fewer complications and a lower risk of developing opioid dependence. Furthermore, regional blocks have been demonstrated to enhance patient comfort, promote early mobilization, and improve overall postoperative results, making them an essential part of comprehensive pain management strategies in cardiac surgery.

Outcome of Interest

The mean pain scale in post-intervention of each included study was the focus of this review. The outcome of interest in this study is the postoperative pain scale, which determines the effectiveness of pain management using different interventions.

RESULT

Study Selection and Identification

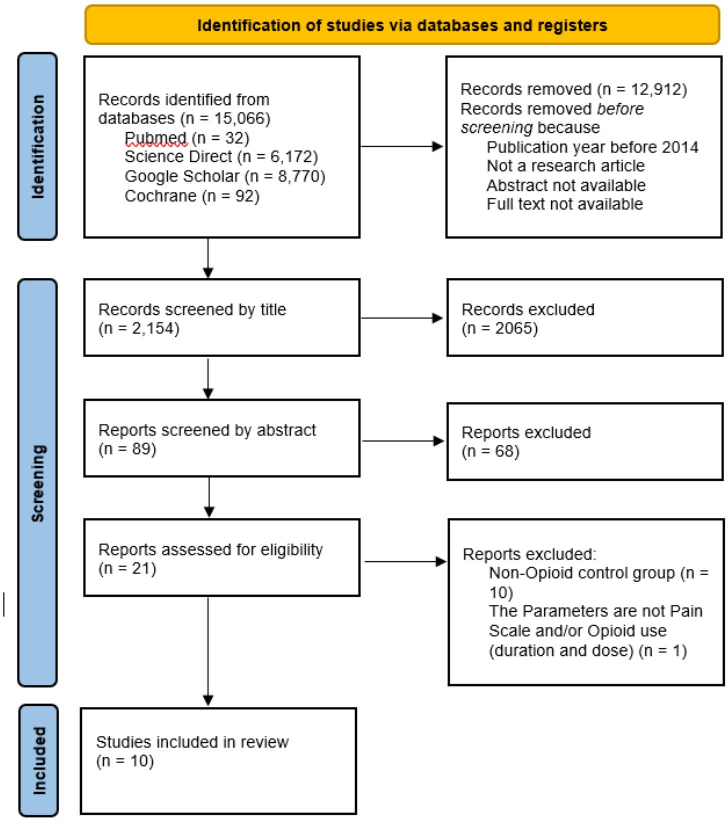

Figure 1. PRISMA Flowchart

Risk of Bias Assessment

The risk of bias evaluation revealed that three studies demonstrated an unclear risk of bias due to ambiguous descriptions and explanations of their methodologies, suggesting non-adherence to the criteria of the first, second, and fifth domains of the Cochrane Risk of Bias Tool 2. The remaining studies were deemed to have a low risk of bias (see Fig. 2). Despite varying levels of bias among the studies, the majority of the data was meticulously analyzed. Reviewers determined that the data were adequately suitable for the analysis.

