Current Therapeutic Research 100 (2024) 100744

Contents lists available at ScienceDirect

Current Therapeutic Research

journal homepage: www.elsevier.com/locate/curtheres

Evaluation of Analgesic Drug Therapy for Postoperative Pain Management in Cardiovascular Surgery

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ARTICLE INFO

Article history:
Received 30 October 2023
Accepted 14 March 2024

Key words:
analgesics
cardiovascular surgery
clinical pathway of analgesic drug therapy
multimodal analgesia
pain management in cardiovascular surgery
postoperative pain

ABSTRACT

Background: Cardiovascular surgery is usually associated with higher degree of postoperative pain that influences a patient's physical recovery. Multiple clinical measures have been taken to avoid overuse of opioid agents for postoperative pain management, which led to the development of clinical pathways for analgesic drug treatment using a multimodal approach.
Objective: To evaluate the effectiveness and safety of a multimodal postoperative analgesic drug pathway (ADP) for pain management following cardiovascular surgery.
Methods: This retrospective, controlled, nonrandomized study evaluated a postoperative ADP in patients undergoing cardiovascular surgery in a tertiary general hospital in Qingdao, China. Effectiveness and safety outcomes were compared before and after the implementation of the ADP. Outcome indicators included postoperative pain scores, consumption of opioids in analgesic pumps, and incidence of adverse events.
Results: Patients who underwent cardiovascular surgery from September to November 2021 before the implementation of the ADP (n = 193) and from September to November 2022 after the implementation of the ADP (n = 218) were enrolled. Pain scores were reduced on day 1, 3, and 5 after surgery and the reduction was most significant in mild pain ($P < .001$). Opioids in analgesic pumps consumption was also significantly reduced and there was decreased incidence of adverse events such as nausea and vomiting ($P = .026$), respiratory inhibition ($P = .027$), and dizziness and headache ($P = .028$) in cardiovascular surgery patients after implementation of the ADP.
Conclusions: Improved effectiveness and safety were observed following the implementation of the ADP. Multimodal analgesic ADP methodology can be effectively used for postoperative pain management in patients undergoing cardiovascular surgery.

Introduction

Postoperative pain is an unpleasant phenomenon and remains an inadequately managed common clinical occurrence.[1,2] In cardiovascular surgery, postoperative pain is caused by surgical procedures, including incision, sternotomy, rib and tissue retraction, conduit harvest, drain tubes, saphenous vein removal, and intraoperative dissection, among others.[1,3] Furthermore, endoscope and surgical instruments placed between the ribs during small incision surgery cause damage to the intercostal nerve and can result in intense and lasting pain.[4] Poorly controlled postoperative pain not only influences prognosis and quality of life, but also complicates recovery following cardiovascular surgery.[5]

In the past, there were 2 major hurdles with respect to postoperative analgesia after cardiovascular surgery. First, when opioids are used in combination with other agents (sufentanil + butorphanol/pentazocine/dezocine), sufentanil acts as a complete opioid μ receptor agonist, whereas butorphanol/pentazocine/dezocine has a dual role of being a κ receptor agonist as well as a μ receptor antagonist. Pharmacological studies suggest that opioid receptor agonist–antagonists may influence the analgesic effect of simple-agonist opioids, thereby influencing patients' recovery.[6–8] Second, NSAIDs, such as celecoxib and di-

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https://doi.org/10.1016/j.curtheres.2024.100744

clofenac, are routinely administered after coronary artery bypass grafting without corresponding medications, resulting in increased risk of adverse events.[9]

Recently, a multimodal opioid-sparing approach was introduced that was shown to decrease opioid consumption during postoperative pain management.[10] Similarly, the current practice guidelines for acute pain management in perioperative settings recommend a multimodal analgesia approach for pain management.[11] The other analgesics include ketamine, gabapentin, and pregabalin. Although their mechanisms of action vary, their combination with opioids can significantly reduce opioid dose and improve pain scores.[12]

To overcome the difficulties in pain management, we have developed a clinical pathway for postoperative analgesic drug treatment (also known as the analgesic drug pathway [ADP]) for patients undergoing cardiovascular surgery in accordance with the relevant guidelines for postoperative pain management. The analgesic drugs for ADP are chosen before and after the surgery and involves standardization of selection, dose, and administration route of analgesic drugs during the perioperative period. At the same time, we hypothesize that such a preventive and multimodal analgesic drug delivery program can achieve better analgesic effect by using smaller doses of analgesic drugs through different channels. On the basis of this rationale, the current study evaluated the analgesic effect in patients who underwent cardiovascular surgery before and after the establishment of a postoperative ADP.

