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Opioid-Sparing Anesthesia in Cardiac Surgery Requiring Cardiopulmonary Bypass

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Requiring Cardiopulmonary Bypass

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Abstract

Background: Traditional anesthesia for cardiac surgery involved high opioid use associated with adverse events and poor outcomes which led to the adoption of multi-modal analgesic approaches. Although improvements in the overall opioid consumption are seen with multi-modal analgesic approaches, recent studies in opioid-sparing anesthesia and regional anesthesia can further reduce the operative use of opioids in cardiac surgery to improve patient outcomes.
Methods: A comprehensive study search was conducted using CINAHL and MEDLINE (ProQuest) to identify research studies from the past three years that have focused on opioid-sparing anesthesia or opioid-free techniques in patients undergoing cardiac surgery with cardiopulmonary bypass.
Results: Six research studies were identified as relevant for review. The studies included in this literature review address opioid-sparing anesthesia in cardiac surgery through different techniques, investigate the feasibility for implementation, the role of regional anesthesia, and individual intraoperative pharmacological adjuvants in cardiac surgery requiring cardiopulmonary bypass (CPB).

Keywords: Opioid-sparing anesthesia, cardiac surgery, cardiac anesthesia, cardiopulmonary bypass, regional anesthesia, opioid crisis, dexmedetomidine.

Problem Identification

To the anesthesia provider, the management of both acute and chronic pain is fundamental as a clinician. Although a multimodal analgesic approach is routinely used by many anesthesia providers, the use of μ opioid receptor agonists is the current paradigm for acute and chronic pain management. Despite the current standard, the perioperative use of opioids may also be detrimental to patient care and may result in opioid-induced side effects including nausea, emesis, ileus, hyperalgesia, somnolence, pruritus, urinary retention, respiratory depression, and death. In addition, up to eight percent of opioid-naive patients who undergo surgery and receive opioids perioperatively may become chronic opioid users.[1] This information has led to the adoption and implementation of non-opioid alternatives and opioid-sparing anesthesia techniques. However, for the last fifty years opioids have been the mainstay in cardiac surgeries.[2] These major surgeries can involve the coronary arteries, heart valves, or other cardiac structures that may need to be accessed by the surgeon.

Traditionally, a high-dose opioid induction and maintenance was considered gold standard for cardiac patients in the 1980s. However, that concept came packaged with side effects of prolonged mechanical ventilation, increased length of stay in the intensive care unit and hospital,[2] increasing awareness and allowing for other methods to be introduced. Although providers use a multi-modal approach to analgesia with non-opioid adjuvants, intraoperative opioid usage ultimately varies between patient, procedure, and anesthesia providers.[3] Focusing on the anesthesia provider, an educational tool on opioid sparing analgesic strategies will help improve provider knowledge.

Background

Opioid use and abuse along with addiction has become a significant issue for the last decade. In fact, opioid overdose in now one of the leading causes of unintentional death in the United States, surpassing motor vehicle accidents.[4] Most surgical patients often receive some form of opioid narcotic throughout the perioperative period and then postoperatively. Reason being, that opioids are potent with a rapid onset of action without an analgesic ceiling,[4] but with the increasing use of opioids, it has become a realization that its benefits might be overshadowed by the potential downsides.[5] Researchers have shown that opioid-naïve patients often can become dependent on narcotic administration after surgery. The anesthesia provider plays a paramount role in the primary stage of the patient's exposure to such potent drugs, and therefore can be a leading agitator to these key issues.

One of the leading causes of the opioid prescription crisis was the call to awareness of treating pain as the "fifth vital sign", and idea presented by Dr. James Campbell in 1995. In 1997, the Robert Wood Johnson Foundation funded The Joint Commission to develop pain standards. Dr. Dennis O'Leary, President of the Joint Commission on Accreditation of Healthcare Organizations, announced standards for health care organizations to improve pain management, and emphasized the need for organizations to do systematic assessments and use quantitative measures of pain.[6] This led to a national focus in assessing patients' perception of pain; often by practitioners without much experience treating pain.[5] Dr. Max emphasized the conventional wisdom of the day that "therapeutic use of opiate analgesics rarely results in addiction," although this was based on only a single publication that lacked detail about how the study was done.[6] Nonetheless, physicians obtained the "green light" to prescribe opioids to patients that reported high levels of pain on a numerical pain scale. In the 1980's through 2000's in the United States, although the rate of opioid overdose deaths increased drastically, patients

continued to report the same levels of pain.[5] The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse alone in the United States is $78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement.[7]

The opioid epidemic has allowed for the ability to analyze and make changes to how pain was being treated. As stated by The Joint Commission, our goal is to ensure that the pendulum of medical practice does not swing back toward the poor pain control of the past, but instead comes to rest in a position that balances effective pain treatment with safe opioid prescribing for individual patients and the general population.[6] By improving the knowledge of anesthesia providers on opioid-sparing analgesic techniques in cardiac surgery, efforts to adhere to the call of The Joint Commission will remain preserved.

Scope of the Problem

Numerous factors contribute to the current practice of perioperative opioid usage. The scope of the problem addresses patients undergoing cardiac surgery but also focuses on the anesthesia provider, and the system or institution. Cardiovascular disease is the leading cause of global death with an estimated seventeen million deaths per year, and the number is set to increase to twenty-three million by the year 2030. Coronary artery disease, peripheral vascular disease, and risk for CAD increase operative risk. Recent myocardial infarction, congestive heart failure, and aortic stenosis are important risk factors in the anesthetic management of these patients. Anesthesia for the cardiac patient requires extensive knowledge of the pathophysiology of the disease process, intraoperative monitoring, and anesthetic management. This includes a careful selection of anesthetic, analgesic, neuromuscular, and autonomic blocking drugs.[8] In the providers armamenterium, the provider should also be familiar with opioid-sparing strategies to

decrease opioid consumption and will benefit from current research regarding the use of opioid-sparing anesthesia in cardiac surgery. The hospital system or medical institution in which the provider practices, has a role in the adoption of certain anesthetic techniques. Therefore, a compilation of evidence and research in the practice of opioid-sparing anesthesia in cardiac surgery is required for adoption of new policy and the translation of evidence into practice.[9] Fortunately, the increasing discussions on the liberal use of opioids during anesthesia care being called into question, and research is demonstrating that adverse effects limit their effectiveness in perioperative care.[10] An educational intervention tool in this sub facet of cardiac surgery will not only ensure the anesthesia provider has up-to-date information and the necessary ability to implement opioid sparing strategies, in an effort to combat the issue of opioid usage and lack of provider knowledge.

Consequences of the Problem

Cardiac surgery is associated with moderate to severe pain that is related to median sternotomy, chest tubes, and costovertebral joint distention. Vascular access sites and saphenous graft harvest sites cause significant pain. Ineffective pain control after major cardiac surgery can lead to sympathetic activation, resulting in unstable hemodynamics and an increased demand for oxygen, which is undesirable in cardiac patients with limited reserves.[11] Due to this delicate balance, postoperative pain has been traditionally managed with the use of intravenous opioids.[12] However, the use of fentanyl and remifentanil are associated with two clinical phenomena specific to opioids. The first is antinociceptive tolerance, which is the decrease in the analgesic activity with a previous exposure to the same or a similar drug. Thus, requiring higher doses to exhibit the same amount of pain relief. And the second problem is opioid-induced hyperalgesia. When hyperalgesia is present, prolonged, or acute administration of opioids results in a

paradoxical decrease in the pain threshold. The lowered threshold causes increases of atypical pain that appears to be unrelated to the original nociceptive stimulus.[13] Other undesired clinical effects from high narcotic analgesia include respiratory depression, chest wall rigidity, impaired gas exchange, difficult mask management, gastrointestinal alterations, nausea, vomiting, inflammation modulation, immunologic alteration, postoperative thermal hyperalgesia, tactile allodynia, and the need for higher rescue analgesia postoperatively.[10,13,14]

Despite the associated downsides, opioids remain the primary agents used in most cardiac surgeries for the treatment of acute and chronic pain.[13,15] The lack of provider knowledge on opioid sparing analgesic strategies intraoperatively in cardiac surgery can have some unbeknownst negative outcomes of the patients they treat. After implementation of the educational tool, the anesthesia provider will gain knowledge that can lead to quicker extubation times, improved cardio protection and decreased postoperative morphine consumption, indications for which populations to implement opioid-sparing anesthesia, and methods to prevent some of the overall consequences of habitual intraoperative opioid usage.

Knowledge Gaps

Despite modern enhanced recovery after surgery (ERAS) and fast-track protocols that aim to reduce opioid usage perioperatively, there is still room for decreasing the use of intraoperative opioids, even in major cardiac surgery. One potential reason for this knowledge gap as described by White et al., could be from the wealth of knowledge that is available today to the clinician. Constant publishing from new journals and research articles can be overwhelming. For instance, in 1995, it was estimated that clinicians would need to read 19 articles a day, 365 days a year to stay abreast of new clinical information. Today, the challenge to stay current with the latest research is harder, which speaks to the importance of finding new evidence-based

practices to bridge this research-practice gap.[9] Also, this knowledge gap may be present due to the existence of conflicting clinical practice guidelines with differing recommendations regarding the same intervention or population, which tend to undermine the use of the new findings. One study mentions that although modern fast-track cardiac programs use multimodal analgesia regimens including paracetamol, non-steroidal anti-inflammatory drugs, and opioids, the technique has been shown to be suboptimal after pediatric open cardiac surgery. Fifty-two percent of pediatric patients still report moderate to severe pain on the day of surgery and thirty-three percent experience pain on postoperative day one, along with 42% of patients reporting vomiting.[12]

Proposal Solution

To increase knowledge and improve the adoption of opioid-sparing anesthesia amongst anesthesia providers, demonstrating the effectiveness of opioid-sparing analgesic techniques in one of the most challenging operating room theatres being cardiac surgery, will help strengthen the research to practice gap. Opioid-sparing anesthesia does not focus on the use of one single drug, but instead encompasses a polypharmacy approach to anesthesia and analgesia.

Drugs commonly used include premedication with gabapentin or pregabalin, the intraoperative use of dexmedetomidine, magnesium, lidocaine, ketamine, and postoperative medication such as paracetamol, diclofenac, intravenous ibuprofen, and IV acetaminophen. Opioid-sparing anesthesia is paired with regional anesthesia to control pain transmission, decrease opioid use, emphasize early extubation, and mobilization.[2,13]

Several opioid-sparing techniques have recently been published in major cardiac surgery requiring on-pump cardiopulmonary bypass in both adult and pediatric populations. One 2019

study focused on the effects on opioid-free anesthesia on CABG surgery postoperatively.[10] The use of intraoperative dexmedetomidine was not used in the first study but included in the 2021 study focused on the feasibility of dexmedetomidine in CABG surgery requiring CPB.[16] In the both studies the reduced opioid group was associated with lower morphine consumption, shortened intubation times, and decreased ICU stay.[13] Additionally, the second study mentions that the protocol used could reduce opioid consumption when compared to the multi-modal and ERAS approaches by half, and also revealed that dexmedetomidine reduced the incidence of new-onset atrial fibrillation, has myocardial protective qualities, and is associated with a decreased incidence of postoperative delirium.[16]

Regarding the pediatric population, in 2020 Wolters Kluwer published an article with an opioid-sparing ERAS protocol using a single dose of IV methadone in children undergoing major cardiac surgery requiring CPB. Methadone, lidocaine, and ketamine boluses were given prior to incision, then ketamine and lidocaine were continued for maintenance. Prior to emergence, a regional parasternal infiltration with ropivacaine 0.2% was completed and IV acetaminophen bloused. Of the 24 participants in the study, no child required supplemental opioid intraoperatively, and all but one child was extubated on the OR table.[17] In 2019, the British Journal of Anaesthesia published a study on dexmedetomidine aimed in determining the safety of usage in neonates and infants undergoing cardiac surgery on CPB, and concluded that dexmedetomidine can be a feasible addition to the anesthetic regimen, and results in low incidence and severity of adverse safety events in infants undergoing cardiac surgery with cardiopulmonary bypass and validates the pursuance of opioid-sparing modalities in the pediatric population and major cardiac surgeries.[18]

As previously discussed, the use of regional anesthesia in cardiac surgery along with opioid-sparing use has also been the topic of research with multiple studies having described major success in mitigating the use of opioids with an erector spinae plane block in both the pediatric and adult population.[12] ESPB is an inter-fascial plane block where local anesthetic is injected beneath the iliocostalis, longissimus, and spinalis muscles to achieve analgesia for pediatric thoracic, cardiac, or abdominal surgery. The effect appears to be due to local anesthetic spread close to the paravertebral space, reaching the dorsal and ventral rami of the thoracic spinal nerves that cover dermatomes, which include the midline sternotomy. The ESPB achieves local anesthetic diffusion to the thoracic paravertebral space when the anesthetic solution is located in between the erector spinae muscles and the paravertebral compartment.[12] In one study, the ESPB was done preoperatively with catheters in place for redosing ropivacaine along with an intraoperative multimodal opioid free approach using dexmedetomidine, ketamine, magnesium, and esmolol, allowed the patient to be extubated after CPB. A single dose of oxycodone was given to the patient in the ICU.[17]

Conducting a thorough literature analysis will provide anesthesia providers with the most up-to-date information possible. The findings are correlative with recent literature and appear to be of vast significance in the development of opioid-sparing anesthetic techniques with benefits in multiple surgical procedures, and in various patient populations. This project will include an educational intervention to improve the knowledge of anesthesia providers in opioid sparing strategies; more specifically, in major cardiac surgery requiring cardiopulmonary bypass.

Methodology

Eligibility Criteria

Studies evaluated for this literature review were chosen based on the inclusion and exclusion criteria set to best discern the objectives. Inclusion criteria included only studies written in English with full-text availability. Exclusion criteria included the studies where subjects were undergoing non-cardiac surgeries using opioid-sparing anesthesia. The studies included for review focus on the open-heart surgery requiring on-pump or off-pump CPB. Clinical database sources used to guide research were accessed via Florida International University library services.

Information sources

Based on the clinical question, the following search keywords were identified using the appropriate Boolean operators and search symbols: Opioid sparing anesthesia, Coronary Artery Bypass Graft, Opioid-free anesthesia, and Cardiac surgery. The databases utilized for the search included The Cumulative Index to Nursing and Allied Health Literature (CINAHL) and MEDLINE (ProQuest)

Search Strategy

The key search terms were further expanded to include: (“Opioid free anesthesia” OR Nonopioid anesthesia” OR “OFA” OR Opioid Sparing OR Dexmedetomidine OR ESPB OR Regional anesthesia) AND (“Cardiac surgery” OR “Heart surgery” OR “Coronary artery bypass” OR Cardiovascular OR Cardiopulmonary bypass OR Valve surgery) The CINAHL search yielded 434 articles and MEDLINE produced 4,299 articles. To ensure the most relevant and recent articles were reviewed, only articles published from 2018 to 2021 and those written in English were included. This yielded 625 for MEDLINE and 119 articles for CINAHL. Duplicate articles were removed, and the CINAHL search was narrowed even further. Titles were excluded if they did not meet inclusion criteria. Articles that included the use of nonopioid drugs solely in

the postoperative phase were excluded. Studies that were not completed or letters to the editors were excluded from further review. The populations accepted included neonates, pediatrics, and adults.

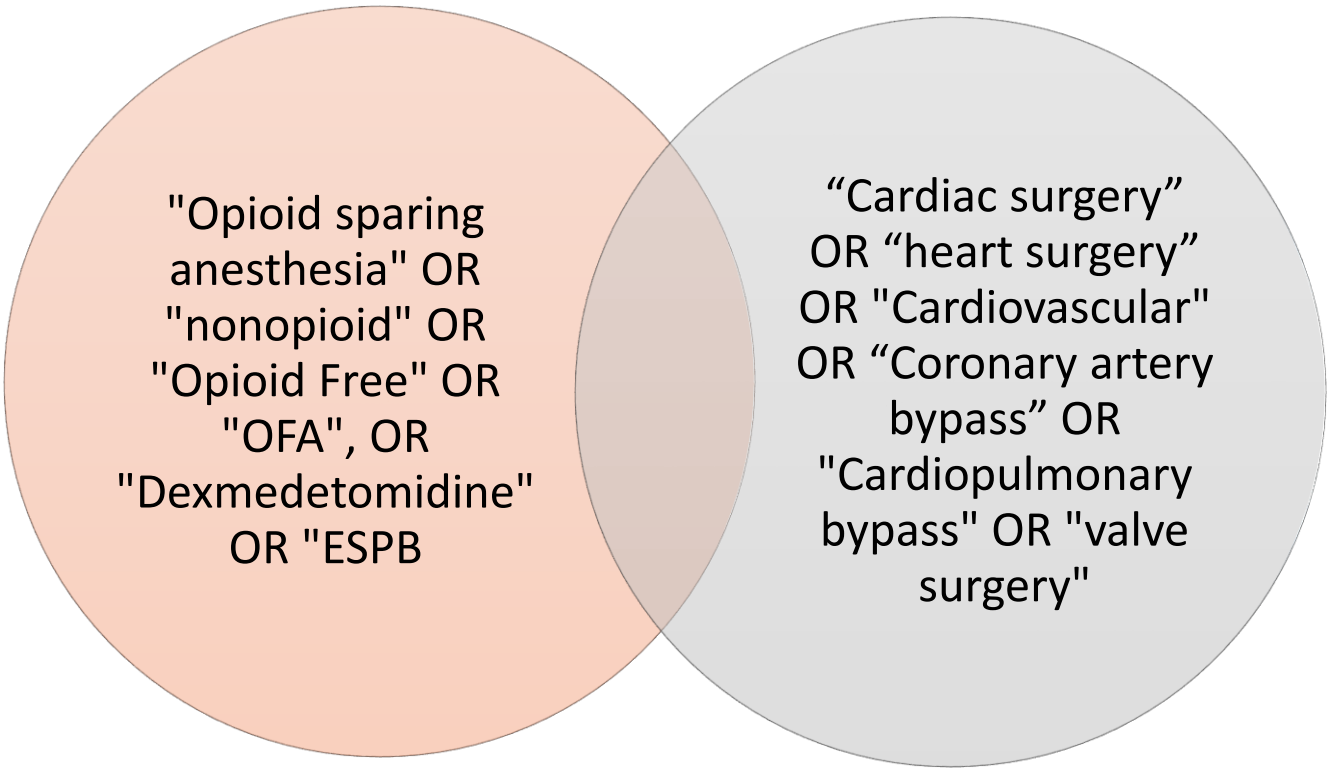


Diagram 1. Search Keywords

Author(s)	Purpose	Methodology / Research Design	Intervention(s)/ Measures	Sampling/Setting	Primary Results	Relevant Conclusions
Guinot et al. (2019)	To demonstrate the feasibility of an opioid-free anesthesia (OFA) protocol in cardiac surgery to improve patient care. To demonstrate that compared with OA, OFA lowers postoperative morphine consumption. To evaluate the effect of OFA on operative hemodynamic stability, postoperative complications assessed by a composite criterion and the length of stay (LOS) in the ICU and in hospital.	Retrospective matched cohort study, Level III	Retrospective matched cohort study on cardiac surgery patients with cardiopulmonary bypass between 2018 and 2019. Patients were divided into two groups: OFA (lidocaine, dexamethasone and ketamine) or opioid anaesthesia (OA) (sufentanil).	Participants were 18 or over requiring cardiac surgery with the use of cardiopulmonary bypass (CPB), coronary artery bypass grafting (CABG), the surgical correction of valve disease (aortic, mitral), combined surgery (CABG and valve disease), ascending aortic disease, and left ventricular assist device implantation). The exclusion criteria were off-pump cardiac surgery, preoperative analgesic use, gabapentin use, antidepressant therapy and preoperative	The total morphine consumption was higher in the OA group than in the OFA group (15 (6–34) vs 5 mg (2–18), p = 0.001). The pain score during the first 48 post-operative hours did not differ between the two groups. Creatinine values did not differ on the first post-operative day (80 (IQR: 66– 115) vs 77 mmol/l (IQR: 69–95), p = 0.284). Incidence of the composite endpoint was lower in the OFA group (25 patients (43%) vs 38 patients (68%), p = 0.021). The time to extubation and the ICU stays were shorter in the OFA group (3 (1–5) vs 5 (3–6) hours, p = 0.001 and 2 (1–3) vs 3 (2–5) days, p = 0.037).	The use of OFA was associated with lower morphine consumption. OFA might be associated with shorter intubation time and ICU stays. OFA might have beneficial effects of on the post-operative course of patients undergoing cardiac surgery with CBP