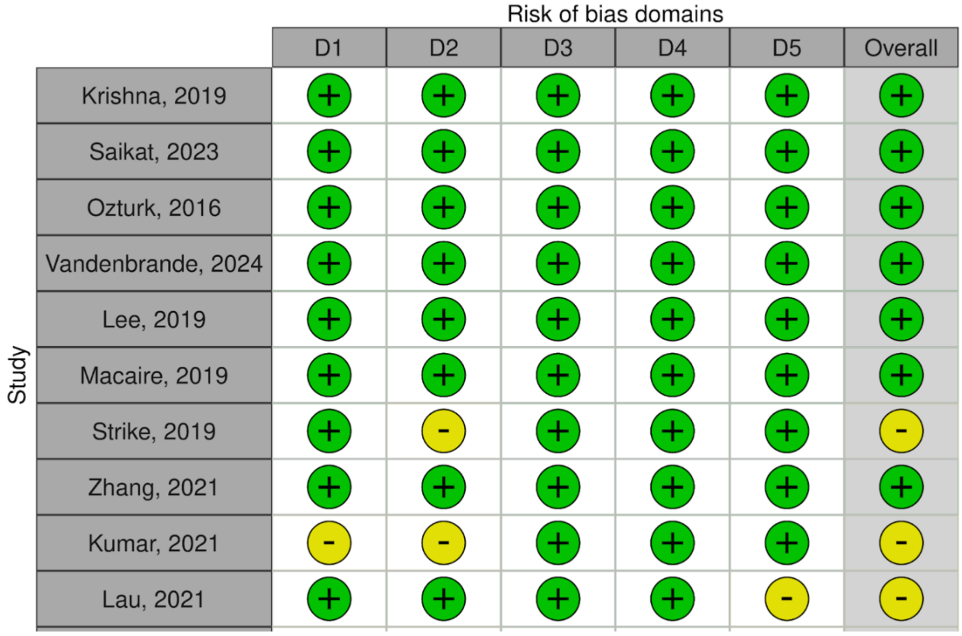

Figure 2. Cochrane Risk of Bias Tool 2 for Randomized Controlled Trial Studies

Table 1. Summaries of The Included Studies

No	Author, year	Number of treatment/ control	Regional Block	Outcomes
1.	Vandenbrande J. *et al.*, 2024	38/37	SAPB	• Pain management Significantly lower post-intervention NRS pain scores on SAPB group at 4-hour (p=0.05 vs. control), 8-hour (p=0.03 vs. control), and 24-hour intervals (p=0.04 vs. control). • Opioid use Significantly reduced post-intervention piritramide consumption in SAPB group at 24-hour intervals (p<0.01 vs. control). • Length to extubation No significant differences between groups (p=0.26).
2.	Lee C. *et al.*, 2019	41/38	PSB	• Pain management No significant difference in post-intervention pain scores at 72-hour intervals between groups (p > 0.05). • Opioid use Significantly reduced post-intervention fentanyl consumption in PSB group at 2-hour intervals (p=0.047 vs. control). • Length to extubation

				No significant differences between groups (p=0.722). • Adverse Effects On both groups: diaphoresis (69.4%), constipation (66.7%), nausea (55.6%), restlessness (50%), dizziness (50%), somnolence (50%), anxiety (44.4%), tachycardia (41.7%), premature ventricular contractions (PVCs) (41.7%), atrial fibrillation (38.9%), weakness (33.3%), metallic taste (27.8%), paresthesias (27.8%), nonsustained ventricular tachycardia (VT) (22.2%), vomiting (22.2%), palpitations (19.4%), first-degree atrioventricular (AV) block (19.4%), pyrexia (16.7%), bradycardia (16.7%), chills (11.1%), miosis (11.1%), tremors (8.3%), and ST-segment changes (8.3%).
3.	Zhang Y. *et al.*, 2021	49/49	PIFB	• Pain management Significantly lower post-extubation NRS pain scores on PIFB group at 2, 4, 8, and 24-hour intervals both at rest and while coughing (p<0.05 vs. control). • Opioid use Significantly reduced intra and post-surgery sufentanil consumption in PIFB group (p<0.01 vs. control). • Length to extubation Significantly less extubation time in PIFB group (p<0.01 vs. control). • Length of ICU and hospital stay Significantly shorter ICU and hospital stay on PIFB group (p<0.05 vs. control).
4.	Kumar A. *et al.*, 2021	20/20	PIFB	• Pain management Significantly lower post-extubation NRS pain scores on PIFB group at 6 and 12-hour intervals at rest (p=0.001 vs. control) and at 0, 3, 6, and 12-hour intervals while coughing (p=0.001 vs. control). • Opioid use Significantly reduced post-surgery fentanyl consumption on PIFB group (p=0.001 vs. control).
5.	Krishna S.N. *et al.*, 2019	53/53	ESPB	• Pain management Significantly lower post-extubation NRS pain scores on ESPB group at 0, 2, 4, 6, 8, 10, and 12-hour intervals (p=0.0001 vs. control). • Opioid use Significantly reduced intra and post-surgery fentanyl consumption in ESPB group (p=0.0001 vs. control). • Length to extubation Significantly less extubation time in ESPB group (p=0.0001 vs. control). • Length of ICU and hospital stay Significantly shorter ICU and hospital stay on ESPB group (p=0.0001 vs. control).
6.	Saikat S. *et al.*, 2023	40/40	SAPB	• Pain management Significantly lower post-surgery VAS pain scores on SAPB group at 15 min, 1, 2, 4, 6, 10, 24, and 48 hour intervals (p<0.0001 vs. control). • Length of ICU and hospital stay Significantly shorter ICU and hospital stay on SAPB group (p<0.0001 vs. control).
7.	Ozturk NK. *et al.*, 2016	38/37	PSB	• Pain management Significantly lower post-extubation VAS pain scores on PSB group at 4, 5, 6, 7, and 8 hour intervals (p<0.001 vs. control). • Opioid use Significantly reduced post-surgery morphine consumption in PSB group (p<0.001 vs. control). • Length to extubation No significant differences between groups (p=0.344). • Length of ICU and hospital stay No significant differences between groups in length of ICU (p=0.975) and hospital stay (p=0.456).
8.	Macaire P. *et al.*, 2019	47/20	ESPB	• Pain management Significantly lower post-extubation VAS pain scores on ESPB group at 2-hour (p=0.008) and one-month intervals (p=0.05). • Opioid use: Significantly reduced intra-surgery sufentanyl dosage in ESPB group (p<0.001). • Length to extubation