Materials and Methods

Study design and setting

This was a retrospective, controlled, and nonrandomized study aimed to assess the efficacy and safety of a postoperative ADP in patients undergoing cardiovascular surgery. Patients' data such as gender, age, body mass index, and surgery data before and after the implementation of the analgesic route were retrieved from the hospital information system. Patients who met the following criteria were included in this study: discharged from the department of cardiovascular surgery and have undergone cardiovascular surgery. Patients who met the following criteria were excluded from the study: younger than age 18 years; missing clinical data; discharged within 24 hours of hospitalization; tonsillectomy and/or adenoidectomy; significant respiratory depression; acute or severe bronchial asthma in the absence of appropriately monitored settings and/or resuscitative equipment; and gastrointestinal obstruction, including paralytic ileus (known or suspected) (Figure 1). The study was conducted in a tertiary general hospital in Qingdao, China, that integrates medical care, teaching, and scientific research. It is an urban tertiary medical institution with 5 campuses and a total of 5723 beds. It is the among the main referral centers in large cities.

Ethics

The study was approved by the ethics committee of The Affiliated Hospital of Qingdao University (study approval No.: QYFY WZLL 27782) and was conducted in accordance with the International Conference on Harmonization guidelines on Good Clinical Practice, China's regulatory requirements, and the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all patients who participated in the study.

Development of the ADP

The ADP was developed by a multidisciplinary team composed of physicians, clinical pharmacists, and nurses and was introduced to clinical practice (Figure 2) on August 9, 2022. The pathway was

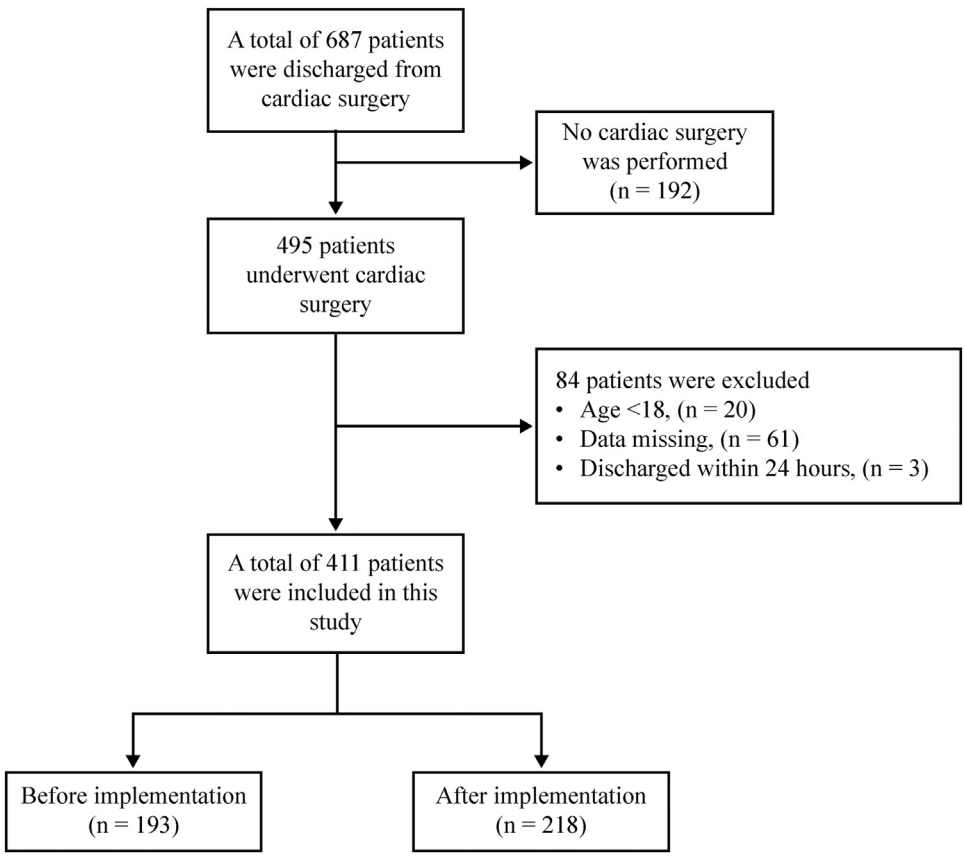

Fig 1. Patient disposition.