				cognitive dysfunction. 110 patients met criteria for inclusion in the study, 55 in the OA group and 55 in the OFA group.		
Aguerreche et al., (2021)	To investigate a dexmedetomidine-based opioid-free anesthesia (OFA) protocol in cardiac surgery. The main objective of this study was to evaluate the feasibility and the postoperative opioid- sparing effect of dexmedetomidine-based OFA in adult cardiac surgery patients.	Retrospective review. Level III	A retrospective review was performed on patients who underwent on-pump cardiac surgery between November 2018 and February 2020. The primary endpoint was the total amount of opioid consumed in its equivalent of intravenous morphine during the first 48 postoperative hours. Secondary outcomes included perioperative	80 patients were divided into two groups: OFA (lidocaine, ketamine, dexmedetomidine, MgSO4) or opioid-based anaesthesia (remifentanil and anti- hyperalgesic medications such as ketamine and/or MgSO4 and/or lidocaine at the discretion of the anesthesiologist). Patients undergoing off-pump cardiac surgery and/or with pre-operative	The median total amount of opioid consumed in its equivalent of intravenous morphine during the first 48 postoperative hours was lower in the OFA group (15.0 mg [8.5–23.5] versus 30.0 mg [17.3–44.3], $p < 0.001$). While no differences were seen with rest pain (2.0 [0.0–3.0] versus 0.5 [0.0–5.0], $p = 0.60$), the maximal pain score during coughing was lower in OFA group (3.5 [2.0–5.0] versus 5.5 [3.0–7.0], $p = 0.04$). In OFA group the incidence of atrial fibrillation (18% versus 40%, $p = 0.03$) and non-invasive ventilation use (25% versus 48%, $p = 0.04$) were lower. The incidence of bradycardia	Dexmedetomidine-based OFA in cardiac surgery patients is feasible and could be associated with a lower postoperative morphine consumption and better postoperative outcomes. Further randomized studies are required to confirm these promising results and determine the optimal associations, dosages, and infusion protocols during cardiac surgery.

			hemodynamics, post-operative maximal pain at rest and during coughing and adverse outcomes. Data are expressed as median.	hemodynamic instability and/or with atrio-ventricular block grade 2 or 3 and/or hypersensitivity to opioids were excluded.	and the intraoperative use of norepinephrine were similar between both groups.	
Kaushal et al., (2020)	To test the hypothesis that the administration of bilateral ESPB with ropivacaine 0.2% would improve postoperative analgesia after pediatric cardiac surgery. The requirement of additional rescue analgesic medication and adverse events associated with ESPB also were studied.	Prospective, randomized, single-blind, comparative study Level III	The subjects were allocated randomly into 2 groups: ESPB (group B, n = 40) received ultrasound guided bilateral ESPB at the level of T3 transverse process and control (group C, n = 40) receiving no block. The postoperative pain was assessed using Modified Objective Pain Scores (MOPS) which were evaluated at 0, 1, 2, 4, 6, 8, 10, and 12	Eighty children with acyanotic congenital heart disease undergoing cardiac surgery through midline sternotomy. Patients with preoperative ejection fraction <35%, low-cardiac-output syndrome, recurrent ventricular arrhythmias, preoperative inotropic support, allergic to the amide type of local anesthetics (LA),	Group B demonstrated significantly reduced MOPS as compared with group C until the 10th postoperative hour ($p < 0.0001$), with comparable MOPS at the 12th hour. The consumption of postoperative rescue fentanyl was also significantly less in group B in comparison to group C ($p < 0.0001$) with a longer duration to first rescue dose requirement in group B. In addition, the group B showed lower postoperative sedation scores and intensive care unit stay in contrast to group C.	Ultrasound-guided bilateral ESPB presents a simple, innovative, reliable, and effective postoperative analgesic modality for pediat- ric cardiac surgeries contemplated through a midline sternotomy.

			hours after extubation	requiring intubation for more than 3 hours or re-exploration, and requiring redo or emergency surgery were excluded from the study.		
Macaire et al., (2020)	To determine if bilateral ESPB with a programmed intermittent bolus (PIB) regimen decreases postoperative morphine consumption at 48 hours and improves analgesia in children who undergo cardiac surgery.	Randomized, double-blind, placebo-controlled trial Level III	Children who underwent cardiac surgery through midline sternotomy randomly allocated into two groups: ultrasound- guided bilateral ESPB at the level of T3–T4 transverse process then PIB with saline infusion (group 1, n=23) or PIB with 0.2% ropivacaine (group 2, n=27). Intravenous morphine at 30 µg/kg/hour was used as rescue analgesia	This randomized, double-blind, placebo-controlled study was performed from August 2018 to March 2019, initially with 104 children with an American Society of Anesthesiologists physical status class II scheduled for cardiac surgical procedures through midline sternotomy at Vinmec Central Park International Hospital, Ho Chi Minh City, Vietnam. Exclusion criteria were as follows:	The total dose of morphine in 48 hours was significantly decreased in patients receiving a bilateral ESPB with ropivacaine (120±320 µg/kg) compared with patients with saline infusion (512±560 µg/kg; p=0.03). Fourteen per cent of patients required rescue analgesia with morphine in group 2 compared with 41% in group 1 (p=0.05). The patients in group 2 demonstrated significantly reduced COMFORT-B scores at extubation, drain removal, and mobilization compared with those in group 1 and had reduced FLACC scale levels	In pediatric cardiac surgery, the results of this study confirms that bilateral ESPB analgesia with ropivacaine decreases the postoperative morphine consumption at 48 hours and demonstrates better postoperative analgesia compared with a control group.

			Postoperative pain was assessed using the COMFORT-B score for extubation, drain removal, and mobilization, and the FLACC (Face, Legs, Activity, Cry, Consolability) scale at 0, 2, 4, 6, 8, 12, 16, 20, 24, 36, and 48hours after surgery. Adverse events were noted.	the patient's family refused, a preoperative ejection fraction <35%, ventricular arrhythmia/dysrhythmia, preoperative inotropic support, redo or emergency surgical procedures, and an allergy to amide-type LAs.	at 20 and 24 hours postoperatively (p=0.05 and p=0.001, respectively). No differences were reported for extubation and drain removal times or for length of hospital stay. In addition, vomiting episodes were decreased in group 2 (p=0.01).	
Iguidbashian et al., (2020)	Assess the efficacy and safety of a multimodal pain regimen centered around single-dose intraoperative IV methadone in pediatric cardiac surgical patients.	Retrospective analysis, Level III	A retrospective analysis of all pediatric cardiac surgical patients for whom early extubation was intended. A multimodal analgesic regimen was used for all patients, consisting of methadone (0.2–0.3 mg/kg), ketamine (0.5 mg/kg plus 0.25 mg/kg/h), lidocaine	A total of 24 children were included in the study. Fifteen were male; 22 had procedures performed on bypass, and 11 involved a reentry sternotomy. The youngest and smallest patient was 8 months old and weighed 6.2 kg. Four patients	None of the children required intraoperative supplemental opioids; 23 (96%) were extubated in the operating room. Time to first supplemental opioid administration was 5.1 (3.5–9.5) h. Cumulative total supplemental opioids (in intravenous morphine equivalents) at 24 and 72 h were 0.2 (0.09–0.32) and 0.42 (0.27–0.68) mg/kg.	A methadone-based multimodal regimen facilitated early extubation without appreciable adverse events. Further investigations are needed to confirm efficacy of this regimen and to assess whether the excellent safety profile seen here holds in the hands of multiple providers caring for a larger,

			(1 mg/kg plus 1.5 mg/kg/h), acetaminophen (15 mg/kg), and parasternal ropivacaine (0.5 mL/kg of 0.2%). Average methadone dosing was 0.26 (0.23–0.29) mg/kg	had single-ventricle physiology	One child required postoperative bilevel positive airway pressure support, but none required reintubation. None had pruritus; three (13%) experienced nausea	more heterogeneous population.
Ming et al., (2021)	This study aimed to investigate the effects of dexmedetomidine on hemodynamics and organ protection in congenital heart disease (CHD) children who underwent open-heart surgery under cryogenic cardiopulmonary bypass.	Randomized Controlled Trial	90 children were randomly allocated to group C (0.9% saline 0.2 mg/kg/hour), group D1 (Dexmedetomidine 0.2 mcg/kg/hour), and group D2 (Dexmedetomidine 0.4mcg/kg/hour) (n=30 per group). All participants received fentanyl, propofol and 1% sevoflurane for anesthesia induction. Hemodynamic data	Children who were scheduled for repair of atrioventricular septal defect during CPB under elective general anesthesia were enrolled in this study from July 1st, 2017 to February 28th, 2018 at the Ruikang Hospital of Guangxi University of Traditional Chinese Medicine. Patients aged 1 to 6years, diagnosed	Compared with group C, group D1, and D2 exhibited reduction in hemodynamic parameters, myocardial and brain injury indicators, and tracheal extubation time. There were no significant differences in blood urea nitrogen and neutrophil gelatinase- associated lipocalin or incidence of AKI among the 3 groups. Besides, the incidence of tachycardia, nausea, vomiting and moderate agitation, and the FLACC scale in group D1 and D2	Anesthesia with dexmedetomidine can effectively maintain hemodynamic stability and diminish organ injuries in CHD children.

			were measured from T0 (before the induction) to T7 (30 minutes after extubation). The difference of arterial internal jugular vein bulbar oxygen difference and cerebral oxygen extraction ratio were calculated according to Fick formula. Enzyme-linked immunosorbent assay was performed to detect the serum myocardial, brain and kidney injury markers. The incidence of acute kidney injury (AKI) was calculated by serum creatinine level. Tracheal extubation time, postoperative pain score and	with CHD or AVSD, with an ASA class II-III. Patients with severe malnutrition and cyanosis were premature and low birth weight; 2. a previous cardiac surgery; 3. allergic to narcotic drugs; 4. pulmonary hypertension; 5. combined with cerebral palsy, severe renal or hepatic disorders, metabolic dysfunction, or other congenital diseases affecting the brain, liver, and kidney, such as Trisomy 21 syndrome were excluded from the study.	were lower than those in group C. Dexmedetomidine 0.4 g/kg/hour could further reduce the dosage of fentanyl and dopamine compared with Dex 0.2g/kg/hour.	

			emergence agitation score were also recorded			

Results of Literature

Study Characteristics

The articles reviewed are centered on cardiac surgery requiring cardiopulmonary bypass along with measurable outcomes during the intraoperative and postoperative phases of their surgical management. Three articles are retrospective studies (Aguerreche et al., Guinot et al., and Iguidbashian et al.), two articles are RCTs (Macaire et al. & Ming et al.) with Macaire et al. being a double-blind and placebo-controlled trial. The last study is a prospective, randomized, single-blind, comparative study (Kaushal et al.). Subjects in the retrospective studies were analyzed before and after intervention without randomization.

The articles analyzed the feasibility of opioid-sparing anesthesia techniques in open-heart surgery. The study methods by Macaire et al. and Kushal et al. analyzed the use of regional anesthesia with ESPB blocks to reduce opioid consumption postoperatively. Guinot et al., Aguerreche et al., and Iguidbashian et al. analyzed the use of a non-opioid-based anesthetic regimen during heart surgery on CPB in efforts to minimize opioid administration while analyzing the feasibility of an opioid spared approach. The article Aguerreche et al. specifically focused on the use of dexmedetomidine intraoperatively as an IV infusion, and Iguidbashian et al. focused on the pediatric population with a focus on the postoperative minimization of opioids. The final study by Ming et al. offers further support for the use of opioid-sparing anesthesia in children with congenital heart disease. Lastly, in the single-blind comparative study by Kaushal et al., subjects were analyzed before and after intervention without randomization.

Summary of the Evidence

This 2019 study by Guinot et al. is the first of its kind to specifically focus on the feasibility of OFA in cardiac surgery undergoing CPB. The findings by Guinot et al. supporting

the use of OFA, or a minimal opioid approach in cardiac surgery became the basis for further studies such as that by Aguerreche et al. The retrospective study by Aguerreche et al. demonstrates the potential for dexmedetomidine as the foundation in an opioid-sparing anesthesia approach to cardiac surgery. Dexmedetomidine offered numerous benefits in the cardiac patient having cardiac surgery and compounded to the information presented in the article by Guinot et al., which focused on the use of other non-opioid adjuvants without dexmedetomidine (due to unavailability) in open-heart cardiac surgery.

Multiple articles supported the use of regional anesthesia in the preserving opioid usage, however the ESPB offered multiple advantages, as demonstrated in the study by Kaushal et al. The article was chosen for literature review as it demonstrated the ability of the ESPB to have a major opioid-sparing effect in cardiac surgery. The bilateral ESPB as a newer regional technique in cardiac surgery proved to reduced opioid consumption, demonstrated efficacy, was safe, and simple to implement for the anesthesia provider. The following article by Macaire et al. provided further insight into the opioid-sparing effects of bilateral ESPB in cardiac surgery. Where the article by Kaushal et al. demonstrated the analgesic benefits to using the ESPB in pediatric cardiac surgery, Macaire et al. found that the addition of PIBs of ropivacaine can further prolong analgesia and diminish post-operative morphine consumption beyond 12 hours (Kaushal et al.) to 48 hours without causing LA systemic toxicity in pediatric cardiac patients undergoing open-heart surgery via midline sternotomy.

The article by Iguidbashian et al. is one of the first to propose the use of IV methadone as the cornerstone of an analgesic regimen in pediatric cardiac surgery. Iguidbashian et al. focused on the use of methadone in the pediatric cardiac population versus the use of more traditional approaches using short-acting analgesics and explains that in traditional methods, pain levels

tend to wax and wane in relation to the varying plasma drug levels. Iguidbashian et al. hypothesized that methadone due to its long duration of action of approximately 24-36 hours may provide steadier, basal pain control during the period of greatest surgical pain. Alternatively, methadone also displays antagonizing effects on the N-methyl-D-aspartate (NMDA) receptor, may prevent the hyperalgesia related to chronic pain syndrome, and has fewer respiratory side effects[19] when compared to other rescue analgesics such as fentanyl, morphine. Also, of the articles reviewed for inclusion of the literature review, the intraoperative approach to this study is amongst the most opioid sparing by design with the inclusion of dexamethasone, ketamine, lidocaine, acetaminophen, ketorolac, and regional anesthesia, with a focus in OR on-table extubation.

Having adequate information to start an implementation guide based on dexmedetomidine, regional anesthesia with ESPB, and methadone as an alternative to short acting opioids, the study by Ming et al. solidifies the use of a dexmedetomidine based opioid-sparing anesthesia in cardiac surgery with the findings that dexmedetomidine at a rate of 0.4mcg/kg/hr is clinically safe and diminishes organ injuries in children undergoing open-heart surgery. Ming et al. explained the strong physiological stress response that is seen during open-heart surgery. For instance, when the ascending aorta is blocked during CPB it significantly diminishes normal blood perfusion to various organs of the body. Meanwhile, the blood in CPB is directly exposed to extracorporeal circulation pipeline and oxygenator, resulting in the generation of numerous inflammatory cytokines and cascade release, which can precipitate systemic inflammatory response syndromes. Hyperglycemia and hyperlacticacidemia are caused by this strong stress response, and hemodynamic instability during surgery can cause ischemia

and reperfusion injuries. These hemodynamic and physiologic changes can cause organ damage to the heart, lung, brain, and kidneys.