				No significant differences between groups (p=0.16). • Adverse Effects Significantly less postoperative adverse effects in the ESPB group, including hypotension (40% vs 5%), nausea/vomiting (35% vs 7%), and hyperglycemia (15% vs 2%) (p<0.01).
9.	Strike E., *et al*, 2019	22/22	PVB	• Pain management No significant differences in post-surgery VAS scores between groups (p=0.64). • Opioid use Significantly reduced intra-surgery fentanyl (p=0.044) and postoperative hydromorphone (p<0.05) consumption in PVB group. • Length to extubation Significantly less extubation time in PVB group (p = 0.001).
10.	Lau WC. *et al.*, 2021	65/19	CryoNB	• Pain management Significantly lower post-surgery VAS pain scores on control group at 72-hour (p=0.02), 96-hour (p=0.01), and 120-hour intervals (p=0.02). • Opioid use Significantly reduced post-surgery opioid consumption in CryoNB group (33.43 [29.77] vs. 38.31 [31.05) respectively. • Length to extubation: No significant differences between groups (p=0.44). • Length of ICU and hospital stay: No significant differences between groups in length of ICU (p=0.29) and hospital stay (p=0.10).

SAPB, serratus anterior plane block; NRS, numeric rating scale; PSB, parasternal block; VT, ventricular tachycardia; AV block, atrioventricular block; PIFB, pecto-intercostal fascial block; ICU, intensive care unit; ESPB, erector spinae plane block; VAS, visual analog scale; ESPB, bilateral erector spine plane block; PVB, paravertebral block; CryoNB, intercostal cryo nerve block

Pain Scale Analysis

There were 8 studies that presented data on the changes in pain scale after the intervention was given. Vandenbrande *et al.* observed that the SAPB group's pain reductions post-intervention were notably greater than the control group's on 4 hours period (median NRS 2; quartiles 0–3 vs. 3; quartiles 1–5; p=0.05), 8 hours (median NRS 1; quartiles 0–2 vs. 3; quartiles 1–4; p=0.03), and 24 hours (median NRS 2; quartiles 1–4 vs. 4; quartiles 2–5; p=0.04).[15] Macaire *et al.* found that those who received bilateral Erector Spinae Plane Block (ESPB) with ropivacaine reported significantly lower pain scores compared to the patients given morphine and nefopam, both 2 hours after tube removal (1 vs. 2; p = 0.008) and 1-month post-surgery (0.5 vs. 2; p = 0.05).[16] Similarly, Zhang *et al.* and Saikat *et al.* noted substantial pain reductions with regional anesthesia in cardiac surgery patients (1.55 [1.15] vs. 3.42 [1.19]; p<0.0001).[17,18] Krishna *et al.* also reported lower pain scores with erector spinae block using ropivacaine compared to the only paracetamol and tramadol group (NRS <4 for 8.98±0.14 hours vs. 4.6±0.12 hours; p = 0.0001).[19] Ozturk *et al.* found significantly lower pain levels with parasternal block compared to morphine and

