

# The Efficacy of Different Modes of Analgesia in Postoperative Pain Management and Early Mobilization in Postoperative Cardiac Surgical Patients: A Systematic Review

## Abstract

Cardiac surgery induces severe postoperative pain and impairment of pulmonary function, increases the length of stay (LOS) in hospital, and increases mortality and morbidity; therefore, evaluation of the evidence is needed to assess the comparative benefits of different techniques of pain management, to guide clinical practice, and to identify areas of further research. A systematic search of the Cochrane Central Register of Controlled Trials, DARE database, Joanna Briggs Institute, Google scholar, PUBMED, MEDLINE, EMBASE, Academic OneFile, SCOPUS, and Academic search premier was conducted retrieving 1875 articles. This was for pain management postcardiac surgery in intensive care. Four hundred and seventy-one article titles and 266 abstracts screened, 52 full text articles retrieved for critical appraisal, and ten studies were included including 511 patients. Postoperative pain (patient reported), complications, and LOS in intensive care and the hospital were evaluated. Anesthetic infiltrations and intercostal or parasternal blocks are recommended the immediate postoperative period (4–6 h), and patient-controlled analgesia (PCA) and local subcutaneous anesthetic infusions are recommended immediate postoperative and 24–72 h postcardiac surgery. However, the use of mixed techniques, that is, PCA with opioids and local anesthetic subcutaneous infusions might be the way to go in pain management postcardiac surgery to avoid oversedation and severe nausea and vomiting from the narcotics. Adequate studies in the use of ketamine for pain management postcardiac surgery need to be done and it should be used cautiously.

**Keywords:** “Pain” management, pain guidelines, cardiac surgery, cardiothoracic intensive care, critical care, intensive care unit, local anesthetic subcutaneous infusions, meta-analyses, open heart surgery, pain, pain busters, pain protocols, paravertebral blocks, patient-controlled analgesia, postcardiac surgery, randomized controlled trials, sternotomy

## Introduction

Pain is known to be an unpleasant sensory and emotional experience associated with potential and actual tissue damage.<sup>[1]</sup> Despite major advances of postoperative pain management,<sup>[2]</sup> it continues to be a significant problem for many patients after major surgery.<sup>[3]</sup> Sternotomy, rib retraction, conduit harvest, and drain tubes are some of the sources of pain in cardiac surgery.<sup>[4]</sup> Therefore, postcardiothoracic surgery, the role of planned pain management is crucial for early mobilization, decreasing pulmonary complications such as atelectasis, shortening the hospital length of stay (LOS),<sup>[5]</sup> and reducing cardiovascular and endocrine complications.<sup>[6]</sup>

Regional anesthetic infiltrations and subcutaneous infusions (pain busters)

around the wound are some of the pain management techniques which carry the advantages of providing superior analgesia and avoiding some of the adverse effects of systemic opioid treatment.<sup>[7]</sup> However, opioid infusions and patient-controlled analgesia (PCA) remain the primary and most commonly used pharmacological therapies immediate postoperative after cardiac surgery in Intensive Care Units (ICUs).<sup>[8]</sup>

Epidural analgesia or blocks for pain management will not be considered in this review because of the controversy and contraindication that surrounds its use in cardiac patients including complications such as hematoma due to perioperative coagulation.<sup>[9]</sup> Mazzeffi and Khelemsky<sup>[8]</sup> stated that, “even if the risk of developing a hematoma in cardiac surgery is known to be

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**Brenda Nachiyunde, Louisa Lam<sup>1</sup>**

Department of Health Sciences, School of Nursing and Midwifery, University of South Australia, City East Campus, Adelaide SA 5001, <sup>1</sup>School of Nursing and Healthcare Professions, Federation University Australia, Berwick, Victoria, 3806, Australia

### Address for correspondence:

Dr. Louisa Lam,  
Deputy Dean, School of Nursing and Healthcare Professions,  
Federation University Australia,  
Office 1121, Building 903,  
Berwick Campus, PO Box 859,  
Berwick VIC 3806, 100 Clyde Rd, Berwick, Victoria.  
E-mail: L.lam@federation.edu.au

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1 in 12000, due to the severity of the consequences related to epidural hematomas, this technique remains underused in postoperative pain management in cardiac surgery.”