As opioid-sparing cardiac surgery gains popularity and interest, there will be more randomized controlled trials about opioid-sparing anesthesia in cardiac surgery. Sorting through search findings in the CINHAL database, numerous case reports validated the methods described above. One example is the Elsevier published case report in the *Journal of Cardiothoracic and Vascular Anesthesia* on opioid-free ultra-fast-track CABG surgery using ESPB catheters.[15] The case report describes a 74-year-old male undergoing CABG surgery with similar anesthetic approaches to those described by Guinot et al., Aguerreche et al., and Iguidbashian et al. with the use of versed, ketamine, propofol, ketamine, and magnesium for the induction of anesthesia, followed by bilateral ESPB with ropivacaine, acetaminophen IV and on-table extubation. In this case report the patient received a total 10 mg oral oxycodone for postoperative pain. A recent 2021 case report from Turkey by the *Anesthesia and Pain Management Journal*[12], describes a similar anesthetic regimen that mainly excluded the use of opioids from the preoperative phase to postoperative in three cardiac patients. Two patients were undergoing CABG surgery and the third patient underwent mitral valve repair, all which were successful under CPB. The ESPB were bilateral with catheters left in place for postoperative ropivacaine infusions. This case report used tramadol as a rescue analgesic versus morphine or fentanyl which was only used in one of the three patients. Unfortunately, these are only case reports and thus were not included in the literature review and are thus a limitation in this review. Further clinical studies are needed to validate the results; however, these two case reports encompass the use of opioid-sparing techniques throughout the perioperative course and includes the ESPB with the epidural catheters for programmed infusions of ropivacaine. The limited amount of research available on opioid-

sparing anesthesia in open-heart cardiac surgery is inherently a limitation to this review. Of the research available, the consensus is that larger, randomized clinical trials are needed to validate the findings

Results of Individual Studies

The first article by Guinot et al.[10] explored the feasibility of opioid-free anesthesia (OFA) protocol in cardiac surgery to improve patient care and then evaluate the end-effect on postoperative morphine consumption and the post-operative course. This retrospective matched study looked at cardiac surgery patients with CPB between 2018 and 2019 that were over the age of eighteen requiring coronary bypass grafting, or valve surgery (aortic, mitral), and or combined coronary and valve surgery. The exclusion criteria were off-pump cardiac surgery, preoperative analgesia use, gabapentin use, antidepressant therapy, and preoperative cognitive dysfunction. 110 patients were matched and were divided into two groups: 55 individuals in the OFA group and 55 individuals in the opioid anesthesia (OA) group. In the OA group, anesthesia was induced with an intravenous bolus of ketamine (0.3-0.5mg/kg), propofol (0.4-2mg/kg), and sufentanil (0.5ng/ml) until the loss of eyelash reflex. Sufentanil was continuously infused using Schneider's target-controlled infusion model. Also, in the OA group, all patients had regional anesthesia by serratus anterior plane block or a continuous parasternal infusion of a local anesthetic. None of the participants in the OA group received lidocaine. In the OFA group, the anesthetic regimen consisted of an intravenous bolus of dexamethasone (0.1mg/kg), an intravenous bolus of ketamine (0.3-0.5mg/kg) intravenous bolus of lidocaine (1.5mg/kg 15 minutes before the start of propofol), and propofol (0.4-2mg/kg) until the loss of eyelash reflex. Lidocaine was continuously administered at 1.5mg/kg/h until the end of surgery. In both groups, intubation was facilitated with the use of cisatracurium (0.15mg/kg) and neuromuscular blockade was ensured using

peripheral nerve stimulation, intermittent boluses were given as needed. The methods used during the time of CPB and ICU management are well documented and clearly explained and remain consistent in both groups to preserve the integrity of the study.

Postoperative analgesia management comprised intravenous paracetamol (1g every 6 hours) and morphine-based patient-controlled analgesia (PCA). Before extubation, all patients received 1 gram of acetaminophen. The study demonstrated a significant difference in the postoperative morphine doses between the OFA and OA groups (5mg vs 15 mg). However, complementary analgesia did not differ significantly. The complementary use of ketoprofen, nefopam, and tramadol remained the same between the two groups. Guinot et al. revealed two findings, one, that the OFA group was associated with lower postoperative morphine consumption, higher operative use of antihypertensive medications, a decrease in orotracheal intubation time including the use of non-invasive respiratory support, and shorter intensive care unit stays. Guinot et al. revealed that dexmedetomidine was not used because it was not available in their department but would have offered several advantages. For example, the combination of dexmedetomidine usage with lidocaine can lead to better postoperative pain relief with a quote by a recent meta-analysis confirming that dexmedetomidine provides good hemodynamic stability with less hypertension and tachycardia.

Limitations to the study include the study method a single retrospective study, which has inherited design-related limitations. Guinot et al., described a second limitation being despite protocol management for sedation and analgesia, biases may have been introduced by the attending physicians and nursing staff. For example, some patients received analgesia in addition to patient-controlled morphine analgesia. To improve on these limitations, controlled randomized

studies can confirm the results that opioid-sparing use in cardiac surgery may be beneficial in cardiac surgery with CPB.

The second article included in this literature review was published by BMC Anesthesiology in 2021 by Aguerreche et al.[16] This study explored the feasibility and postoperative opioid-sparing effect of an OFA approach in cardiac surgery. This study takes the recommendations from Guinot et al. and implements a dexmedetomidine-based approach to opioid-sparing anesthesia. The purpose of the article is disclosed with the research question supporting the hypothesis that dexmedetomidine-based OFA could significantly reduce morphine consumption within the first 48h following on-pump cardiac surgery. The design methods are a retrospective and single-center study conducted in Bordeaux, France that analyzed patients from November 2018 to February 2020. The patients were broken down into two groups, one the OFA group, and the second, the opioid-based group (OBA). 2108 patients underwent on-pump CPB during the time frame; however, it was reduced to 80 patients divided into two groups of 40 with similar statistical variables between them such as similar surgical procedures with equivalent CPB duration. Exclusion criteria included patients undergoing off-pump cardiac surgery, preoperative hemodynamic instability, atrioventricular block grade 2 or 3, and patients with hypersensitivity to opioids.

Intraoperative management for both groups included routine monitoring (five-lead ECG, pulse oximeter, non-invasive arterial pressure) upon arrival to the operating room. A peripheral venous catheter and an arterial catheter were inserted under local anesthesia. After induction of anesthesia, hemodynamic monitors were completed with the insertion of a triple lumen central venous catheter (CVC) in the right internal jugular vein for the infusion of drugs and to monitor the central venous pressure.

In the OBA group, anesthesia was based on simultaneous propofol and remifentanil targeted-controlled infusions using the Schnider and the Minto models. Induction of anesthesia was maintained via target-effect site concentrations for propofol and remifentanil. For maintenance, concentrations of propofol and remifentanil were adapted to maintain the bispectral index (BIS) value between 40 and 60 and to maintain mean arterial pressure (MAP) between 60 and 85 throughout the surgery. A bolus of morphine of 0.10-0.15mg/kg was given 30 minutes before the anticipated end of surgery for postoperative analgesia. The addition of nonopioid adjuncts such as ketamine, lidocaine, or magnesium sulfate in the OBA group was left at the discretion of the attending anesthetist.

In the OFA group, a pre-induction mixture of IV boluses of dexmedetomidine (0.3-0.6 mcg/kg), magnesium sulfate (3g over 15min), dexamethasone (0.1mg/kg), and lidocaine (1.5mg/kg) were given over 15 minutes. A bolus of ketamine (0.3 mg/kg) was followed by continuous infusion (0.25mg/kg/hr), which was stopped at surgical wound closure. Propofol was used for induction and then used in maintenance via TCI infusion. After induction, a continuous infusion of dexmedetomidine was adapted to MAP values. If MAP was below 55 mmHg, dexmedetomidine was discontinued. Conversely, if MAP was higher than 90 mmHg and the BIS between target values, dexmedetomidine was increased up to 0.5 mcg/kg/hr. In both groups, the use of regional anesthesia was not performed. Aguerreche et al. described the specifics of the CPB machine and methods used during this period in the surgery. Both groups received a bolus of nefopam 30 min before the end of surgery and infusion. Also, paracetamol 1gm every 6 hours was administered. In both groups, all medications were stopped at the end of surgical dressing except for propofol which was continued in all patients for the ICU transfer.

Aguerreche et al. revealed the total amount of opioids consumed in its equivalent of IV morphine during the first 48 postoperative hours was significantly lower in the OFA group compared to the OBA group (15mg vs. 30mg). Maximal pain scores were similar between both groups and but were lower in the OFA regarding postoperative coughing. Patients in the OFA group also had a lower incidence of atrial fibrillation and required less non-invasive ventilation. The author supports the hypothesis that a dexmedetomidine-based OFA regimen is feasible in cardiac surgery, has a "statistically significant" opioid-sparing effect, and can be associated with better postoperative outcomes including less new-onset atrial fibrillation, a lower rate of postoperative invasive ventilation use, and a decreased incidence in postoperative delirium. Dexmedetomidine was discontinued in 10 patients due to a MAP less than 55.

There are limitations of this study mainly due to the nature of its retrospective design. The low number of patients in this study limits external validity. The author also mentions that the inclusion of remifentanil in the OBA group is a limitation because of its potential to cause postoperative hyperalgesia. Also, the patients that received postoperative ketamine boluses in the OBA group, the ketamine cannot be converted to morphine equivalents for comparison. The author suggests that for future research, a controlled prospective randomized study will confirm the current results. Despite dexmedetomidine being discontinued in 10 patients, the author quotes other articles that support the use of dexmedetomidine in cardiac surgery due to its opioid-sparing effects via spinal and non-spinal mechanisms, its ability to have a protective effect in on-pump CABG by decreasing myocardial ischemia-reperfusion and improving myocardium perfusion, anti-inflammatory, sympatholytic and parasympathomimetic effect. The author concludes the article by strongly suggesting that dexmedetomidine-based opioid-sparing anesthesia in cardiac surgery is feasible and provides intraoperative hemodynamic stability.

The third study in the literature review is the 2019 study published by the Journal of Cardiothoracic and Vascular Anesthesia by Kaushal et al.[20] The title of Efficacy of Bilateral Erector Spinae Plane Block in Management of Acute Postoperative Surgical Pain After Pediatric Cardiac Surgeries Through a Midline Sternotomy. The prospective, randomized, single-blind study aims to explore the role of a newer regional anesthetic technique involving the erector spinae fascial plane; the erector spinae plane block (ESPB) in pediatric cardiac surgery. The author tests the hypothesis that the administration of bilateral ESPB with ropivacaine 0.2% would improve postoperative analgesia after pediatric cardiac surgery after midline sternotomy.

Patients were selected after explaining the study protocol and obtaining written consent. 100 participants with an American Society of Anesthesiologists physical status class I and II were selected. Children excluded were those with a preoperative ejection fraction less than 35%, low-cardiac-output syndrome, recurrent ventricular arrhythmias, preoperative inotropic support, allergic to amide local anesthetics, requiring intubation for more than 3 hours or re-exploration, and patients requiring redo or emergency surgery. The enrolled children were subsequently randomized into 2 groups using a computer-generated random number table: group B receiving bilateral ESPB with 0.2% ropivacaine and group C without any intervention. The postoperative pain was managed with rescue IV fentanyl. Both the groups received IV acetaminophen 15 mg/kg every 8 hours as a component of multimodal analgesia. Preoperatively all patients received 1mg/kg of promethazine syrup one hour before surgery. Induction was standardized with an inhalation induction with sevoflurane in 50% oxygen and air mixture, followed by peripheral IV cannulation of appropriate size. Midazolam was given IV 0.05-0.1mg/kg, fentanyl 1-2mcg/kg, and rocuronium, 0.6mg/kg, to facilitate endotracheal intubation. After arterial and central venous catheter placement, the child was placed in the right lateral decubitus position to

facilitate the ultrasound guided ESPB. A high-frequency linear ultrasound was used in a longitudinal direction over the T3 transverse process lateral to the spinous process. The identified muscles for the ESPB include the trapezius, rhomboid major, and erector spinae over the transverse process which is hyperechoic. A 5cm 22-gauge stimuplex block needle was inserted in-plane in a cephalo-caudad direction and the needle pointed to the tip of the transverse process, piercing the erector spinae. 1.5mg/kg of 0.2% ropivacaine was administered in this position after positive needle tip confirmation and negative aspiration of blood. The process was repeated on the contralateral side for a cumulative dose of 3mg/kg ropivacaine. Anesthesia was maintained with sevoflurane 0.9-2% in 50% oxygen in air mixture and supplemental boluses of 0.1mg/kg of atracurium, with hemodynamics maintained within 20% of baseline. The patient underwent sternotomy, heparinization, surgical correction, and then weaned off bypass followed by protamine administration and transferred to the ICU after procedural completion.

To assess pain postoperatively, Kaushal et al. used a Modified Objective Pain Score (MOPS) at hours 0,1,2,4,6,8, 10 and, 12 post-extubation. Both groups received acetaminophen 15mg/kg IV every 8 hours. If the MOPS score was greater than 4 at rest, fentanyl 0.5-1mcg/kg was administered IV as rescue analgesia. MOPS at 0,1,2,4,6,8,10, and 12 hours post-extubation were the primary endpoints. The secondary endpoint of this study viewed intraoperative fentanyl requirements, postoperative cumulative fentanyl requirement up to 12 hours, Ramsey sedation score, ICU stays, and the incidence of adverse events.

The MOPS scores for group B were significantly lower than group C until 10 hours post-extubation in comparison to group C with no significance in MOPS at the 12th hour. The intraoperative fentanyl requirements and extubation time were comparable in both groups. All the children in group C required postoperative rescue fentanyl, whereas rescue was required in

28 children in group B. Postoperative fentanyl administration in group B (1.08 +/- 0.91mcg/kg) was significantly less that than in group C (5.52 +/- 3.27 mcg/kg) ($p < 0.0001$). The time duration to the first rescue analgesic dose Postoperative vomiting was noted in 5 children in group B and 8 children in group C, 2 children in group B and 3 children in group C developed temperatures up to 38.7˚C, which subsided within 6 hours. No complications were found from the ESPB technique and LA administration. The author describes the physiology of the ESPB and how it anesthetizes the dorsal and ventral rami of the spinal nerve roots leading to profound analgesia of the ipsilateral hemithorax, where LA then spreads in a craniocaudal throughout the erector spinae fascia. Thus, allowing the single-shot ESPB to cover multiple dermatomes.

Kaushal et al. list the sample size as being a limitation to the study and mentioned that although pain scores were recorded, the inability to assess dermatomal sensory blockade considering the age of subjects posed an impediment to the successful establishment of proposed sternal analgesia. Also, although no adverse events came from the ESPBs, the bilateral nature of the block poses a risk to LA systemic toxicity. Kaushal et al. concluded with the ability for ultrasound-guided bilateral ESPB to provide excellent analgesia with a reduced amount of rescue analgesics after midline sternotomy in pediatric cardiac surgery, and that ESPB promises to be a simple, effective, and safer regional anesthetic technique considering simple visualization of sonographic targets and an injection site that is distant from the neuraxis, pleura, and major vascular structures.

The fourth study in the literature review supporting opioid-sparing anesthesia implementation in cardiac surgery is by Macaire et al.[12] published by the American Society of Regional Anesthesia and Pain Medicine in 2020. The randomized, double-blind, placebo-controlled trial aims to test the hypothesis that bilateral ESPB with a programmed intermittent

bolus (PIB) regimen decreases postoperative morphine consumption at 48 hours and improves analgesia in children undergoing cardiac surgery with midline sternotomy. Macaire et al. included the findings of the previous article by Kaushal et al., on the decreased need for rescue analgesics following 12 hours post-extubation, but now adds the component of the PIB to further decrease opioid consumption up to 48 hours after surgery, with improved postoperative pain relief when compared with multimodal analgesia management without continuous ESPB. Patient selection began with information about the study and written informed consent obtained from all the parents of the children in the study. Initially, 104 children with an ASA status class II were scheduled for cardiac surgery with midline sternotomy. The exclusion criteria consisted of family refusal, a preoperative ejection fraction less than 35%, ventricular arrhythmia/dysrhythmia, preoperative inotropic support, redo or emergency surgical procedures, and allergies to amide-type LAs. 47 patients were not eligible and were excluded from the study. of the 47, eight did not meet inclusion criteria, 11 parents declined the study, and 28 were excluded for organizational problems. Of the 57 patients included in the study, 3 were excluded due to the cancellation of surgery.

The patients were enrolled by a physician blinded to the study and randomized into two groups using a computer-generated random number table. Group 1 patients received an induction single-shot bilateral ESPB with 0.1%/0.2% ropivacaine followed by a PIB regimen for bilateral ESPB with saline for 48 hours. The randomly generated patients that were assigned group 2 received an induction single-shot bilateral ESPB with 0.1%/0.2% ropivacaine followed by a PIB regimen for bilateral ESPB with 0.1%/0.2% ropivacaine for 48 hours. Both groups received intravenous acetaminophen 15mg/kg every six hours and ibuprofen 10mg/kg every 12 hours as a

multimodal analgesic approach. Breakthrough and moderate to severe pain control were managed with rescue intravenous morphine at 30mcg/kg/hour when necessary.

Midazolam 0.25mg/kg was administered two hours before the procedure. Standard monitoring for cardiac surgery was applied including arterial line and central venous catheter placement, and appropriate antibiotic dosing. Induction of anesthesia began with propofol 2mg/kg, sufentanil at 0.5-1mcg/kg, and rocuronium at 0.6mg/kg to facilitate endotracheal intubation. Anesthesia was maintained with sevoflurane (1-2%) in 50% oxygen in air mixture, rocuronium at 0.4-0.6mg/kg/hr, and sufentanil at 0.1-0.4 mcg/kg/hour titrated to vitals within 20% of baseline. The ESPB was completed with the patient in the right lateral decubitus position under aseptic conditions. The ultrasound probe was placed in a longitudinal orientation over T3 or T4 transverse process. After identification of structures, a 50mm 20-gauge Tuohy needle was advanced in-plane, and a 24-gauge epidural catheter was inserted in a cephalo-caudad direction. The catheter tip location was confirmed by hydro location with 0.5mL of dextrose 5% indicating a solution spread in the fascial plane between the transverse process and erector spinae muscle. The catheters were secured with transparent dressings. In children under 1 year, a bolus of 0.25mg/kg/ side of ropivacaine 0.1% was injected as an initial bolus. In children >1year an initial bolus of 0.50mg/kg/side of ropivacaine 0.2% was injected. The procedure was repeated on the contralateral side. A maximum cumulative initial bolus of 6mL (6–12mg) per side was allowed. The surgical procedure continued as usual with sternotomy, heparinization, surgical repair, and then weaning off bypass and protamine administration. The patients were then transferred to the pediatric ICU.