Transcutaneous Electrical Nerve Stimulation (TENS) (1.64 vs. 3.24 vs. 2.94; p < 0.001). On the other hand, a significant reduction in median pain between the intervention and control groups did not found by Lee *et al.*[20,21] Similarly, Strike *et al.* and Kumar *et al.* observed no significant differences in pain scores between groups.[22]

Opioid Dose and Duration

Opioid use outcomes were also notably impacted by the interventions. For example, in the study by Vandenbrande *et al.*, the SAPB group showed a substantial reduction in opioid use during the initial 24 hours postoperatively, with median piritramide use being 9.0 MME compared to 15.0 MME in the control group, confirming the superiority of SAPB with a mean difference of 5.8 MME (p<0.01).[15] Similarly, Zhang *et al.* reported significantly decreased intraoperative and postoperative sufentanil requirements in the PIFB group compared to the control group (76[10] μg vs 118[32] μg, p<0.01; 65[15] μg vs 108[30] μg, p<0.01).[17]

Length to Extubation

The length of extubation was another critical outcome measured in these studies. In the study by Vandenbrande *et al.*, there were no significant differences in time to extubation between the SAPB and control groups (p=0.722).[15] In contrast, Zhang *et al.* found a significantly reduced length to extubation in the PIFB group compared to the SALI group (2.7[1.8] h vs 9.7[3.5] h, p<0.01).[17]

Adverse Effects

In addition to the outcomes, several adverse effects were also observed. In the study conducted by Lee *et al.*, several adverse effects were observed in both groups, the most common adverse effects were diaphoresis (69.4%), constipation (66.7%), and nausea (55.6%).[21] While Strike *et al.*, also reported lower adverse effects in the intervention group such as delirium, atrial fibrillation, and renal insufficiency compared to the control group, but similar rates of reintubation, while control group had higher occurrences of pneumonia, stroke, and in-hospital mortality.[23] Macaire *et al.* also observed similar outcomes reporting adverse effects, in the ESPB group, postoperative adverse events significantly decreased, with the control group experiencing 40% hypotension compared to 5% in the ESPB group, 35%

nausea/vomiting versus 7%, and 15% hyperglycemia versus 2% ($p < 0.01$).[16]

DISCUSSION

To the fullest extent of the author's knowledge, this meta-analysis and systematic literature review is the first to assess the postoperative analgesic efficacy of opioids against local anesthesia following cardiac surgery. Thoracotomy and sternotomy are surgical procedures that cause a lot of post-operative pain.[24,25] Following heart surgery, a variety of pain syndromes can occur which originates from visceral, musculoskeletal, or neurogenic sources. Myofascial tissue like muscle, bone, tendon, and ligaments are the main source of chronic pain following heart surgery. Pain management is essential since neglecting it can have serious consequences.[26] One of the complications that can arise due to inadequate postoperative acute and chronic pain management is the appearance of nociplastic pain which can occur as a comorbidity among those with chronic pain syndromes that are mostly nociceptive or neuropathic.[27] This can complicate pain management and reduce the patient's quality of life.

Several commonly used post-surgery analgesic treatments have demonstrated varying degrees of efficacy. A highly effective multimodal strategy uses pharmaceuticals that inhibit pain signals at numerous points along the pain pathway. Despite this, opioids continue to be the primary therapy for managing postoperative pain.[28] The 2016 prescribing guidelines for opioids issued by the Centers for Disease Control and Prevention recommend that when prescribing immediate-release opioids for acute pain, doctors use the lowest effective dose possible and never prescribe more than what is necessary to address the patient's estimated duration of pain severe enough to warrant opioid use. It's usually sufficient to take three days or less; more than seven days are rarely required.[29] This recommendation arises because while they reduce pain, opioids also have side effects.