The efficacy of ketamine and opioid infusions, paravertebral blocks, PCA, subcutaneous nurse-administered opioids, ropivacaine/bupivacaine local continuous subcutaneous infusions, and infiltrations in cardiac surgery have been assessed in this review of randomized controlled trials. This is in relation to postoperative pain management, early mobilization, and LOS in intensive care and hospital in general.

## Materials and Methods

### Selection criteria

#### Inclusion and exclusion

Included were randomized controlled trial articles for adults eighteen years and over post cardiac surgery. These included the use of subcutaneous anesthetic infusions, paravertebral blocks/infiltrations, PCAs, Ketamine/ opioid infusions and nurse administered subcutaneous (NASC) opioids for pain management in Intensive care. There was no restriction to opioids or anesthetic medications used were made. Included studies were all postcardiac surgery articles, including valve repair or replacement and coronary artery bypass and grafts in intensive care.

All studies using epidural analgesia or blocks for pain management postcardiac surgery were excluded from the study.

#### Search strategy

Two independent reviewers searched the Cochrane Central Register of controlled trials, Joanna Briggs Institute and the Google scholar. EMBASE, DARE, PUBMED, MEDLINE and SCOPUS databases were also searched using the keywords above.

#### Critical appraisal tools

The JBI critical appraisal form for randomized controlled trials was used. Eligible studies were graded using the following scoring system: First, if there was true randomization used for assignment of participants to the treatment groups,<sup>[1]</sup> if the allocation was concealed,<sup>[2]</sup> and if the outcome assessors were blind to the assignment.<sup>[6]</sup> The description of an appropriate method of double blinding was graded as follows: yes, no, and unclear. The studies had to have a YES on criteria 1, 2, and 6 to qualify. The flow diagram is included below and shows how the search strategy was done and articles included and excluded.

#### Data extraction

The JBI data extraction form was used as a model for data extraction but was modified to the specific need of information for this specific systematic review. Any data on patient-reported pain using visual analog scale (VAS) and

numerical rating scores were extracted from the studies. Specific outcomes that were extracted included pain scores at rest and with activity including coughing and need for rescue medication. The complications as described in the outcome measures were indicated where applicable. Data on LOS in ICU and in hospital were extracted where recorded.

### Analysis of outcomes

Information from each included study was recorded in data tables [Table 1]. The primary outcomes were patient-reported pain, LOS, and complications due to inadequate pain management (atelectasis, pneumonia, wound infection, and increase in mortality/morbidity) where reported. Means and standard deviations (SDs) were extracted from the text, tables, or graphs within the studies. Quantitative analysis was limited by heterogeneity in study designs, and the subject numbers were small. The limited number of randomized controlled studies led to a narrative synthesis of the systematic review.

## Results

Database searches yielded 1875 articles. Further screening yielded 873 articles in which inclusion and exclusion titles and abstracts reduced the number of articles to 52; 52 were retrieved, 13 of which were noncardiac articles, 4 were reviews, 8 were cardiac but nonrandomized controlled trials, and 17 articles failed to meet the criteria during data extraction. Ten articles were included in this study. Randomized clinical trials enrolling a total of 511 patients were included for the final narrative analysis [Figure 1]. Flow diagram for pain management postcardiac surgery shows the search criteria.

### Local infiltrations and parasternal blocks

Parasternal block and local anesthetic infiltrations with levobupivacaine versus Saline (P)<sup>[10]</sup> showed significantly less use of morphine as a rescue drug in the levobupivacaine (LB) group ( $P = 0.02$ ) compared to the P group after surgery over the 24 h period. Zero percentage of the LB group needed rescue medication versus 44.4% of the P group. The VAS scores were not significantly different at rest and when coughing, statistically as indicated in Figure 2a and b below. Alveolar-arterial oxygen gradient and partial oxygen were measured and were significantly better in the LB group at the time of extubation and better throughout the first 24 h period.