The ESPB catheters were connected to a pump to deliver the PIB. The children in group 1 received 0.5mL/kg/side PIB of saline every 6 hours, with a maximum volume of 6mL/side.

The patients in group 2 received 0.5mL/kg/side PIB of ropivacaine 0.1%/0.2% every 6 hours into the ESPB catheters, with a maximum volume of 6mL/side. The bolus on the second catheter was delayed by one hour in both groups. All patients received IV paracetamol 15mg/kg every 6 hours and ibuprofen 10mg/kg every 12 hours. Postoperative pain scores were assessed using the COMFORT-B score and the FLACC scale for these patients. Moderate to severe pain was determined by a COMFORT-B score of greater than 17, or a FLACC value greater than 3. If pain persisted despite multimodal analgesia, rescue analgesia with IV morphine 30mcg/kg/hour was administered. Inspection on the catheter site took place twice a day to ensure no redness around the site.

Macaire et al. provided the results for the study with validated figures and data representative of the study methods. In group 1 with the saline infusing ESPB catheters, the total morphine consumption at 48 hours was 512+/- 560mcg/kg. In group 2 with the PIB of ropivacaine, the 48-hour morphine consumption was 120+/- 320mcg/kg; with a P-value of 0.03. 41% of patients in group 1 required rescue analgesia with IV morphine compared to 14% of patients requiring rescue analgesia in group 2. Patients in group 2 also demonstrated lower FLACC scale values at 20 hours and 24 hours compared to the saline group, with no significant differences at other times. No differences between the two groups were observed for extubation time, time to drain removal, time to first active mobilization, and length of ICU and hospital stays. Vomiting episodes were also reduced in group 2 compared to group 1 with saline. The author mentions the inadvertent removal of the catheters occurred in 13 percent of patients in group 1, and 15 percent of patients in group 2.

Macaire et al. concluded by stating that the use of bilateral ESPB with an automated intermittent bolus of ropivacaine significantly reduced postoperative morphine consumption at

48 hours, reduced postoperative pain values at 20 and 24 hours, and specifically after extubation and drain removal, with no effect on time to extubation and length of ICU/hospital stay. The use of bilateral ESPB with PIB also reduced the incidence of vomiting and serves as a useful technique for opioid-sparing postoperative analgesic regimens after pediatric cardiac surgery. The author also mentions that although regional anesthesia is gaining popularity in pediatric cardiac surgery, only approximately 43% of pediatric centers are using these techniques, opting for the use of multi-modal or fast-track approaches without regional anesthesia. From prior studies not using regional techniques, the median equivalent morphine dosages are 102mcg/kg in post-anesthesia care units, approximately 460mcg/kg in the first 12 postoperative hours, and from 400-approximately 630mcg/kg at 24 hours, compared to the 120mcg/kg average of this study. The author hints that the use of IV opioids as rescue analgesics cannot fully provide pain relief. Macaire et al. critiqued the sample size of the study as the first limitation. Another limitation to the study is that the pediatric patients were not enrolled in a fast-track anesthesia with an on-table extubation program, which could be the best situation for the use of bilateral ESPB analgesia, and thirdly, the study did not assess the dermatomal sensory blockade in the participants.

The fifth study in the literature review is titled Enhanced Recovery and Early Extubation after Pediatric Cardiac Surgery Using Single-Dose Intravenous Methadone by Iguidbashian et al.[17] published by Wolters Kluwer in the 2020 Annals of Cardiac Anaesthesia journal. The retrospective study aims to assess the efficacy and safety of a multimodal pain regimen centered around a single-dose intraoperative IV methadone in pediatric cardiac surgical patients. The retrospective case study analyzed children greater than six months of age undergoing cardiac surgery in which a fast-track method to facilitate extubation and ERAS was implemented with a

single anesthesiologist and a single surgeon where the likelihood of postoperative hemodynamic instability, ongoing coagulopathy, or bleeding was anticipated to be low. The multi-modal analgesic regimen consisted of methadone 0.2-0.3mg/kg IV bolus before incision, ketamine 0.5mg/kg IV bolus prior to incision and, lidocaine 1mg/kg IV bolus prior to incision. Anesthesia was induced with sevoflurane and or propofol and maintained with sevoflurane 1-1.2 the minimum alveolar concentration (MAC). Muscle relaxation was induced with rocuronium prior to incision. Dexamethasone (0.15mg/kg) was given prior to incision, and ondansetron (0.1mg/kg) was given prior to emergence as prophylaxis for postoperative nausea and vomiting. A continuous infusion of ketamine at 0.25mg/kg/hr and lidocaine at 1.5mg/kg/hr was started from incision to skin closure. Before emergence a 15mg/kg IV bolus of acetaminophen was given and regional anesthesia using a parasternal block was performed with Ropivacaine 0.2%. Postoperative supplemental analgesics consisted of scheduled oral acetaminophen and IV ketorolac. If needed, breakthrough analgesia with IV fentanyl and IV morphine, and oral oxycodone were available.

A total of 24 children were included in the study. 22 patients had procedures done on CPB of which 11 involved a re-entry sternotomy. The youngest patient was 8 months old and weighed 6.2kg. Four patients had single-ventricle pathology. Surgeries performed included six aortic valve replacements, four Fontan procedures, three repairs of atrial septal defects, two pulmonary valve replacements, amongst other cardiac procedures outlined in article. 23 children were extubated in the OR and transported to the pediatric ICU. Postoperative vital signs were obtained within 30 minutes of arrival. No child required intraoperative supplemental opioid administration. Iguidbashian et al. reported the first respiratory rate in the ICU to be 14, with an arterial partial pressure of carbon dioxide to be 51. One child required non-invasive ventilation

for approximately 60 min due to moderate hypoxemia and then transitioned to a 2L nasal cannula. The median time to first supplemental opioid administration was 5.1 hours, the median morphine equivalent dosing in the first 24 hours was 0.2mg/kg, and a median of 0.42mg/kg at 72 hours postoperatively. The author interprets the supplemental opioid requirements as modest and suggests methadone is accomplishing the bulk of the basal pain control in the initial postoperative period.

The article proceeds to disclose the limitations of the study and system flaws. The study's sample size is small, is not randomized, and does not have a control group to compare the effects of methadone. System flaws with extubating the patients in the OR and then going to ICU while the patient is spontaneously breathing the author mentioned was difficult for the ICU nurses. Larger, randomized controlled studies are needed to validate the use of methadone in cardiac surgery.

The sixth article for review is Medicine journals' 2020 article by Ming et al.[21] This randomized controlled trial studied the effect of dexmedetomidine on perioperative hemodynamics and organ protection in children with congenital heart disease undergoing open-heart cardiac surgery. Ming et al. quoted previous literature that supported dexmedetomidine's anesthetic sparing effects, the attenuated release of inflammatory mediators and neuroendocrine hormones, and the potential to abate ischemic brain damage. The study is aimed at evaluating the efficacy of different dosages of dexmedetomidine on hemodynamics and organ protection including heart, brain, and kidney in CHD children.

Participants chosen were children aged 1-6 with CHD, scheduled for repair of atrioventricular septal defect (ASVD) under CPB, with an ASA class II/III. Participants that were excluded were those with severe malnutrition and cyanosis, were born premature, and had

low birth weight. Also, patients with prior cardiac surgery, with pulmonary hypertension, or those allergic to opioids were excluded, and patients with a history of cerebral palsy, severe renal or hepatic disorders were excluded.127 participants were assessed, 37 were excluded from the study. The remaining 90 children were randomly allocated to group C, group D1, and group D2. Group C received 0.9% saline at 0.2mcg/kg/hr, group D1 received dexmedetomidine at 0.2mcg/kg/hr, and group D2 received dexmedetomidine at a rate of 0.4mcg/kg/hr.

The anesthesia protocol consisted of midazolam (0.1mg/kg), fentanyl (3-8mcg/kg), propofol (1-3mg/kg), and vecuronium (0.1mg/kg) followed by endotracheal intubation, and maintenance with sevoflurane 1% From the start of anesthesia, dexmedetomidine was infused continuously for groups D1 and D2 and their subsequent rates, and saline was continuously infused for group C. After sternotomy and heparinization, the patients were placed on CPB and cooled to 30-34 degrees. After completion, the heparin was reversed at a 1:1 dosage with protamine.

Hemodynamic data included MAP and heart rate, levels of lactic acid in blood samples, and levels of C-reactive protein which were measured at timed intervals starting from before induction (T0) to 30 minutes after extubation (T7). For the detection of organ injury markers, arterial (radial artery) and venous blood (internal jugular vein) samples were obtained before surgery, 30 min after CPB, at the end of CPB, after the surgery, and 24 hours post-procedure. The arterial-venous oxygen concentration difference and cerebral oxygen extraction ratio were calculated using Fick's formula. 3-5mLs of venous blood were removed before and at the end of the surgery, and 6-, 24-, and 48-hours post-procedure followed by centrifugation at room temperature at 4000 revolutions/min for 10 minutes. The supernatant was isolated and stored at -80˚C and allowed for detection and interpretation of serum myocardial injury markers, brain

injury markers, and kidney injury markers via an enzyme-linked immunosorbent assay. BUN and serum creatinine were also analyzed for the incidence of acute kidney injury. Secondary outcomes that were measured included extubation times, emergence agitation, postoperative pain scores, and adverse events. The results of the study demonstrated that compared with group C, group D1 and D2 had lower hemodynamic parameters, lower myocardial and brain injury indicators, and quicker tracheal extubation times. There was no significant difference in the incidence of kidney injury in all three groups. Nausea, vomiting, agitation, and FLACC scale in groups D1 and D2 were lower than those in group C. The intraoperative fentanyl requirement was notably lower in the D2 group. After tracheal extubation, 18 children in group C were given an IV drip of tramadol for analgesia, 13 in group D1, and 10 in group D2.

Ming et al. concluded that in children with CHD undergoing CPB, dexmedetomidine reduces the dosage of other anesthetic drugs, inhibited inflammatory stress response, and maintains perioperative hemodynamic stability. Dexmedetomidine also downregulates the expression of myocardial and brain injury markers, lowers the incidence of tachycardia, nausea, vomiting, and moderate agitation, and shortens tracheal extubation times. Dexmedetomidine at a rate of 0.4mcg/kg/hr can further decrease the dosage of fentanyl and dopamine compared with dexmedetomidine at 0.2mcg/kg/hr. Ming et al. deemed dexmedetomidine at a rate of 0.4mcg/kg/hr a clinically safe and effective anesthesia adjuvant for pediatric open-heart surgery.

Discussion

This 2019 study by Guinot et al. is the first of its kind to specifically focus on the feasibility of OFA in cardiac surgery undergoing CPB. The findings by Guinot et al. supporting the use of OFA, or a minimal opioid approach in cardiac surgery became the basis for further

studies such as that by Aguerreche et al. The retrospective study by Aguerreche et al. demonstrates the potential for dexmedetomidine as the foundation in an opioid-sparing anesthesia approach to cardiac surgery. Dexmedetomidine offered numerous benefits in the cardiac patient having cardiac surgery and compounded to the information presented in the article by Guinot et al., which focused on the use of other non-opioid adjuvants without dexmedetomidine (due to unavailability) in open-heart cardiac surgery.

Multiple articles supported the use of regional anesthesia in the preserving opioid usage, however the ESPB offered multiple advantages, as demonstrated in the study by Kaushal et al. The article was chosen for literature review as it demonstrated the ability of the ESPB to have a major opioid-sparing effect in cardiac surgery. The bilateral ESPB as a newer regional technique in cardiac surgery proved to reduced opioid consumption, demonstrated efficacy, was safe, and simple to implement for the anesthesia provider. The following article by Macaire et al. provided further insight into the opioid-sparing effects of bilateral ESPB in cardiac surgery. Where the article by Kaushal et al. demonstrated the analgesic benefits to using the ESPB in pediatric cardiac surgery, Macaire et al. found that the addition of PIBs of ropivacaine can further prolong analgesia and diminish post-operative morphine consumption beyond 12 hours (Kaushal et al.) to 48 hours without causing LA systemic toxicity in pediatric cardiac patients undergoing open-heart surgery via midline sternotomy.

The article by Iguidbashian et al. is one of the first to propose the use of IV methadone as the cornerstone of an analgesic regimen in pediatric cardiac surgery. Iguidbashian et al. focused on the use of methadone in the pediatric cardiac population versus the use of more traditional approaches using short-acting analgesics and explains that in traditional methods, pain levels tend to wax and wane in relation to the varying plasma drug levels. Iguidbashian et al.

hypothesized that methadone due to its long duration of action of approximately 24-36 hours may provide steadier, basal pain control during the period of greatest surgical pain. Alternatively, methadone also displays antagonizing effects on the N-methyl-D-aspartate (NMDA) receptor, may prevent the hyperalgesia related to chronic pain syndrome, and has fewer respiratory side effects[19] when compared to other rescue analgesics such as fentanyl, morphine. Also, of the articles reviewed for inclusion of the literature review, the intraoperative approach to this study is amongst the most opioid sparing by design with the inclusion of dexamethasone, ketamine, lidocaine, acetaminophen, ketorolac, and regional anesthesia, with a focus in OR on-table extubation.

Having adequate information to solidify an implementation guide based on dexmedetomidine, regional anesthesia with ESPB, and methadone as an alternative to short acting opioids, the study by Ming et al. solidifies the usage of a dexmedetomidine based opioid-sparing anesthesia in cardiac surgery with the findings that dexmedetomidine at a rate of 0.4mcg/kg/hr is clinically safe and diminishes organ injuries in children undergoing open-heart surgery. Ming et al. explained the strong physiological stress response that is seen during open-heart surgery. For instance, when the ascending aorta is blocked during CPB it significantly diminishes normal blood perfusion to various organs of the body. Meanwhile, the blood in CPB is directly exposed to extracorporeal circulation pipeline and oxygenator, resulting in the generation of numerous inflammatory cytokines and cascade release, which can precipitate systemic inflammatory response syndromes. Hyperglycemia and hyperlacticacidemia are caused by this strong stress response, and hemodynamic instability during surgery can cause ischemia and reperfusion injuries. These hemodynamic and physiologic changes can cause organ damage to the heart, lung, brain, and kidneys.

As opioid-sparing cardiac surgery gains popularity and interest, there will be more randomized controlled trials about opioid-sparing anesthesia in cardiac surgery. Sorting through search findings in the CINHAL database, numerous case reports validated the methods described above. One example is the Elsevier published case report in the Journal of Cardiothoracic and Vascular Anesthesia on opioid-free ultra-fast-track CABG surgery using ESPB catheters.11 The case report describes a 74-year-old male undergoing CABG surgery with similar anesthetic approaches to those described by Guinot et al., Aguerreche et al., and Iguidbashian et al. with the use of versed, ketamine, propofol, ketamine, and magnesium for the induction of anesthesia, followed by bilateral ESPB with ropivacaine, acetaminophen IV and on table extubation. In this case report the patient received only 10 mg of oral oxycodone for postoperative pain. A recent 2021 case report from Turkey by the Anesthesia and Pain Management Journal[11], describes a similar anesthetic regimen that mainly excluded the use of opioids from the preoperative phase to postoperative in three cardiac patients. Two patients were undergoing CABG surgery and the third patient underwent mitral valve repair, all which were successful under CPB. The ESPB were bilateral with catheters left in place for postoperative ropivacaine infusions. This case report used tramadol as a rescue analgesic versus morphine or fentanyl which was only used in one of the three patients. Unfortunately, these are only case reports and thus were not included in the literature review and are thus a limitation in this review. Further clinical studies are needed to validate the results; however, these two case reports encompass the use of opioid-sparing techniques throughout the perioperative course and includes the ESPB with the epidural catheters for programmed infusions of ropivacaine. The limited amount of research available on opioid-sparing anesthesia in open-heart cardiac surgery is inherently a limitation to this review. Of the

research available, the consensus is that larger, randomized clinical trials are needed to validate the findings.

Conclusion

Future research on opioid-sparing anesthesia in cardiac surgery with CPB will validate the results presented. The term "opioid-sparing" is subject to multiple interpretations as noted in the literature review. These recommendations serve as a guide and are vary depending on patient history, disease physiology, and surgical procedure. The educational intervention tool to improve the knowledge of anesthesia providers in opioid-sparing cardiac surgery will suggest for the use of short-acting opioids such as fentanyl be minimized to treat breakthrough pain postoperatively, or for a single-dose of methadone, with a longer duration of action and safer pharmacological profile be given prior to incision. The educational tool recommends the use of regional anesthesia to further spare the use of opioids. After the induction of anesthesia, bilateral ESPB with 0.2% ropivacaine with epidural catheters left in place for PIBs of ropivacaine is recommended. The intraoperative use of dexmedetomidine IV infusion at a rate of 0.4mcg/kg/hr is recommended during cardiac surgery. Ketamine per the literature reviewed may be used intraoperatively (IV infusion) or postoperatively (IV boluses). Postoperative redosing of ropivacaine 0.2% via PIBs is recommended to help mitigate pain transmission up to 48 hours. IV acetaminophen around the clock is recommended postoperatively.

Purpose/PICO Clinical Questions/Objectives

PICO Question or Purpose

Population (P): Anesthesia Providers

Intervention (I): Opioid-Sparing Anesthesia for Cardiac Surgery education tool

Comparison (C): None

Outcomes (O): Improved provider knowledge of anesthesia techniques that minimize opioid usage in cardiac surgery.