Opioids can impair expectoration and cause nausea, vomiting, sleepiness, and cough suppression. If combined with pain caused by incisions made for the chest tube entrance and median sternotomy, these individuals may also be unable to cough, immobile, and have inadequate breathing. All those factors may increase the period of ICU and hospital stay, along with the delay in weaning off of mechanical breathing.[20] Eight articles in this review compared the timing of post-op ventilator use, and 4 showed no significant decrease in extubation time.[15–17,19–21,23,30] These conflicting results may be caused by a relatively small number of subjects and emphasize the need for additional research to completely understand the impact of various anesthetic treatments on extubation times, but they also suggest that certain regional blocks may expedite recovery and reduce the duration of mechanical ventilation.

Eight studies presented significant decrease in pain scale after the regional anesthesia intervention. These result is not surprising since regional anesthesia provides analgesia directly to the chest wall, it is also for this reason that opioid use may be significantly reduced in 8 out of 10 studies. The serratus plane block appears to mediate its analgesic action by blocking the intercostal nerves on its lateral cutaneous branches.[31] The parasternal intercostal block and pecto-intercostal fascial block work at a similar branch of nerve. The fascial block protects the anterior branches of intercostal nerves from T2 to T6, whereas the parasternal intercostal blocks the anterior cutaneous branch, which is the terminal component of the main trunk of the intercostal nerve.[32] The erector spinae plane block inhibits neuronal transmission in the intercostal nerve's lateral cutaneous branches and the paravertebral block works by blocking the ipsilateral somatosensory and sympathetic activity of spinal nerves as they emerge from intervertebral foramina which will preserve the contralateral sympathetic activity resulting in lower side effects such as hypotension compared with thoracic epidural.[33–35] The existence of 2 studies that showed no substantial reduction in pain assessment scores and no significant reduction in opioid consumption could be due to several things, namely types of opioids used, differences in sample size, doses of anesthetic drugs used perioperatively or could even indicate the possibility of differences in efficacy between regional anesthesia techniques.

In terms of side effects, only three out of ten articles reported them. All three articles reported side effects occurring in all groups, although at a greater incidence in the control group and almost all side effects that were reported are opioid related. Given that all patients in both groups receive opioid drugs pre and perioperatively, side effects like nausea, delirium, and constipation are not uncommon. This effect can occur because systemic opioids do not only affect the pain center but will affect all opioid receptors in the body and cause different effects. Profound analgesia is produced by activating opioid receptors, which is mediated by presynaptic and postsynaptic combination effects. Opioid analgesics work pre-synaptically by inhibiting calcium channels in primary nociceptive afferents. This inhibits the release of neurotransmitters such as glutamate and substance P that are contributing in nociceptive transmission. The post-synaptically effect is achieved by hyperpolarizing cell membranes through the activation of potassium channels, which directly inhibits postsynaptic neuronal activity.[36] In the other hand, opioid analgesics also have a wide range of negative side effects because of wide distribution both inside and outside the neurological system. For example, the effect of constipation is triggered by the binding of opioids to the receptors in enteric neurons, delaying the gastrointestinal tract (GI) transit time, stimulating the pylorus and ileocecal sphincters as well as non-propulsive GI motility.[37] None of the articles we reviewed mentioned side effects associated with regional anesthesia like hypotension, pneumothorax, spinal cord damage, epidural abscess, epidural hematoma, dural puncture, and ipsilateral Horner syndrome.[38]

The findings of our review are constrained by substantial variations in local anesthesia and surgical techniques. Furthermore, variations in fundamental analgesia regimens may result in disparities in pain assessments. As a result, there is significant heterogeneity among investigations, and the findings cannot be statistically synthesized and interpreted.

CONCLUSION

This systematic review demonstrates that regional anesthesia interventions significantly reduce postoperative pain compared to control groups, as evidenced by lower pain scale scores across multiple studies. The findings indicate that regional blocks effectively decrease opioid consumption, thereby minimizing associated risks and side effects. However, the impact on extubation times remains inconclusive, with mixed results suggesting the need for further investigation. Overall, regional anesthesia appears to be a promising alternative to traditional opioid use in managing postoperative pain following cardiac surgery, although variability in study results emphasizes the necessity for more consistent and comprehensive research in this study field.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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