**Table 1: Intravenous patient-controlled analgesia consumption**

Intravenous patient-controlled analgesia consumption			
	Bupivacaine (n=19)	Sham group (n=19)	P
24 h	26.8±11.0	36.3±17.3	0.095
48 h	56.4±22.4	67.6±30.3	0.092
72 h	70.5±26.4	91.4±40.7	0.117

IV PCA consumption. Chiu *et al.*, 2008<sup>[15]</sup>

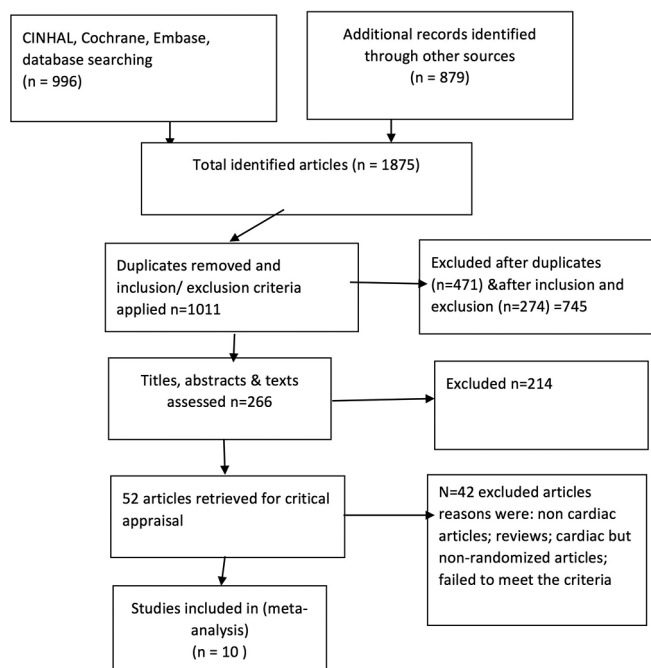


Figure 1: Pain management post cardiac surgery. Flowchart describing the search criteria

Parasternal intercostal block with ropivacaine for pain management after cardiac surgery, was used in a double blind randomized controlled trial with saline.<sup>[11]</sup> The ropivacaine group had almost 50% visual analogue pain scores less than those in the saline group with a mean of 29.5, SD = 24.3 versus 53.2 = 24.1, ropivacaine versus saline respectively,  $P = 0.001$ . Numerical rating scale scores were similarly significantly less for patients in the ropivacaine group at extubation with a mean = 2.7 (SD = 1.6) versus 5.2 (SD = 2.0), respectively; (95% CI: -3.3 to -1.7,  $P = 0.01$ ). The use of morphine PCA in the ropivacaine patients was approximately 50% less for the first 12 h after surgery (12.0 [SD = 5.4] vs. 23.2 [SD = 8.3] total morphine equivalent in milligrams R vs. S respectively;  $P < 0.001$  [95% CI, -14.3 to -8.1]) as indicated in the graph [Figure 3].

The Efficacy of parasternal injection of bupivacaine on postoperative pain for early extubation in patients undergoing coronary artery bypass surgery was assessed. The VAS pain score in the bupivacaine group remained 0–3 with a mean (1.38 ± 1.19) and none of the patients required rescue pain medication, while in the placebo group, the mean of 6.13 ± 2.92 which was very significant, the difference in the mean VAS between the two groups ( $P = 0.001$ ), rescue medication was required in 8 (53.3%) whereas non from Bupivacaine.

Partial oxygen (PaO<sub>2</sub>) showed a trend to be higher in the Bupivacaine group with a mean of 208.23 ± 42.57, whereas in the placebo, a mean was 126.40 ± 23.15. These results reflected the respiratory comfort and ease of vital capacity whose difference was statistically significant ( $P < 0.001$ ).