Primary DNP Project Goal

Opioid use and abuse along with addiction have become a significant issue for the last decade. In fact, opioid overdose is now one of the leading causes of unintentional death in the United States, surpassing motor vehicle accidents.[4] Most surgical patients often receive some form of opioid narcotic throughout the perioperative period and then postoperatively. The reason being, that opioids are potent with a rapid onset of action without an analgesic ceiling,[4] but with the increasing use of opioids, it has become a realization that its benefits might be overshadowed by the potential downsides.[5] Researchers have shown that opioid-naïve patients often can become dependent on narcotic administration after surgery. The anesthesia provider plays a paramount role in the primary stage of the patient's exposure to such potent drugs, and therefore can be a leading agitator to these key issues.

Cardiovascular disease is now the leading cause of global death with an estimated seventeen million deaths per year, and the number is set to increase to twenty-three million by the year 2030.[8] Cardiovascular surgery typically involves the coronary arteries, heart valves, or other cardiac structures that may need to be accessed by the surgeon for repair. Cardiac surgery is associated with moderate to severe pain from median sternotomy, chest tube insertion, and costovertebral joint distention.[2,11] Vascular access sites and saphenous graft harvest sites also cause significant pain. However, ineffective pain control after cardiac surgery can lead to sympathetic activation, resulting in unstable hemodynamics and increased demand for oxygen[2]

Traditionally, high-dose opioid induction and maintenance were considered the gold standard for cardiac patients in the 1980s. However, that concept came packaged with side effects of prolonged mechanical ventilation, increased length of stay in the intensive care unit and hospital[2], increasing awareness, and allowing for other methods to be introduced. Although providers use a multi-modal approach to analgesia with non-opioid adjuvants, intraoperative opioid usage ultimately varies between patient, procedure, and anesthesia providers.[11] Focusing on the anesthesia provider, the objective of the development of an opioid-sparing anesthesia guide for cardiac surgery requiring cardiopulmonary bypass is to reexamine traditional practices and replace them with evidence-based guidelines in order to achieve early postoperative recovery and mobility while establishing comparable levels of pain control by a significant reduction in the amount of perioperative opioid administration to reduce the potential for opioid-related adverse effects, and subsequently improve the current knowledge of anesthesia providers on the implementation of an opioid-sparing anesthetic approach in cardiac surgeries.

Goals and Outcomes

To guide the development of the goal objectives, the acronym SMART was utilized. SMART details that the objectives should be specific, measurable, achievable, realistic, and timely.[22] These goals will guide the implementation of the quality improvement project.

Specific

Anesthesia providers will receive an educational intervention tool with evidence-based information for the implementation of an opioid-sparing anesthesia technique in cardiac surgery.

Measurable

The effectiveness of the opioid-sparing anesthesia technique or protocol in cardiac surgery will be derived through the analysis of a questionnaire that will be provided to participants before and after an educational intervention. Outcomes will be measured by evaluating the variations in the anesthesia providers' knowledge of opioid-sparing anesthesia and its role in cardiac surgery, the pharmacological agents and techniques utilized, intraoperative and postoperative pain management, and indications/contraindications for use, pre, and post-intervention. In order to generate reports, Qualtrics® software will be used to create the surveys and analyze data.

Achievable

Anesthesiologists, Certified Registered Nurse Anesthetists (CRNA), Certified Anesthesiologist Assistants (CAA) and other anesthesia providers will benefit from the educational intervention tool on opioid-sparing anesthesia in cardiac surgery.

Realistic

Anesthesia providers will be educated on the new opioid-sparing technique in cardiac patients undergoing CPB. Clinical informatics will develop an electronic order set for easy access in fast-track or on-table-extubation candidates.

Timely

The opioid-sparing anesthesia in cardiac surgery implementation guide will be completed and available to anesthesia providers within a 1-month time frame. The outcome of this initiative will be as follows: within a 1-month period, anesthesia providers will have access to an evidence-based opioid-sparing implementation guide for patients who undergo cardiac surgery to improve postoperative outcomes and optimize patients for extubation and mobilization, while reducing the perioperative consumption of opioids.

Program Structure

The development of an opioid-sparing anesthesia pathway in cardiac surgery will require collaboration amongst anesthesia providers. A comprehensive assessment will be performed via a pre-test to identify where opportunities exist and the importance, value, and significance the project will have to all stakeholders.[22] The educational module will serve as the educational intervention for anesthesia providers to learn more about opioid-sparing anesthesia and its role in open-heart cardiac surgery. Then after the intervention, a post test will be administered to the anesthesia providers to determine if the intervention was successful. The strength, weakness, opportunities, and threats analysis assessment tool will be utilized to evaluate the internal and external characteristics and threats to the program's development.

Because the project aims to improve anesthesia provider's knowledge of opioid-sparing anesthesia techniques when caring for cardiac patients who have undergone cardiac surgery with CPB, the first step will be to identify a team of expert stakeholders. The expert stakeholders will guide the development of the opioid-sparing anesthesia protocol and the anesthesia providers' educational intervention. The participants will first be provided with a questionnaire to measure their knowledge of opioid-sparing anesthesia, anesthesia in cardiac surgery, fast-track and ERAS protocols, and pharmacological agents used in opioid-sparing anesthesia. Participants will then be provided with an educational course addressing the care of the cardiac patient with cardiac disease who undergoes cardiac surgery with CPB and the use of opioid-sparing anesthesia. This course will be provided to anesthesia providers through in-services and huddles. After the intervention, participants will be asked to take a survey that will analyze the variations in their knowledge before and after the educational course.

Strengths

Opioid-sparing anesthesia in cardiac surgery has been the recent topic of discussion in research. Multiple strengths have been identified, one being, the support through literature demonstrating a benefit in a broad range of patient populations from neonates to pediatric patients, and from adults to the elderly undergoing open-heart surgery requiring CPB. Furthermore, there is strength in the feasibility of clinical application in comparison to traditional methods and the subsequent reduction in opioid requirements postoperatively. Apart from the reduction of opioids, positive patient outcomes are prevalent with opioid-sparing anesthesia for cardiac surgery and are associated with quicker extubation times, a decreased need for post-operative non-invasive ventilation, a decreased incidence of postoperative delirium, intraoperative organ protection, and the facilitation of on-table extubation.[16,17,21] Also, opioid-sparing anesthesia in cardiac surgery is not limited to open-heart surgery requiring CPB and has been recorded to be beneficial in other cardiac cases such as in transfemoral transcatheter aortic valve implantations.[23] As most of these high-acuity cardiac surgery cases are regularly seen at the current clinical site, the clinical site thus serves as a major strength for this project and adoptions that may come from it.

Another strength in opioid-sparing anesthesia in cardiac surgery is that the goal of sparing opioids can be met by the implementation of one, or some, or all, of the opioid-sparing anesthetic strategies. For instance, the anesthesia provider can choose to "spare" the use of opioids by inserting bilateral epidural catheters and giving a bolus and infusion of ropivacaine via an erector spinae plane block (ESPB) and perhaps not start a dexmedetomidine infusion. Because the goal of reducing opioids would be met with either method, there is strength in the variety available to the anesthesia provider. Lastly, a strength of an opioid-sparing anesthesia

approach to cardiac surgery lies in its potential to guide future clinical application in other subspecialties as more research becomes available. Adhering to the nationwide call to combat the opioid crisis, there is insurmountable strength in the ability for opioid sparing techniques to help save lives, decrease opioid-dependence in opioid-naïve patients, and help purvey the shifting of the current paradigm in cardiac surgery.

Weakness

As defined by Moran et al.[22], the plan's weaknesses are any internal issues that may be damaging to the program. There are weaknesses to implementing an opioid-sparing anesthetic technique in cardiac surgery requiring CPB such as the requirement for the anesthesia provider to be proficient with multiple pharmacological agents as well as regional anesthesia. This may be seen as a weakness by stakeholders due to the additional risk involved with adding more drugs to achieve analgesia during CPB. For instance, a patient cannot have an allergy to amide anesthetics to maximize the benefits of opioid-sparing anesthetic and analgesic effects if an ESPB is to be done. This is also true for the additional pharmacological agents involved in an opioid-sparing approach to anesthesia in cardiac surgery on CPB. Therefore, hindering the ability to standardize an opioid-sparing technique in cardiac surgery requiring CPB. Another weakness to the implementation of opioid-sparing anesthesia in cardiac surgery requiring CPB is the lack of research available, and the variability amongst the methods of anesthesia management for induction, maintenance, and post-operative phases, and certain biases present in the articles that are present. This variability in anesthesia care for the patient is seen in the current clinical site, with some providers being open to the idea and other providers refusing its use in cardiac surgery due to the way things have been done before. Standardization is needed to validate the results of

an inclusive opioid-sparing anesthesia technique for cardiac surgery with the use of multi-modal non-opioid adjuvants for intraoperative management such as dexmedetomidine, ketamine, dexamethasone, magnesium, propofol, gabapentin, non-steroidal anti-inflammatory agents, regional anesthesia with the ESPB with bolus and continuous infusions of ropivacaine, and the consideration for methadone over the use of short-term opioids.

Opportunities

The implementation of an opioid-sparing anesthetic guide for cardiac surgery requiring CPB can provide opportunities for other anesthesia team members to learn and become involved in the adoption of opioid-sparing open-heart surgery. Learning about this process will also provide an opportunity for other anesthesia providers to learn about the power of the different non-opioid adjuvants and utilize them in their practice. For example, the organ protecting effects of dexmedetomidine as described by Ming et al.[21], is not only suitable for open-heart surgery but could provide the opportunity to be used in other surgeries where organ protection is desired. Also, an opportunity for the use of opioid-sparing anesthesia in cardiac surgery may be present in hospital facilities where the culture is to embrace and implement evidence-based practices, these facilities could recruit participants looking for the latest advancements in care. An example where these observations can translate and transition into patient care has been seen in the current clinical site, where the culture is one that is embracing of change. The current clinical site provides an opportunity for this project to become embraced.

There is also a large amount of opportunity in the application of opioid-sparing anesthesia in cardiac patients who are at high-risk for opioid dependence or have suffered adverse reactions to opiates in the past. With the use of opioid-sparing anesthesia in this patient population, opioid-related adverse effects are minimized without jeopardizing quality care or

pain control. Also, opioid-sparing anesthesia in cardiac surgery with the use of regional anesthesia can help improve ERAS protocols into "fast-track", or "ultra-fast track" (to extubation) methods in select candidates in efforts to extubate post-open-heart patients on the table.[17,24]

Threats

Factors that may potentially harm the process or interfere with the program's ability to achieve its objectives must be evaluated.[22] The largest threat to the implementation of opioid-sparing anesthesia for open-heart cardiac surgery requiring CPB is the resistance to change from the anesthesia providers, the cardiac surgeons, and the institutions/facilities where the operations are performed. The institute of medicine reported that the average time lag from discovery to knowledge to its application in practice is 17 years.[9] Opioids such as fentanyl are still considered the standard analgesic agent in cardiac surgery, because of this notion, providers might not be accepting of potential changes to their practice. Older practicing anesthesia providers may not feel comfortable with the thought of a patient having open-heart cardiac surgery, on CPB, and the restriction of opioids for pain. These providers have been trained to do things a certain way with effectiveness, and to abandon what has worked to implement a new strategy will be met with resistance. It is expected that this level of resistance will be seen when demonstrating the current literature at the current clinical site. However, White et al. explains that a resultant decline in best care knowledge for patient care occurs due to the rate of growth of new knowledge and the delays of implementing that new knowledge. Because there is so much information for the clinician to read and evaluate for its use in practice, it is widely recognized that the knowledge of best care has a negative correlation with the year of graduation.[9]

Organizational factors

The implementation of the opioid-sparing anesthesia for cardiac surgery protocol will be conducted within a collaborative team approach amongst anesthesia providers. We will first determine the steps needed to develop the opioid-sparing anesthesia for cardiac surgery protocol. A flowchart will be formed to represent the visualization of the process steps. Data can be analyzed and compared with the goals and expectations devised during the planning phase through chart reviews that assess the total opioid consumption, individual patient outcomes, and length of stay pre, and post-implementation of the opioid-sparing anesthesia protocol for cardiac surgery. In the evaluation phase, the anesthesia providers will be interviewed to obtain their input on the educational tool and the overall effectiveness evaluated by the difference in knowledge obtained by the anesthesia provider through a pre- and post-educational intervention tool exam.

Conceptual Underpinning and Theoretical Framework of the Project

Pertinent to the implementation of an opioid-sparing anesthesia protocol in cardiac surgery for open-heart procedures, a translation theory will be used to guide the process. Translation theories focus on the interrelationships and complex organizational dimensions that are relevant to the translation and research of new knowledge into practice. Rogers's Diffusion of Innovations Theory is useful in understanding individuals' reactions to change. Change in this theory occurs when innovation is introduced and is perceived as new by an individual. Opioid-sparing anesthesia in cardiac surgery on CPB will be perceived by many as new, and hence, would serve as a catalyst for translating innovation towards change. The second part of the theory describes a five-step innovation-decision process in which the individual transitions from the knowledge phase, which begins when the individual becomes aware of the innovation, to the

implementation and confirmation phase where the individual implements the innovation and then decides on whether to continue the use of the innovation or not.[9] The model ties in with the interventional educational tool to be presented to anesthesia providers in which the information is made available, and tested on the retention of new knowledge, and then left to the anesthesia provider to adopt, implement, and continue to use upon favorable results.

Methodology

Setting and Participants

This project took place at Memorial Regional Hospital in the surgical department where there were many scheduled and emergent surgical procedures, including elective cardiac, and emergent cardiac surgeries. There are approximately 30 anesthesia providers currently providing care at this practice and they vary from anesthesiologists, to AAs, and CRNAs. This practice is in Hollywood, FL, and the anesthesia providers themselves, as well as all the population they serve, are of diverse backgrounds.

Description of Approach and Project Procedures

The DNP project intervention began with inviting the anesthesia providers of this practice to participate in the QI project. The results of the pretest/posttest design were used to measure self-reported knowledge on opioid-sparing anesthesia in cardiac surgery. The data collected before the educational intervention includes demographic information, years of practice, and history of previous cardiac surgery experience in years. The education program contained the information regarding implementation and indication for an opioid-sparing approach, its pharmacological techniques, regional anesthesia approaches, and alternatives to current opioid-based practice. Throughout the training, providers were invited to speak openly about their own experiences with opioid-sparing anesthesia, opioid-related adverse events, and their thoughts for

use in both their professional and personal capacities. The training lasted approximately 60 minutes, and after the educational segment participants completed a post-test survey.

Protection of Human Subjects

All anesthesia providers from the previously described practice were invited to participate via email. Florida International University Institutional Review Board (IRB) approval was obtained for the project with minimal risk. Participants consented via Qualtrics, with the opportunity and right to withdraw their consent at any time. Benefits of participation included the improvement of knowledge in cultural competency, minority cultures, and self-reflection on their own culture and how it affects their care. No identifiable data was collected during this project, however, due to the size of the sample participants were identified through indirect identifiers. The data collected was stored in a password-protected online database only accessible to the primary investigator.

Data Collection

Demographic data collected included gender, race, ethnicity, and education. Additionally, participants provided an approximation of the number of years they have been practicing and whether they have previously used opioid-sparing or opioid-free anesthesia during cardiac surgery. Data collected consisted of a pre-test that gauged the anesthesia providers' knowledge of opioid-sparing anesthesia in cardiac surgery, and the post-test determined the knowledge acquired following the educational intervention.

Data Management and Analysis Plan

Data collected was stored in an electronic database. Only the primary investigator had the password to this database. No direct identifiers were collected in this investigation and all results

were reported in aggregate. Questionnaires were collected and scored; the means of the total scores and sub-scores were compared before and after the intervention.

Results

Demographics

The demographics of the participants surveyed are represented below.

Consent to participate

Answer	%	Count
Consent to Participate	100.00%	7
Withdraw from survey	0.00%	0
Total	100.00%	7

Gender

Answer	%	Count
Male	42.86%	3
Female	57.14%	4
Total	100%	7

Ethnicity

Answer	%	Count
Hispanic	28.57%	2
Other	71.43%	5
Total	100%	7

Level of Education

Answer	%	Count
Masters	28.57%	2
Doctorate	57.14%	4
JD or MD	14.29%	1
Total	100%	7

Years as an anesthesia provider

Answer	%	Count
0-5	71.4%	5
5-10	0.00%	0
10-15	0.00%	0
Greater than 15	28.6%	2
Total	100.00%	7

A total of 42 invitations were distributed via email to anesthesia providers to participate in the pre-and post-test educational intervention. Seven participants consented to participate, no surveys were left incomplete, totaling seven participants for the quality improvement project. The demographics of those who participated are represented by the following: male (n = 3, 42.9%), female (n = 4, 57.1%), Hispanic (n = 2, 28.6%), other (n=5, 71.4%). Six participants were certified registered nurse anesthetists (n = 6), with either a Master's degree (n = 2, 28.6%), or Doctorate (n = 4, 57.1%), and less than 5 years experience (n = 5, 71.4%) or 15 or more years experience (n = 1, 14.3%) as an anesthesia provider. One participant was an MD (n=1, 14.3%) with 15 or more years experience (n = 1,14.3%, group total n=2, 28.6%)

Pre-Test Knowledge of Opioid-Sparing Anesthesia for Cardiac Surgery

The pre-test consisted of 12 questions that assessed the current knowledge of opioid-sparing anesthesia in cardiac surgery. Five (n = 5, 71.4%) of the seven participants correctly answered that respiratory depression was the most common opioid-related adverse complication. The same number of participants also successfully historically associated cardiac surgery with high-opioid inductions. None of the seven participants were able to identify the percentage of opioid-naïve patients that go on to become chronic users. Six (n = 6, 85.7%) participants correctly answered and understood the clinical phenomena of hyperalgesia and tolerance, however only four participants (n=4, 57.1%) correctly answered the definition of hyperalgesia. One question was marked as invalid, due to a selection error, in which, all participants received credit for their responses. 1 participant (n=1, 14.3%) successfully answered a question regarding the timing of pain relief following the erector spinae plane block in the pre-test section.