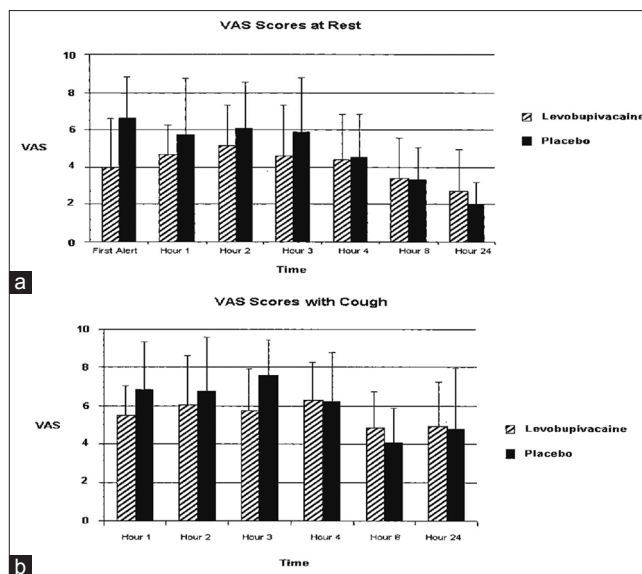


Figure 2: Verbal analog scores for pain at rest (a) and with cough (b) on a standard 0 to 10 scale over the first 24 h after surgery. Values are a mean ± standard deviation. (McDonald et al. 2005)<sup>[16]</sup>

### Local subcutaneous infusions

Results of a randomized double blind clinical trial of ropivacaine (0.2%) versus saline showed improved pain control after cardiac surgery. Patients in the ropivacaine group reported significantly less pain than the saline group with a mean overall VAS pain score significantly lower than the saline group (1.6 vs. 2.6,  $P = 0.005$ ). This also reflected in the total narcotic use where ropivacaine versus the control group 47.3 versus 78.7 mg ( $P = 0.038$ ), respectively, and day 2 postoperatively (15.5 vs. 29.4 mg,  $P = 0.025$ ). The mean LOS for the patients in the ropivacaine group was 5.2 ± (1.3) days, with a range of 3–7 days, whereas the mean LOS in the control group was 8.2 ± 7.9 days with a range of 4–39 days. There was a trend toward improvement in pulmonary function in the ropivacaine group.

The analgesic effects of a bilateral sternal infusion of ropivacaine after cardiac surgery<sup>[14]</sup> in the first 48 hours proved lower pain scores in the ropivacaine group during mobilization ( $P = 0.0004$ ) and at rest ( $P = 0.0006$ ), and the analgesic effects were mostly apparent on day 2 postsurgery. The amount of morphine consumption reduced in the ropivacaine group and their satisfaction and rehabilitation improved; however, no effects were noted on respiratory outcomes. Clinical tolerance and comfort were also better in the ropivacaine group. The ropivacaine plasma levels remained beneath the mean level observed for occurrence of neurologic symptoms.

Local infusion of bupivacaine combined with patient controlled analgesia provides better pain relief than intravenous patient controlled analgesia alone in patients undergoing a minimally invasive cardiac surgery.<sup>[15]</sup> In this study, there were no differences in time to extubation, ICU, or hospital stay. There appeared to be a trend in



reduction in PCA requirements when bupivacaine was infused into the wound. The Sham infusion group had greater and more persistent pain than the bupivacaine infusion group even at 24 h, 48 h, and at 3 months after the operation [Table 2].

The analgesic efficacy of continuous paesternal bupivacaine infusion through a single catheter after cardiac surgery<sup>[16]</sup> proved to reduce pain scores in the bupivacaine group. The overall morphine requirements over the first 48 h in ICU were significantly less in group B than group C, mean = 8.6 mg ± (0.94) vs. 18.83 mg ± (3.4), respectively, *P* = 0.02. The mean VAS scores were also significantly less in Group B than Group C at most time points.

The time to extubation was shorter in Group B compared to Group C, with a mean of 117 min (±10) versus 195 min ± (19), respectively, *P* = 0.03. However, there was no statistical difference between the two groups in the ICU and hospital stay duration. The respiratory parameters such as PaO<sub>2</sub>/FiO<sub>2</sub> and partial carbon-dioxide were better in Group B at extubation, 6 h, 12 h, and 24 h mark compared to Group C [Table 3].

### Ketamine infusions

S (+) ketamine versus a placebo as an analgesic adjunct proved to reduce opioid consumption after cardiac

surgery.<sup>[17]</sup> During the first 48h postoperatively, the consumption of oxycodone in the S (+) ketamine group was less, mean = 103 mg ± (44) compared to mean of 125 mg ± (45) in the placebo group: mean difference was 22 mg and 95% confidence interval (CI) for the difference of 3–40 mg, *P* = 0.023. The time after tracheal extubation to the first dose of oxycodone with PCA was longer in the S (+) Ketamine group 134 min ± (125) and 101 min ± (197) respectively, *P* = 0.013. The VAS pain scores during the 48 h period were comparable both at rest and during a deep breath with no statistical difference. When asked if they could use the same type of analgesia, 41 (93%) of the 44 patients in the S (+) Ketamine group and 41 (89%) of the 46 in the placebo group replied affirmatively.

Pulmonary function tests, mobilization tests, walking exercises with physiotherapists, maximal oxygen capacity (VO<sub>2</sub>) and Vco<sub>2</sub> and postoperative PCO<sub>2</sub> levels were higher in the placebo group than the in the S (+) Ketamine group (*P* = 0.021).

### Patient-controlled analgesia and opioids

Patient controlled analgesia of remifentanyl(RM) versus morphine (M)<sup>[18]</sup> post cardiac surgery, did not show a significant difference in effectiveness. After 24 h of PCA use, no statistically significant difference in both groups in pain management. The LOS of the patients in ICU was 46.83± (4.6) h for remifentanyl (RM) group and 45.44± (5.6) h for M group. The overall LOS in hospital after the operation was 5.2± (1) days versus 5.1± (1) days, respectively. Each group had 14% of the patients present with atelectasis postoperatively which was treated with chest physiotherapy. However, the overall effectiveness was rated very good or good in 87% by RM group compared to 72% of the patients in the M group.

Nurse administered subcutaneous morphine is a satisfactory alternative to intravenous patient controlled analgesia of morphine after cardiac surgery.<sup>[19]</sup> There was no statistically significant difference found between the two groups in any of the variables measured. Median VAS pain scores at rest and with movement; on day 1, it was 0 and 3 in the NASC and 0 and 2.5 in the intravenous (IV) PCA, and on day 2, it was 0 and 2.5 in NASC group and 0 and 2 in the IV PCA group. Unblind physiotherapists scored the success of mobilization and the difficulty the patients had in obtaining additional analgesia before physiotherapy for the two groups. For the IV PCA group (VAS scale 1–10), it was 8 (6–9) and 7 (7–8) for the NASC group. Total morphine administered postoperatively was 42.7 ± 32.4 mg in the IV PCA group and 53.3 ± 29.3 mg in the NASC group. Morphine consumption through IV PCA or NASC in the first 24 h after extubation was 33 ± 22 mg and 37 ± 20 mg in the IV PCA group and NASC group, respectively.

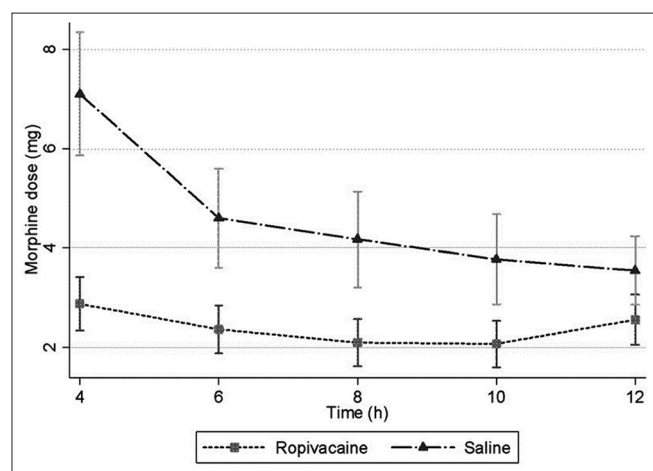


Figure 3: Consumption of patient-controlled analgesia Morphine in the 12 h period (Barr et al.)

Table 2: Morphine consumption and recovery times after surgery

Outcomes	Group B (n=19)	Group C (n=18)	<i>P</i>
Morphine consumption over the 48 h (mg)	8.6±0.94	18.83±3.4	0.02
Extubation time (min)	117±10*	195±19	0.03
ICU stay (h)	56.1±30	55.4±22	0.36
Hospital stay (days)	5.5±1.2	5.7±1.6	0.3

Nasr et al., 2015. B: Bupivacaine, C: Saline group, ICU: Intensive Care Unit

**Table 3: Demonstrates the patient demographics employed by the included studies, the comparisons used and the recorded and reported outcomes**