Post-Test Knowledge of Opioid-Sparing Anesthesia for Cardiac Surgery

After the PowerPoint educational intervention, participants answered a post-intervention questionnaire consisting of the same questions found in the pre-test. Results assess the knowledge gained from the educational intervention and are listed below (table 1). All questions demonstrated an increase in the correct answer when the pre-and post-intervention tests were compared. The most significant increase in provider knowledge was noted in the response regarding the percent of opioid naïve patients, where in the pre-test none of the participants answered correctly and in the post-test six participants answered correctly; demonstrating an increase in provider knowledge of 85.7%. The same percentage increase in provider knowledge was seen following the educational PowerPoint regarding the erector spinae plane block.

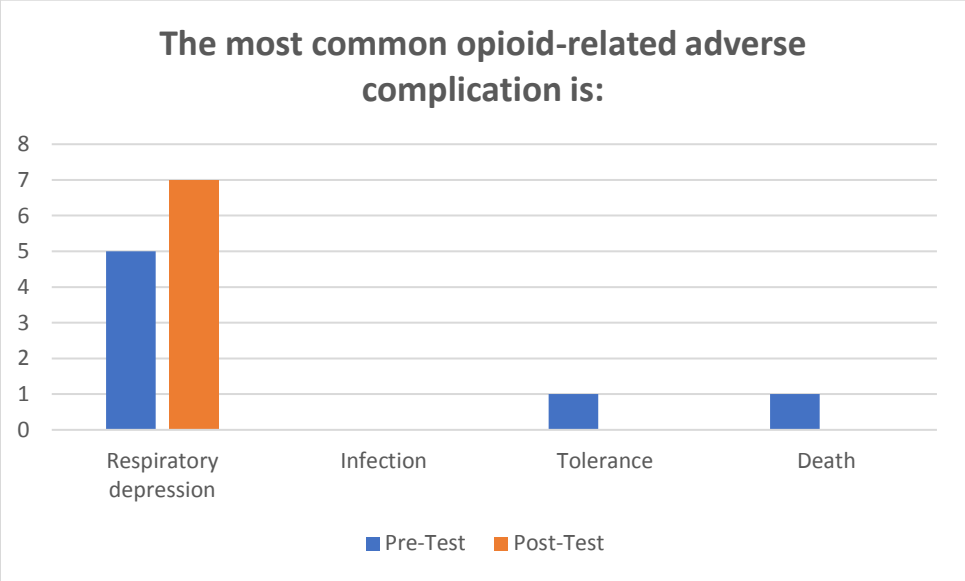
Table 1

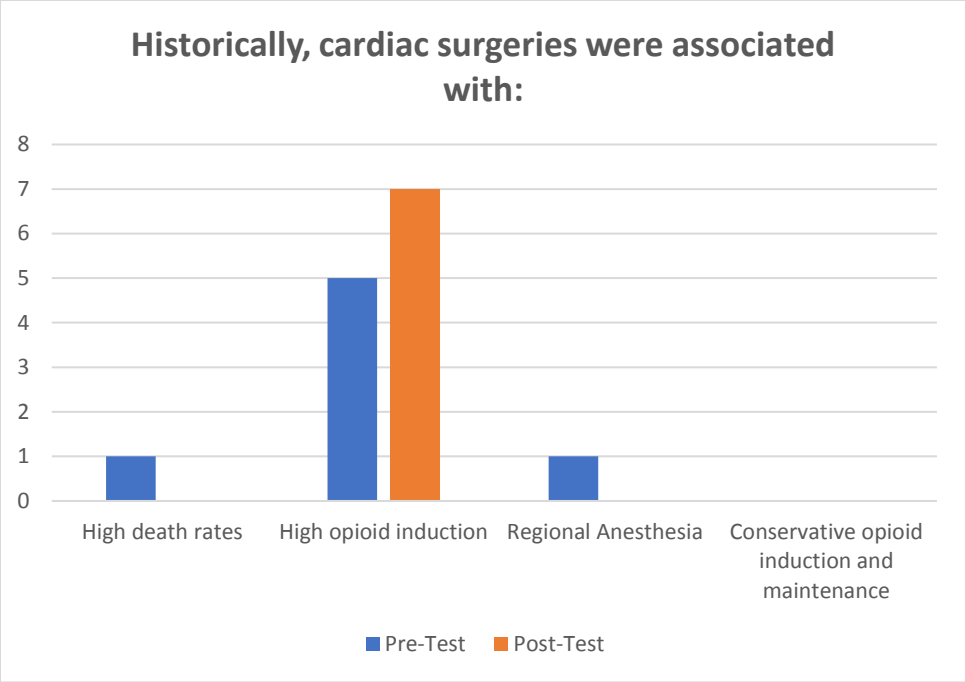
Question	**Pre-Test** (n=7)	**Post-Test** (n=7)	**Difference** (%)

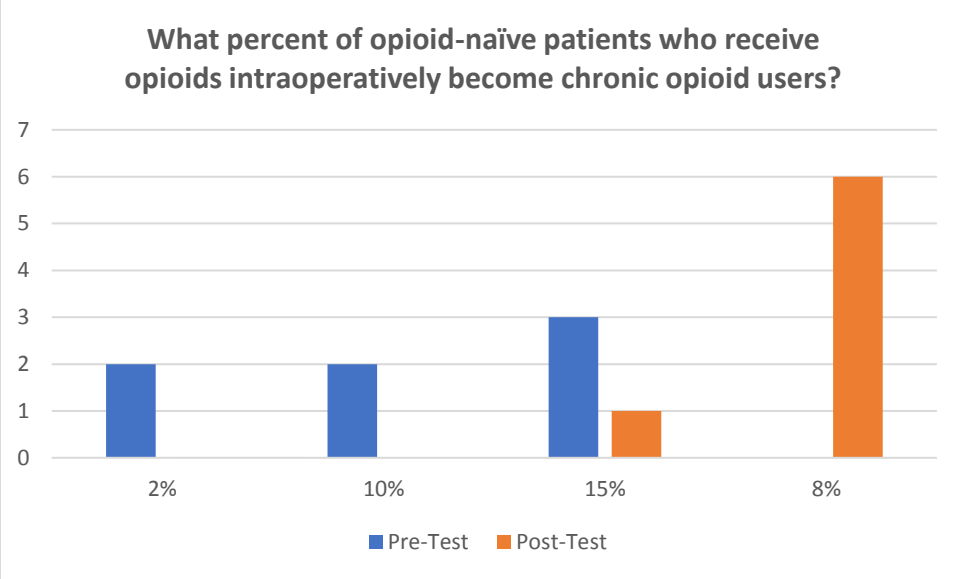
The most common opioid-related adverse complication is:	5	7	+14.3
Historically cardiac surgeries were assosciated with:	5	7	+28.6
What percent of opioid-naïve patients who receive opioids intraoperatively become chronic opioid users?	0	6	+85.7
A patient had a successful valve replacement surgery 48 hours ago, this patient received opioid-based anesthesia, and a total of 600 mcg of fentanyl intraoperatively. Postoperatively the patient has been requiring opioids (Fentanyl/Dilaudid) for breakthrough pain, which are now becoming more frequent. The anesthesia provider rounds on the patient and realizes that these may be signs related to:	6	7	+14.3
Dexmedetomidine at 0.4mcg/kg/hr can reduce the need for postoperative opioid consumption and has organ protective properties:	5	7	+28.6
The administration of the opioid methadone causes respiratory depression similar to morphine or fentanyl:	4	5	+14.3
The lowering of pain thresholds that causes increases in atypical pain appearing to be unrelated to the original nociceptive stimulus is known as?	4	6	+28.6
Regional anesthesia has been shown to be beneficial in reducing pain and opioid requirements in cardiac patients. Which are true of the erector spinae plane block?	7	7	0
Traditional anesthetic management for cardiac surgery included high-opioid inductions:	6	7	+14.3
According to the literature about erector spinae plane blocks in pediatric subjects, the addition of epidural catheters for programmed intermittent boluses with 0.2% ropivacaine can decrease postoperative opioid requirements for up to:	1	7	+85.7
Methadone has properties that act on the NMDA receptor and avoids hyperalgesia compared to morphine/fentanyl.	4	6	+28.6
What are some benefits to opioid-sparing approaches in cardiac surgery?	4	6	+28.6

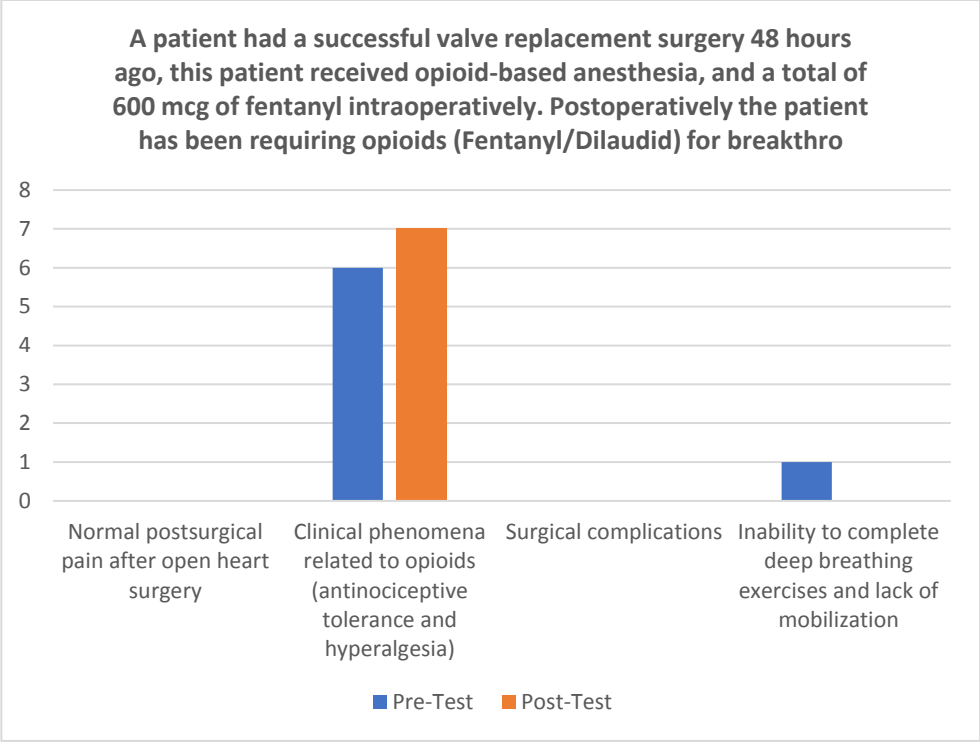
Summary of Data

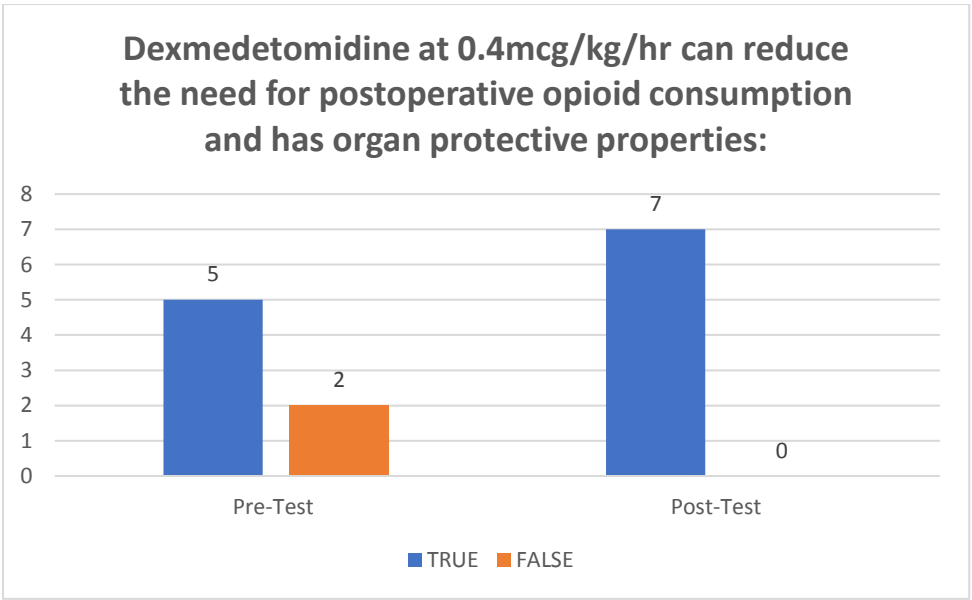
Overall, the results of the educational intervention demonstrated a knowledge increase of 32.2% between the pre-test and post-tests. One question was omitted due to selection error in both the pre and post test. The most notable increase in provider knowledge was observed in the question asking to identify the percent of opioid naïve patients that become chronic opioid users. Also, a notable increase in knowledge was seen in the length of postoperative pain relief following a bilateral erector spinae plane block with programmed intermittent boluses of ropivacaine. The following graphs illustrate the differences between the pre-and post-test answers for each question.

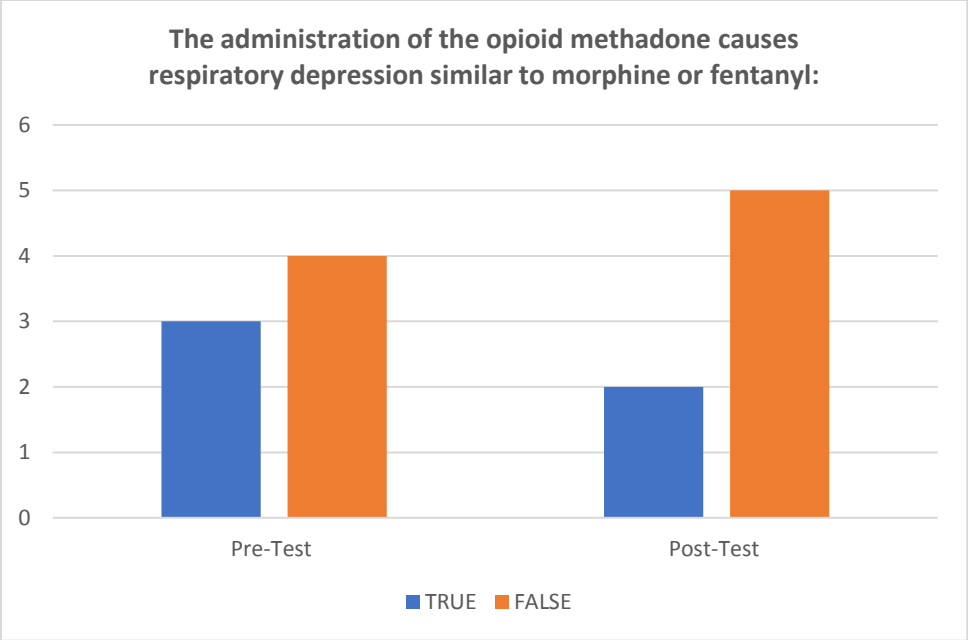


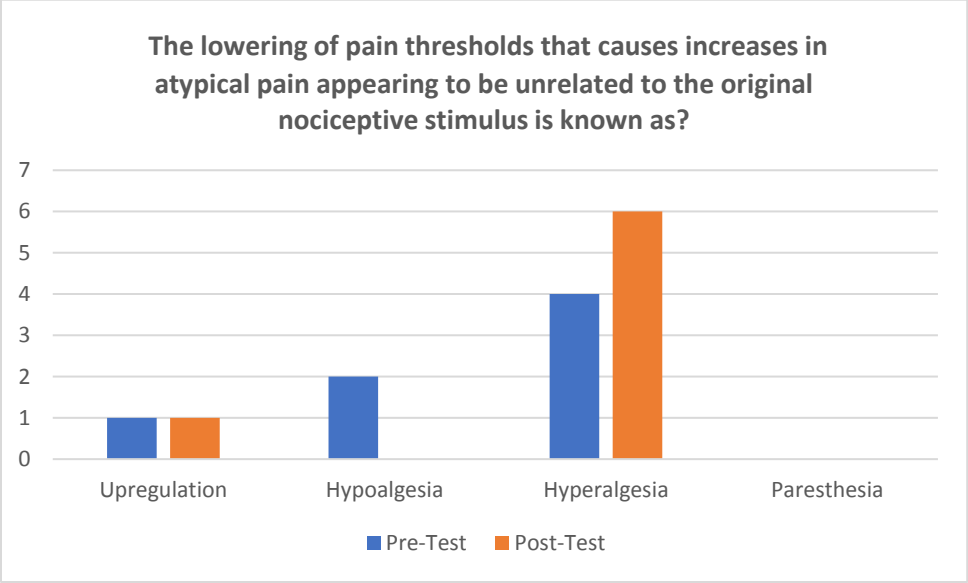

Historically, cardiac surgeries were associated with:
8
7
6
5
4
3
2
1
0
High death rates
High opioid induction
Regional Anesthesia
Conservative opioid induction and maintenance
Pre-Test
Post-Test

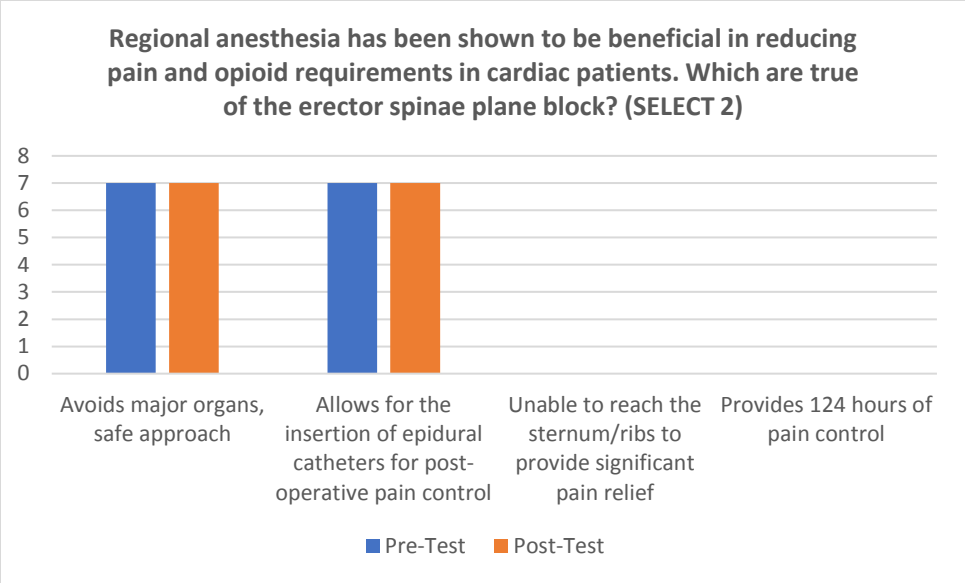

What percent of opioid-naïve patients who receive opioids intraoperatively become chronic opioid users?
7
6
5
4
3
2
1
0
2%
10%
15%
8%
Pre-Test
Post-Test