Included Studies	Population	Patient Demographics: sex (S), age (A), weight range body surface area (BSA) or body mass index (BMI) whichever is available		Comparisons	Main Outcomes Patient reported pain (VAS) scores, length of stay in ICU & hospital and respiratory/immobility complications
		Control group	Treatment group		
McDonald <i>et al.</i> 2005 <sup>[10]</sup>	Patients 18-80 years of age undergoing either single valve replacement or coronary artery bypass grafting with or without cardiopulmonary bypass without complications	Placebo=9 S (m/f):8/1 A: 64±11 BMI: 28.1±4.2	Levobupivacaine=8 8/0 61±9 29.7±1.9	54mls of 0.25% levobupivacaine (LB) with 1:400000 epinephrine or 54mls normal saline with no epinephrine added as a parasternal block.	Less morphine used in treatment group-20.8±6.2 vs. 33.2±10.9 (control) Reported VAS scores not significantly different. Better oxygenation at time of extubation in the LB group.
Barr <i>et al.</i> 2007 <sup>[11]</sup>	Patients to be extubated within 6hrs post primary non-emergency multi-vessel CABG on or off cardiopulmonary bypass, aortic and mitral valve replacements or repair, atrial septal defect repair	N=Normal saline (45) S (m/f):35/8 A: 60±15 BSA (Mean): 1.9 (1.8-2.0)	Ropivacaine (43) 34/11 62±18 1.9 (1.9-2.0)	0.75% ropivacaine via parasternal intercostal block or Saline before closure of sternal wound	At extubation parasternal block patients with ropivacaine had visual analogue and numerical rating scores approximately 50% less than the normal saline group Over the first 24 hrs. Low oxygen saturation was significantly more in the saline group. No difference in the incidence of postoperative pneumonia between the groups.
Rahman <i>et al.</i> 2016 <sup>[12]</sup>	Female or male, adults undergoing first time for isolated coronary artery bypass surgery. Without complications	Placebo (normal saline) =15 S (m/f):9/6 A: no age W: no weight or height specified H:	Bupivacaine 0.5% =13 S (M/F): 8/5	Bupivacaine 0.5% @ 2mg/kg and normal saline 0.9% infiltrated in the parasternal wound	The VAS remained at a mean of 1.38±1.19 in the Bupivacaine (B) group, while 6.13±2.92 in the placebo group. Pao <sub>2</sub> remained high in the B and lower in the placebo group. ICU or hospital stay was not reported
Dowling <i>et al.</i> 2003 <sup>[13]</sup>	Patients undergoing elective CABG alone or combined with laser trans-myocardial revascularization	Normal saline n=19 S (m/f):14/5 A: 56±8 BSA: (95%): 2.1 (2.0-2.2)	Ropivacaine 0.2% n=16 13/3 55±11	0.2% ropivacaine at 4mls/hr. with narcotic PCA and Normal saline with narcotic PCA	The mean overall pain scores for the ropivacaine were significantly less than those for normal saline (1.6 vs. 2.6). Length of stay 5.2 days for ropivacaine vs. 8.2 days for normal saline group. No difference in assessment of pulmonary function.
Eljezi <i>et al.</i> 2012 <sup>[14]</sup>	18-90 year old scheduled for open heart surgery with sternotomy for valve replacement or CABG with cardiopulmonary bypass with no complications	N=placebo (19) S (m/f):16/3 A: 64±12 W: 76±14 H: 168±10	Ropivacaine 0.2% n= (20) S (m/f) not indicated 68±13 77±9 170±9	4mls/hr. of 0.2% Ropivacaine and 0.9% Normal saline	VAS: pain scores lower in the ropivacaine group during mobilization. No effects on respiratory functions, quality of rehabilitation was improved except on respiratory outcomes. ICU and hospital stay were not reported
Chiu <i>et al.</i> 2008 <sup>[15]</sup>	Adult Patients undergoing minimally invasive cardiac surgery without complications	N Saline=19 S (m/f): 12/7 A: 57.4±15.2 W: 63.6±12.9 H: 1.59±0.08	Bupivacaine 0.15% =19 S (M/F): 13/6 59.7±13.8 63±10.4 1.62±0.10	0.15% bupivacaine @ 2mls/hr. and Normal saline	No differences in time of extubation, ICU or hospital stay. The bupivacaine group had reduced pain in the first 48hrs including 24hrs after cessation of the infusion.