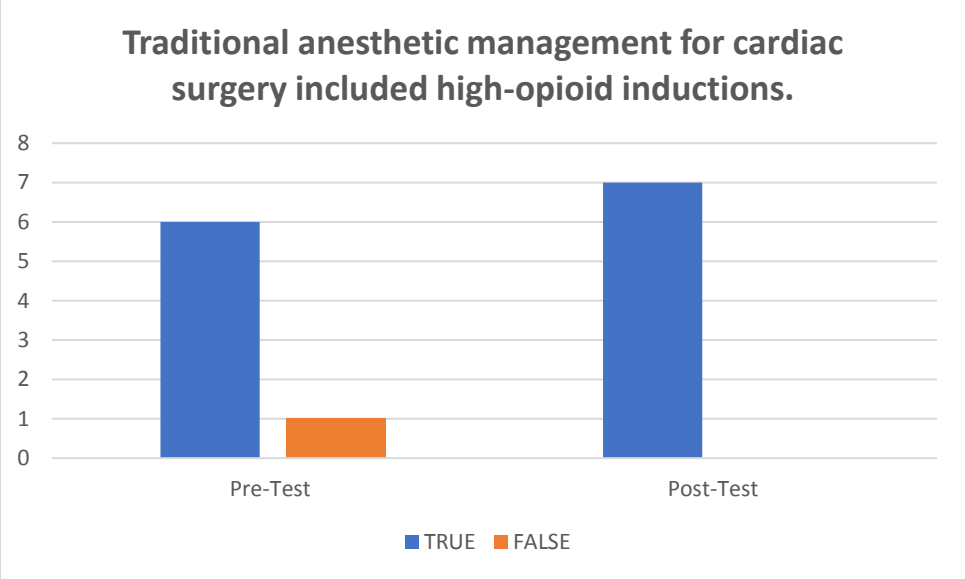

A patient had a successful valve replacement surgery 48 hours ago, this patient received opioid-based anesthesia, and a total of 600 mcg of fentanyl intraoperatively. Postoperatively the patient has been requiring opioids (Fentanyl/Dilaudid) for breakthro
8
7
6
5
4
3
2
1
0
Normal postsurgical pain after open heart surgery
Clinical phenomena related to opioids (antinociceptive tolerance and hyperalgesia)
Surgical complications
Inability to complete deep breathing exercises and lack of mobilization
Pre-Test
Post-Test

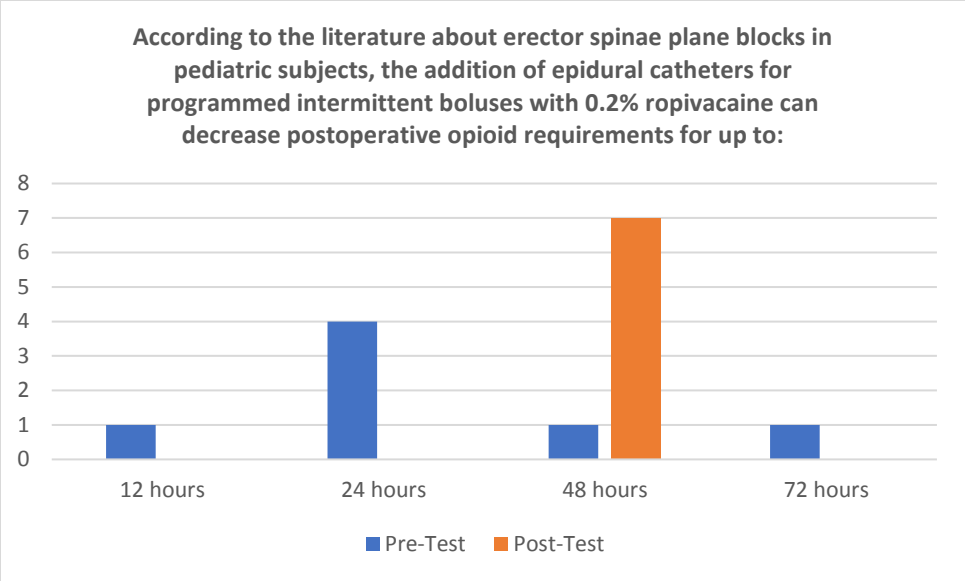

Dexmedetomidine at 0.4mcg/kg/hr can reduce the need for postoperative opioid consumption and has organ protective properties:
8
7
6
5
4
3
2
1
0
5
2
7
0
Pre-Test
Post-Test
TRUE
FALSE

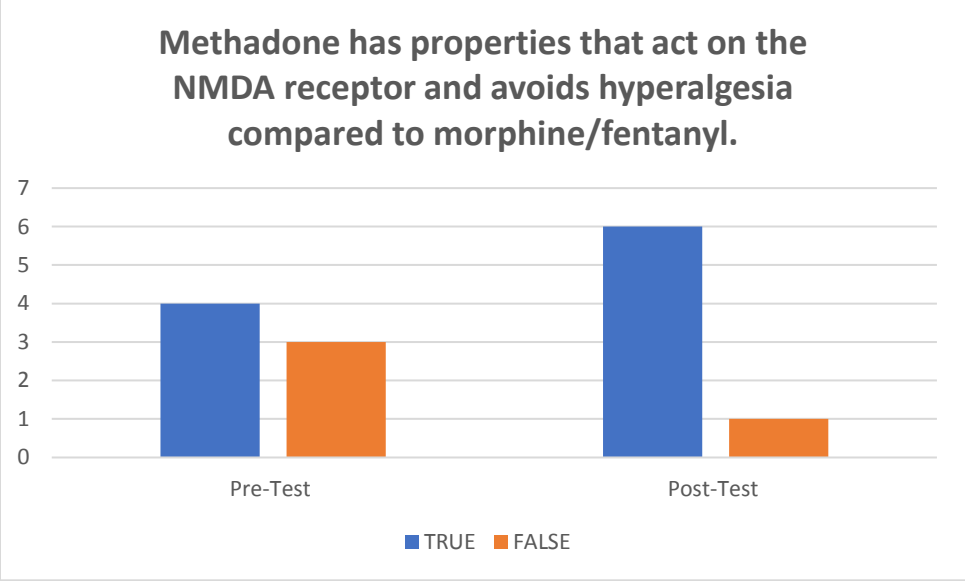

The administration of the opioid methadone causes respiratory depression similar to morphine or fentanyl:
6
5
4
3
2
1
0
Pre-Test
Post-Test
TRUE
FALSE

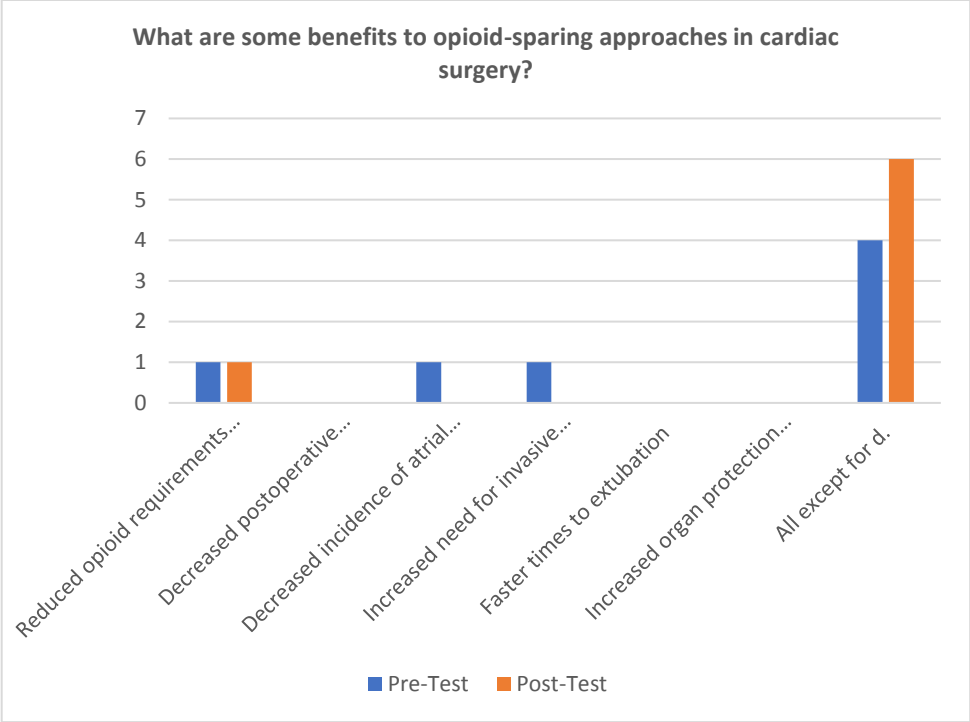

The lowering of pain thresholds that causes increases in atypical pain appearing to be unrelated to the original nociceptive stimulus is known as?
7
6
5
4
3
2
1
0
Upregulation
Hypoalgesia
Hyperalgesia
Paresthesia
Pre-Test
Post-Test

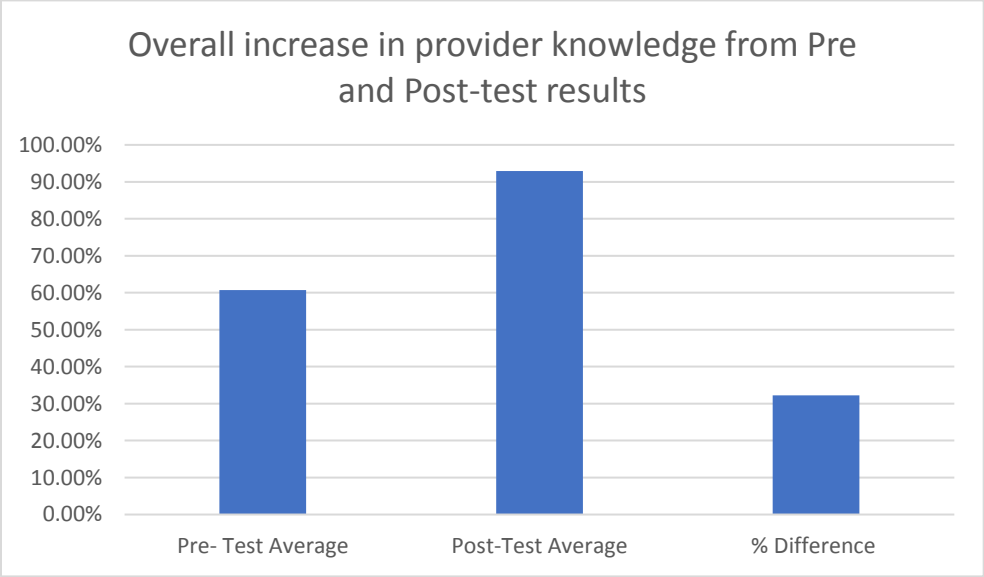

Regional anesthesia has been shown to be beneficial in reducing pain and opioid requirements in cardiac patients. Which are true of the erector spinae plane block? (SELECT 2)
8
7
6
5
4
3
2
1
0
Avoids major organs, safe approach
Allows for the insertion of epidural catheters for post-operative pain control
Unable to reach the sternum/ribs to provide significant pain relief
Provides 124 hours of pain control
Pre-Test
Post-Test


Traditional anesthetic management for cardiac surgery included high-opioid inductions.
8
7
6
5
4
3
2
1
0
Pre-Test
Post-Test
TRUE
FALSE


According to the literature about erector spinae plane blocks in pediatric subjects, the addition of epidural catheters for programmed intermittent boluses with 0.2% ropivacaine can decrease postoperative opioid requirements for up to:
8
7
6
5
4
3
2
1
0
12 hours
24 hours
48 hours
72 hours
Pre-Test
Post-Test


Methadone has properties that act on the NMDA receptor and avoids hyperalgesia compared to morphine/fentanyl.
7
6
5
4
3
2
1
0
Pre-Test
Post-Test
TRUE
FALSE





Limitations

This quality improvement project had several limitations including small sample size. Forty-two surveys were distributed via email to anesthesia providers at one location, however, only 7 participants completed the pre-test, educational intervention, and post-test in its entirety. A larger, more diverse sample size would allow for a more accurate representation of the

preexisting knowledge of the opioid-sparing anesthetic management for patients undergoing cardiac surgery. A larger sample size would also validate the effectiveness of the educational module and intervention. The time frame for the responses is also a limitation, as participants were given two weeks to complete the survey. Another limitation is sending out the surveys to only one facility instead of multiple facilities to maximize the amount of participation, instead of just one community.

Discussion of the Results with Implications for Advanced Nursing Practice

Because anesthesia providers directly maintain anesthesia and analgesia for their patients during cardiac surgery with the medications of their choosing, whether the provider decides to administer opioids or consider opioid-sparing alternatives, the result of the anesthesia provider's decisions lies directly on the patient. Therefore, a valid hypothesis may have many positive implications. First, it would indicate that a short intervention can be an effective way to reduce opioid consumption and potential opioid-related adverse events while providing effective analgesia using newer techniques that are gaining popularity in research. Secondly, a valid hypothesis would demonstrate that sparing opioids in cardiac surgery can lead to improved patient outcomes by reducing the incidence of PONV, atrial fibrillation, the need for postoperative non-invasive ventilation, extubation time, and ICU/Hospital LOS. Also, validity would ensure that opioid-naïve patients or patients that have struggled with opioid dependence obtain adequate pain control and lower the total morphine equivalent dosing given perioperatively, thus giving patients the best chance to avoid opioid dependence or relapse during major cardiac surgery where surgical pain is significant. This project can have good implications for health care organizations that wish to offer the latest research and evidence-based practice approaches to their patients, offering an alternative angle to traditional on-pump

cardiac surgery. Lastly, this project will help guide future research and standardization options for initiating opioid-sparing anesthesia in cardiac surgery.

Conclusion

With an increasing rate of cardiovascular disease and the subsequent number of cardiac surgeries, the responsibility of the anesthesia provider for the most up-to-date care concerning opioid administration in a variety of patients can help optimize postoperative care and outcomes and can help reduce the number of patients that unfortunately become chronic opioid-users. Arming providers with multiple techniques to reduce opioid consumption and improve outcomes can help shift the paradigm of traditional cardiac surgery. The studies provided have their limitations, mainly being small sample sizes and the need for further research. With time, advances leading to the adoption of opioid-sparing cardiac approaches to anesthesia care will flourish.

Appendix: A IRB Exemption

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Office of Research Integrity
Research Compliance, MARC 414

MEMORANDUM

To:	Dr. Charles Buscemi
CC:	Daniel Baez
From:	Elizabeth Juhasz, Ph.D., IRB Coordinator EJ
Date:	March 25, 2022
Protocol Title:	**"Improving the knowledge of clinicians of opioid-sparing anesthesia for cardiac surgery: A quality improvement project "**

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #:	IRB-22-0100	**IRB Exemption Date:**	03/25/22
TOPAZ Reference #:	111350		

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
3) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

EJ

Appendix B: QI Project Consent

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CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT

"Improving the Knowledge of Clinicians of Opioid Sparing Anesthesia for Cardiac Surgery: A Quality Improvement Project."

PURPOSE OF THE PROJECT

You are being asked to be in a quality improvement project. The goal of this project is to improve the knowledge of opioid-sparing anesthesia techniques used in open-heart cardiac surgery, amongst anesthesia providers to reduce perioperative opioid consumption, reduce adverse effects, and improve patient outcomes.

NUMBER OF PROJECT PARTICIPANTS

If you decide to be in this project, you will be one of thirteen people participating in this research project.

DURATION OF THE PROJECT

Your participation will require about 90 minutes of your time in the first session and 20 minutes in the second session that will occur four weeks after your first session.

PROCEDURES

If you agree to be in the project, we will ask you to do the following things:

1. At your first session, you will complete a demographic questionnaire, which includes general information such as age, gender, position in practice; and a pre-test with the opioid-sparing anesthesia for cardiac surgery management guideline knowledge
2. In the first session, you will receive a 60-minute educational program about opioid-sparing anesthesia for cardiac surgery, implementation guide, and literature to support patient outcomes.
3. Four weeks later, you will be asked to complete the opioid-sparing anesthesia for cardiac surgery post-test.

RISKS AND/OR DISCOMFORTS

There are no foreseeable risks with you for participating in this project.

BENEFITS

The following benefits may be associated with your participation in this project: An increase in provider knowledge on opioid-sparing anesthesia for cardiac surgery, which will help you to better assess anesthetic delivery with guidelines for the implementation of opioid-sparing anesthesia for cardiac surgery to reduce the risk of opioid-related adverse events. The overall objective of the program is to increase the quality of healthcare delivery, improving the health indicator of our patients, and increase patient engagement.

ALTERNATIVES
There are no known alternatives available to you other than not taking part in this project. However, if you like to receive the educational material given to the participants in this project, it will be provided to you at no cost

CONFIDENTIALITY
The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, we might publish, we will not include any information that will make it possible to identify you as a participant. Records will be stored securely, and only the project team will have access to the records.

COMPENSATION & COSTS
There is no cost or payment to you for receiving the health education and/or participating in this project.

RIGHT TO DECLINE OR WITHDRAW
Your participation in this project is voluntary. You are free to participate in the project or withdraw your consent at any time during the project. Your withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove you without your consent at such time that they feel it is in the best interest.

RESEARCHER CONTACT INFORMATION
If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Daniel E. Baez at 786-797-9002, dbaez007@fiu.edu or Dr. Charles Buscemi at 305-348-4870, cbuscemi@fiu.edu.