Contd...

Table 3: Contd...

Included Studies	Population	Patient Demographics: sex (S), age (A), weight range body surface area (BSA) or body mass index (BMI) whichever is available		Comparisons	Main Outcomes Patient reported pain (VAS) scores, length of stay in ICU & hospital and respiratory/immobility complications
		Control group	Treatment group		
Nasr <i>et al.</i> 2015 <sup>[16]</sup>	45-60 years scheduled for open heart surgery for CABG with CPB without complications	Saline solution=18 S (m/f): 10/8 A: 53±5.8 W: H	Bupivacaine 0.25%-19 S (M/F): 11/8 54±4.5	5ml/hr. bupivacaine 0.25% and normal saline	Lower post-operative pain scores, better respiratory parameters, shorter extubation times with no incidence of wound infection in the Bupivacaine group; no differences in ICU or hospital stay duration
Lahtinen <i>et al.</i> 2004 <sup>[17]</sup>	Adult Pts scheduled for CABG with CPB and younger than 70 years of age Non complicated	Normal saline n= (46) S (m/f):43/3 A: 58±7 W: 83±10 H: 173±6	S(+) Ketamine N= (44) 37/7 59±5 85±13 172±8	S (+) Ketamine-75µg/kg bolus+infusion of 1.25µg/kg/min and normal saline infusion	VAS scores were comparable in the first 48hrs both at rest and during deep breaths. Tracheal extubation times were similar, PCO <sub>2</sub> levels were higher in the placebo group. Respiratory effects and length of stay was not reported.
Baltali <i>et al.</i> 2009 <sup>[18]</sup>	Adult Cardiac surgical patients undergoing CABG non-complicated	N=R (29) S (m/f): 21/8 A: 57±8 W: 80±11 H:	N=M (29) 22/7 58±8 79±13	Remifentanyl 0.05µg/kg/min, Morphine 1mg bolus, 0.3mg/hr. PCA	On coughing the NRS values were significantly lower in Remifentanyl than Morphine, not much difference in overall effectiveness. 4 patients in each group developed atelectasis, which needed routine physiotherapy. ICU or Hospital stay was not reported
Munro <i>et al.</i> 1998 <sup>[19]</sup>	All patients scheduled for non-emergency cardiac surgery without complications	IV PCA of Morphine-39 S (m/f):32/7 A: 61.1±12 W: 81±11.9 H: not recorded	NA SC Morphine-41 S (M/F): 32/9 58.7±10.1 84.4±12.8 H:	IV PCA with morphine 1mg bolus, 6 min lock out and 10mg/h limit, and nurse-administered subcutaneous morphine 0-7.5mg given every 1-2hrs	VAS scores at rest and with movement, daily verbal pain relief scores and side effect profiles were not significantly different. Hospital or ICU stay was not reported

S: sex, M/ F -Male or female, W: weight, H: height, VAS: visual analogue scale, ICU: Intensive Care Unit, IV PCA; intravenous Patient controlled analgesia, NA SC: nurse administered subcutaneous; BMI- body mass index, BSA- body surface area, CABG-coronary artery bypass graft, CPB-cardiopulmonary bypass, R- Remifentanyl, M-Morphine

## Discussion

### Major findings

Use of opioids analgesics alone postcardiac surgery is an acceptable and established way of pain management worldwide.<sup>[20]</sup> We performed a systematic review of randomized controlled trials and found that parasternal and intercostal blocks, local anesthetic infiltrations, and local anesthetic continuous infusions when used with background of opioid PCA appeared to be effective pain management in patients postcardiac surgery and improved patient outcomes.