IRB CONTACT INFORMATION
If you would like to talk with someone about your rights of being a subject in this project or about ethical issues with this project, you may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT
I have read the information in this consent form and agree to participate in this project. I have had a chance to ask any questions I have about this project, and they have been answered for me. I understand that I will be given a copy of this form for my records.

Appendix C: Recruitment Letter

Recruitment Email for Improving the Knowledge of Clinicians of Opioid Sparing Anesthesia for Cardiac Surgery: A Quality Improvement Project

Dear Memorial Regional Hospital clinician,

My name is Daniel E. Baez, and I am a student from the Graduate Nurse Anesthesia Department at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to improve clinicians' knowledge of opioid sparing anesthesia or cardiac surgery. You are eligible to take part in this project because you are a anesthesia provider at Memorial Regional Hospital, and you provide or may provide care to patients requiring cardiac surgery. I am contacting you with the permission of your department director and the Chief Nurse Anesthetist at Memorial Regional Hospital.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. You will complete a pre-test questionnaire, which is expected to take approximately 10-15 minutes. Then, you will then be asked to view an approximately 20-minute-long educational presentation online. After watching the video, you will be asked to complete the post-test questionnaire, which is expected to take approximately 10-15 minutes. *No compensation will be provided.*

Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate please click on the link provided (link for Qualtrix questionnaire). If you have any questions about the study, please email or contact me at dbaez007@fiu.edu or 786-797-9002.

Thank you very much.

Sincerely,

Daniel E. Baez

Appendix D: Letter of Support

Envision
PHYSICIAN SERVICES

February 1, 2022

Charles Buscemi, PhD, APRN
Clinical Associate Professor,
Florida International University

Dr. Buscemi,

Thank you for inviting Memorial Regional Hospital to participate in the Doctor of Nursing Practice (DNP) project conducted by Daniel Baez entitled "Improving the Knowledge Opioid Sparing Cardiac Surgery: A Quality Improvement Project" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthetist Practice at Florida International University. I have warranted him permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This project intends to evaluate if a structured education improving knowledge of opioid-sparing cardiac surgery

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password-encrypted digital cloud, and only be accessible to the investigators of this study: Daniel Baez and Dr. Buscemi We expect that Daniel Baez will not interfere with normal hospital performance, behave in a professional manner and follow standards of care.

Prior to the implementation of this educational project, the Florida International University Institutional Review Board will evaluate and approve the procedures to conduct this project. Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

Suzanne Hale

Suzanne Hale, MSN, CRNA, ARNP
Advanced Practice Provider Director, Broward and Dade
Chief, Memorial Regional Hospital
Envision Physician Services
954-265-2044

3501 Johnson Street | Hollywood, FL 33021

Appendix E: Pre-test/Post-test Questions

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Pretest and Posttest Questionnaire:

Improving the Knowledge: Opioid-Sparing Cardiac Surgery

INTRODUCTION

The primary aim of this QI project is to improve the knowledge of anesthesia providers on opioid-sparing anesthesia for cardiac surgery in order to improve provider education and patient outcomes in this population.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format. These questions are meant to measure knowledge and perceptions on identification, referral, management, and patient education on opioid-sparing techniques in cardiac surgery.

PERSONAL INFORMATION

1. **Gender:** Male Female Other
2. **Age:** _____
3. **Ethnicity:**

   Hispanic Caucasian African American Asian Other
4. **Position/Title:** _____
5. **Level of Education:** Associates Bachelors Masters

   Other
6. **Years of Practice** (e.g. RNC): Yes No

QUESTIONNAIRE

1. **The most common opioid-related adverse complication is:**
    a. Respiratory Depression
    b. Infection
    c. Tolerance
    d. Death
2. **Historically, cardiac surgeries were associated with:**
    a. High death rates
    b. High opioid induction
    c. Regional anesthesia
    d. Conservative opioid induction and maintenance
3. **What percent of opioid-naïve patients who receive opioids intraoperatively become chronic opioid users?**
    a. 2%
    b. 10%
    c. 15%
    d. 8%
4. **A patient had a successful valve replacement surgery 48 hours ago, this patient received opioid-based anesthesia, and a total of 600 mcg of fentanyl intraoperatively. Postoperatively the patient has been requiring opioids (Fentanyl/Dilaudid) for breakthrough pain, which are now becoming more frequent. The anesthesia provider rounds on the patient and realizes that these may be signs related to:**

a. Normal postsurgical pain after open heart surgery
b. Clinical phenomena related to opioids (antinociceptive tolerance and hyperalgesia)
c. Surgical complications
d. Inability to complete deep breathing exercises and lack of mobilization

5. **Dexmedetomidine at 0.4mcg/kg/hr can reduce the need for postoperative opioid consumption and has organ protective properties:** True False
6. **The administration of the opioid methadone causes respiratory depression similar to morphine or fentanyl**: True False
7. **The lowering of pain thresholds that causes increases in atypical pain appearing to be unrelated to the original nociceptive stimulus is known as?**
    a. Upregulation
    b. Hypoalgesia
    c. Hyperalgesia
    d. Paresthesia
8. **Regional anesthesia has been shown to be beneficial in reducing pain and opioid requirements in cardiac patients. Which are true of the erector spinae plane block? (SELECT 2)**
    a. Avoids major organs, safe approach
    b. Allows for the insertion of epidural catheters for post-operative pain control
    c. Unable to reach the sternum/ribs to provide significant pain relief
    d. Provides 124 hours of pain control
9. **What are some benefits to opioid-sparing approaches in cardiac surgery?**

a. Reduced opioid requirements intraoperatively and postoperatively
b. Decreased postoperative nausea and vomiting
c. Decreased incidence of atrial fibrillation
d. Increased need for invasive postoperative ventilation
e. Faster times to extubation
f. Increased organ protection during CPB
g. All except for d.

10. Traditional anesthetic management for cardiac surgery included high-opioid inductions.

True False

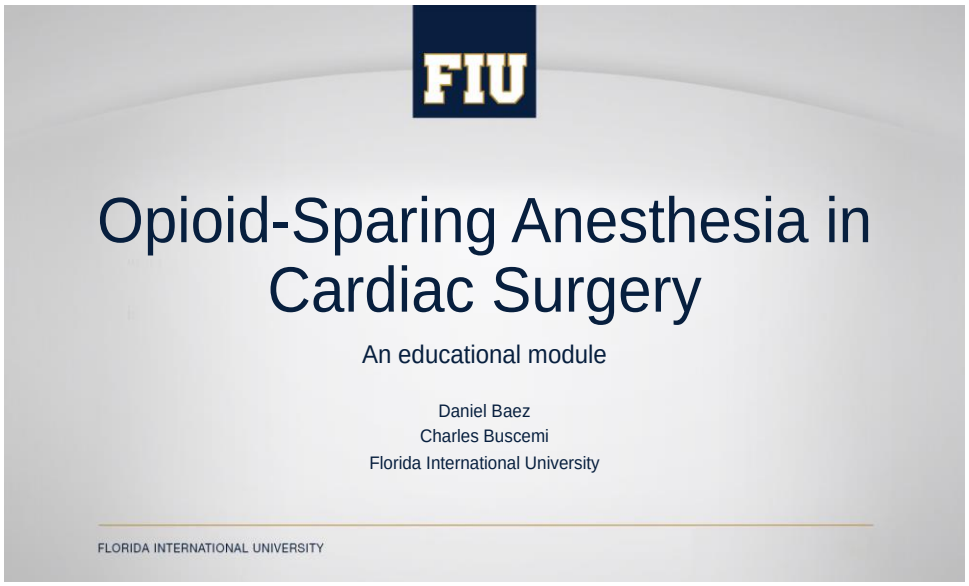
11. According to the literature about erector spinae plane blocks in pediatric subjects, the addition of epidural catheters for programmed intermittent boluses with 0.2% ropivacaine can decrease postoperative opioid requirements for up to:

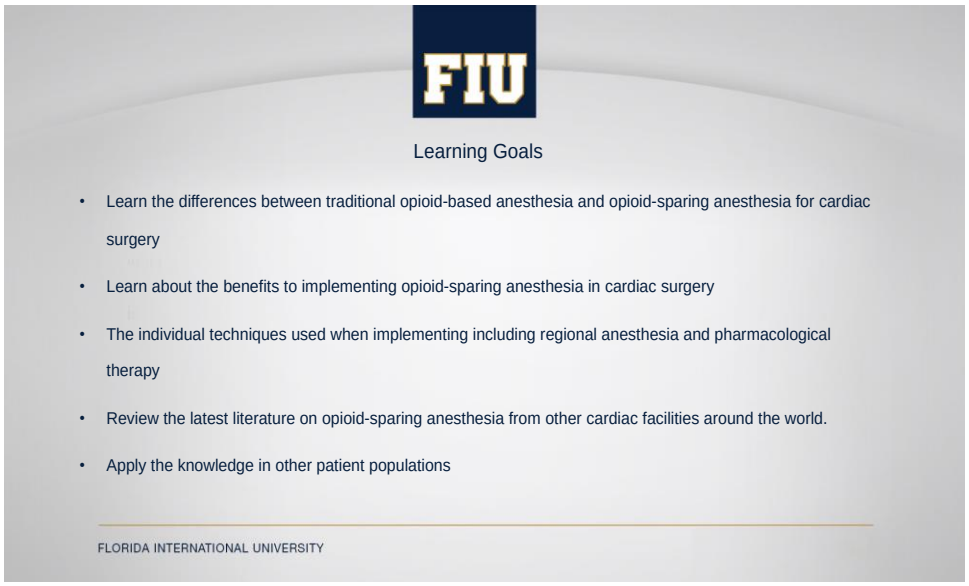
a. 12 hours
b. 24 hours
c. 48 hours
d. 72 hours

12. True or False: Methadone has properties that act on the NMDA receptor and avoids hyperalgesia compared to morphine/fentanyl.

True False

Appendix F: QI educational module





Background of Problem

- Opioid overdoses are one of the leading causes of death, surpassing motor vehicle accidents.[1]
- The CDC estimates the total economic burden of prescription opioid misuse in the United States to be 78.5 billion dollars a year. [2]
- Cardiovascular diseases are expected to rise within the next 5-10 years along with the number of cardiac surgeries performed[3]
- Cardiac procedures are painful and are traditionally managed with the use of intraoperative short-acting opioids such as fentanyl
- **Up to 8% of opioid-naïve patients that are administered opioids during surgery may become chronic users**. [4]

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Cardiac surgery and Opioids

- Despite today's multi-modal approaches to anesthesia, the use of short-acting opioids remain the pharmacological norm in cardiac surgery
- **Historically, cardiac surgeries were associated with high-opioid inductions and maintenance.**[5]
- This caused awareness with the rise of opioid-related adverse events, and the need for multi-modal pain control, ERAS protocols, and 'Fast-Track' approaches
- With the need for pain to be controlled, there is a fine balance between narcotic administration and side effects which include:
  - **The most common is respiratory depression**, then ileus, emesis, hyperalgesia, somnolence, urinary retention, allodynia, hypercarbia, and death[4]

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Pain Control During Cardiac Surgery: A Delicate Balance

- In cardiac surgery there is significant pain from median sternotomy, insertion of chest tubes, costovertebral joint distention, saphenous vein grafting[6]
- Ineffective pain control during major cardiac surgery can lead to sympathetic activation that results in unstable hemodynamics and an increased demand for oxygen[6]
- This is undesirable in cardiac patients with limited reserves [6]
- Short acting opioids for this reason have been the mainstay of cardiac surgery
- However, what if we could achieve the same level of hemodynamic stability, address the significant pain that is associated with open-heart cardiac surgery, and, also improve patient outcomes such as extubation times and PONV?

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Continued…

- The answer might be found in using opioid-sparing anesthesia in patients having open-heart cardiac surgery
- The use of short-acting opioids are associated with two main clinical drawbacks including
- 1)**antinociceptive tolerance, in which less analgesic effect is seen with equal repeat doses**
- 2)**hyperalgesia, which causes a paradoxical decrease in the pain threshold**. This decrease in the pain threshold increases the incidence of atypical pain, which is pain that is unrelated to the original nociceptive stimulus[7]
- The following six studies are centered on open-heart cardiac surgery requiring CPB with measured outcomes during the intraoperative and postoperative periods in both adult and pediatric open heart surgery patients

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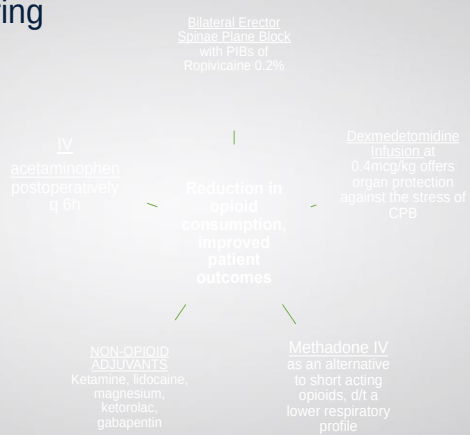
Literature on Opioid Sparing Cardiac Surgery

Authors	Title	Evidence Level
Guinot et al. (2019)[8]	Effect of opioid-free anaesthesia on post- operative period in cardiac surgery: a retrospective matched case-control study	Retrospective matched cohort study, Level III
Aguerreche et al. (2021)[9]	Feasibility and postoperative opioid sparing effect of an opioid-free anaesthesia in adult cardiac surgery: a retrospective study	Retrospective review. Level III
Kaushal et al. (2020)[10]	Efficacy of Bilateral Erector Spinae Plane Block in Management of Acute Postoperative Surgical Pain After Pediatric Cardiac Surgeries Through a Midline Sternotomy	Prospective, randomized, single-blind, comparative study Level III
Macaire et al. (2020)[11]	Bilateral ultrasound-guided thoracic erector spinae plane blocks using a programmed intermittent bolus improve opioid-sparing postoperative analgesia in pediatric patients after open cardiac surgery: a randomized, double-blind, placebo-controlled trial	Randomized, double-blind, placebo-controlled trial Level III
Iguidbashian et al. (2020)[12]	Enhanced Recovery and Early Extubation after Pediatric Cardiac Surgery Using Single-Dose Intravenous Methadone	Retrospective analysis, Level III
Ming et al. (2021)[13]	Effect of dexmedetomidine on perioperative hemodynamics and organ protection in children with congenital heart disease	Randomized Controlled Trial

Improving Patient Outcomes with an Opioid-Sparing Approach



Pre-op Implementation

- Gabapentin or pregabalin PO administered the night before surgery
- IV Tylenol preoperatively
- Dexmedetomidine infusion can be started preoperatively and is also good alternative to midazolam in elderly patients to preserve cognitive function
- Methadone IV before sternal incision-
  - Alternative to short acting opioids
  - Long-acting opioid, great for treating basal surgical pain of cardiac surgery, can last up to 36 hours.
  - Safer side effect profile, as it **avoids respiratory depression compared to fentanyl/morphine family**
  - **Unique in that it also acts on NMDA receptors involvement**

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IV Intraoperative Implementation

- VAA titrated to BIS (Iso, Sevo)
- Dexmedetomidine-based opioid-sparing anesthesia
  - **Start the infusion at 0.4mcg/kg/hr**
    - Good starting point for both adults and pediatrics
    - Can be started in the pre-operative setting (especially in patients at risk for POCD)
    - Pharmacological profile decreases intraoperative opioid requirements
    - **Organ protectant-** from the inflammatory stress response of surgery and from CPB
    - Standardize as part of the open-heart set up for optimal patient results
- Ketamine infusion and/or boluses
- Lidocaine and Magnesium infusions
- Regional anesthesia

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Regional Intraoperative Implementation

- Bilateral Erector Spinae Plane Block
  - Perform the ESPB block after the induction of anesthesia
  - Good results in both adults and pediatrics
  - **Simple to perform, avoids large organs/blood vessels, easy to locate landmarks**
  - Anesthetizes the dorsal and ventral rami of the spinal nerve roots
  - Profound analgesia of the ipsilateral hemithorax
  - 0.2% ropivacaine is typically used
  - Without bilateral epidural catheters- can provide up to 12 hours of pain relief
  - **With the addition of bilateral epidural catheters, up to 48 hours of postoperative pain control**

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Postoperative Implementation

- IV Tylenol
  - 15mg/kg or 1g q 6 hours
- Programmed intermittent boluses of Ropivacaine via bilateral **epidural catheters**
  - **Up to 48 hours of pain control**
  - Reduction in morphine requirements
- Short acting IV opioids
  - Fentanyl, Morphine, Hydromorphone
  - Reserve for the treatment of breakthrough pain in efforts to improve post surgical outcomes by decreasing opioid consumption

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Take home points

- The information presented today serves as a guide with improving the knowledge of anesthesia providers in opioid-sparing techniques in open-heart cardiac surgeries
- **Open-heart surgery is very painful, which is why high-opioid techniques have remained the norm**
- Opioid-sparing anesthesia in major cardiac surgery is the topic of newer research, demonstrating analgesic equipotency with improved patient outcomes over opioid-based approaches
- Further research is needed for larger adoption as there is a large theory-to-practice gap
- The addition of regional anesthesia further reduces the overall need for perioperative opioids for up to 48 hours with the ESPB and epidural catheters for postoperative pain control

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Take home points

- **A good alternative to shorter acting opioids (i.e Fentanyl) for open heart surgery is the use of IV methadone prior to surgical incision to provide 36-hour pain relief without respiratory depression or hyperalgesia/tolerance**
- Dexmedetomidine infusion has many applications in cardiac surgery for both adults and pediatrics and varies from open-heart surgery to TAVRs. Those include improved cognition and a decreased incidence of postoperative agitation in the elderly, reduction in the incidence of a-fib arrythmias, organ protection from the physiological stress response of CPB, reduction in morphine requirements, facilitation of deep, and on-table extubation, and lack of respiratory depression/cessation with use
- With **up to 8 percent of opioid-naïve patients possibly becoming chronic opioid users,** anesthesia providers can help combat this statistic, and help fight the opioid crisis
- The application of opioid-sparing anesthesia in cardiac surgery can become the future of forward-thinking institutions and can be offered as an anesthetic option for the patient to choose. (Think “GETA”/”RA”/”Opioid-sparing”)

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