Application of anesthetics directly to wounds provides analgesia by blocking transmission of pain from nociceptive afferents in the wound surface and by inhibiting local inflammatory response to injury, thereby reducing the

release of inflammatory mediators from neutrophils and decreasing edema formation.<sup>[21]</sup>

### Infiltrations and parasternal blocks and continuous subcutaneous anesthetic infusions

The local infiltrations and parasternal blocks<sup>[10-12]</sup> appeared to be much more effective in the first 4–6 up to 24 h postoperatively. This result is in line with previous systematic reviews conducted on evaluating regional techniques for postthoracotomy analgesia.<sup>[22]</sup> Previous systematic reviews were not able to detect the appreciable benefit from single injection of local anesthetics in abdominal operation or laparoscopy.<sup>[23,24]</sup>

The continuous subcutaneous anesthetic infusions<sup>[13-16]</sup> were effective much longer and associated with reduced LOS as indicated in previous review.<sup>[21]</sup>

In the local anesthetic groups, whether infiltrated, nerve block, or subcutaneous infusions, all patients in the control and treatment groups used opioids to cover other discomforts associated with the operation and ICU admission. The use of both local anesthetic infusions with PCA<sup>[15]</sup> demonstrated superior analgesia to PCA alone in reducing pain post minimally invasive cardiac surgery. This was also demonstrated in other studies<sup>[13,14,16,20,25]</sup> and led to the reduction in the use of opioids and consequent reductions in hospital stay. Nasr *et al.*<sup>[16]</sup> also demonstrated early extubation in the bupivacaine group with better respiratory parameters as indicated by the arterial blood gases (ABG) analyses at the time of extubation and the subsequent readings compared to the control group. On the contrary, Eljezi *et al.*<sup>[14]</sup> did not demonstrate any improvement in the respiratory function with improvement in analgesia in their study group. This could have been due to the use of different parameters of assessing respiratory functions, for example, ABGs versus pulmonary function tests. This review also demonstrates why it is important to consider the dosages of the local anesthetics being used to avoid toxicity leading to neurological and cardiac complications.

#### Opioid administration and patient-controlled analgesia

Administration of opioids is considered a cornerstone of postoperative pain management; greater analgesic efficacy and higher patient satisfaction are achieved with opioid PCA.<sup>[26]</sup> PCA not only improves patient comfort but also it improves resource utilization.<sup>[27]</sup> Baltali<sup>[18]</sup> demonstrated that RM PCA was a better analgesic on the basis of pain scores during coughing and movement. Gurbet *et al.*<sup>[28]</sup> in a study, where they compared fentanyl, morphine, and RM, found that PCA of RM provided equal and adequate pain relief at rest after cardiac surgery such as morphine and fentanyl. Munro *et al.*<sup>[19]</sup> did not show significance difference in the use of PCA and NASC morphine. In a meta-analysis comparing PCA with nurse-controlled analgesia,<sup>[27]</sup> there was a 25% reduction in VAS scores for patients who used PCA compared to nurse-controlled analgesia between 24 and 48 h postoperatively.

#### Ketamine

Ketamine has been used successfully for pain management in various trials.<sup>[29-32]</sup> Lahtinen *et al.*<sup>[17]</sup> used S (+) ketamine as an analgesic adjunct and proved that it reduced opioid consumption in patients' postcardiac surgery. Epidural S (+) ketamine was used effectively to reduce pain postknee arthroplasty when it was applied with ropivacaine in epidural anesthesia;<sup>[33]</sup> S (+) Ketamine was given as an infusion post knee arthroscopy,<sup>[34]</sup> and neither enhanced analgesia, nor provided opioid sparing effect. In Lahtinen *et al.*,<sup>[17]</sup> four patients developed transient hallucinations during the infusion versus none in the placebo group; however, opioid consumption in the S (+) Ketamine group decreased in the first 48 h.

#### Limitations to this study

Methodological quality of the randomized controlled trials in this systematic review varied. Due to the strict inclusion and exclusion criteria, the number of studies and ultimately patients for analysis was limited. Not all studies reported on all the outcome measures of interest to this study like complications, LOS. Despite these challenges, the information extracted was in line with previous studies, and the recommendations may lead to new and better ways of pain management in patients postcardiac surgery.

#### Conclusion

The use of PCA with opioids in conjunction with local subcutaneous anesthetic continuous infusions is much more effective longer. This approach might eventually be the cornerstone for pain management postcardiac surgery in ICUs. There is a need, therefore, for anesthetists and acute pain service teams to consider the use of mixed methods in pain management postcardiac surgery. There is a need to be cautious with Ketamine use postcardiac surgery until more dose-related studies are done and concerns pertaining to psychotomimetic adverse reactions are addressed.

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#### Conflicts of interest

There are no conflicts of interest.

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