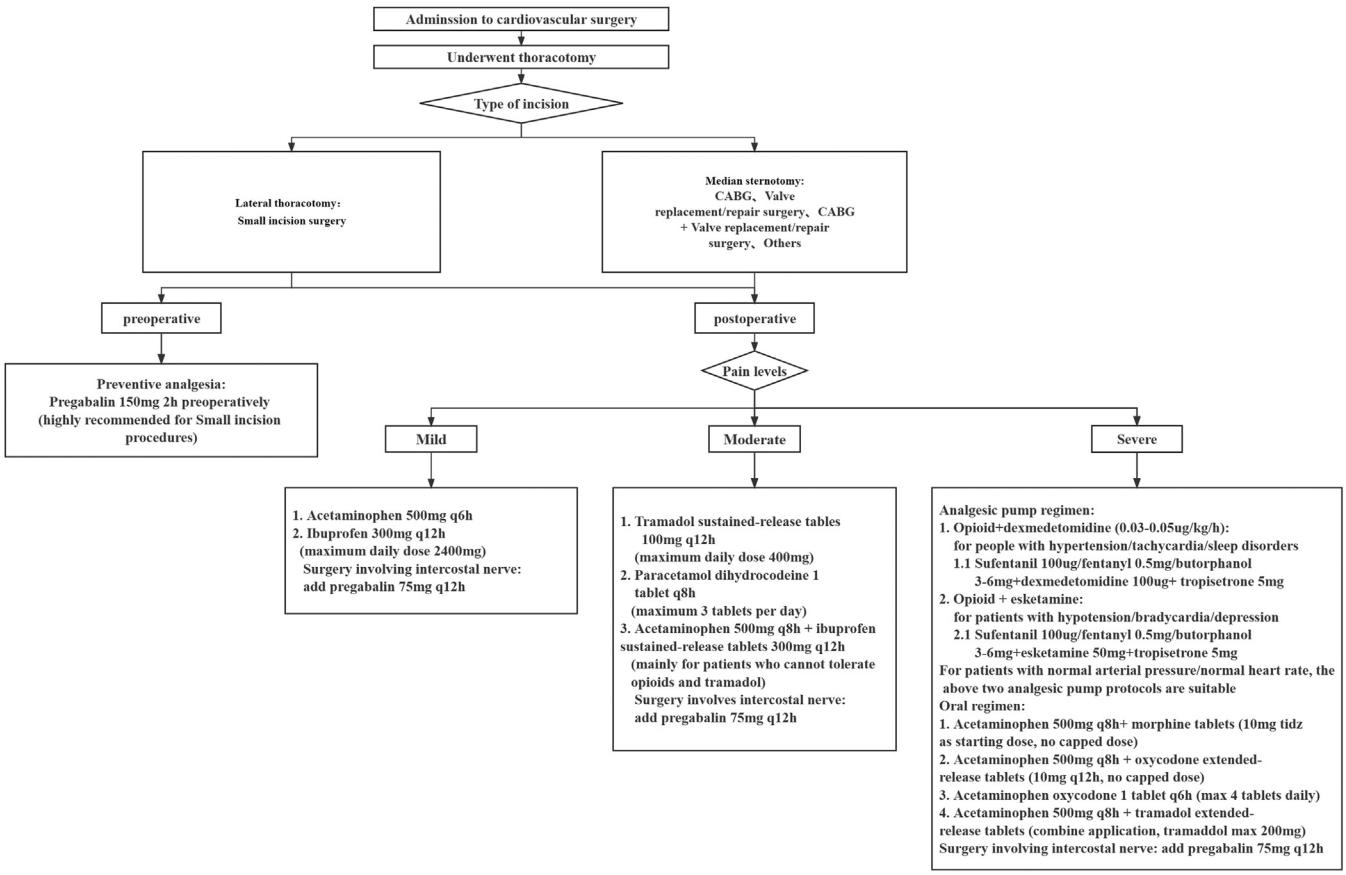

Fig 2. Clinical flow of postoperative analgesic drug therapy in cardiovascular surgery. CABG = coronary artery bypass graft.

developed based on the review of existing US guidelines for postoperative pain management, which are translated into consensus-based analgesic protocols (guidelines for analgesic protocols).[13] The ADP was used in patients undergoing cardiovascular surgery with thoracotomy. Patients were stratified according to the type of incision (median sternotomy or lateral thoracotomy) and the timing of the operation (preoperative or postoperative). For patients undergoing lateral thoracotomy, the preoperative use of pregabalin for prophylactic analgesia was recommended. Patients were further stratified postoperatively by assessing their pain level (mild, moderate, or severe) based on a numerical rating scale (NRS) pain score. For mild pain, acetaminophen or ibuprofen was prescribed. Tramadol or aminophenol dihydrocodeine was prescribed for patients with moderate pain. Acetaminophen was prescribed for patients who cannot tolerate opioids and tramadol.

For patients with severe pain, the analgesic pump regimen or an oral regimen was recommended. An analgesic pump regimen containing different analgesic drugs was used as the first choice in a multimodal approach to preserve opioid effects and also to achieve more effective pain management through central and peripheral antinociceptive mechanisms.[14] In this, opioids + dexmedetomidine hydrochloride injection (0.03–0.05 μg/kg/h) was given to patients with hypertension/tachycardia/sleep disorders, whereas opioids + esketamine hydrochloride injection was given for patients with hypotension/bradycardia/depression. Dexmedetomidine is a highly selective $\alpha 2$ adrenergic receptor agonist and produces sedative and analgesic effects by acting on $\alpha 2$ receptors in the central and peripheral nervous systems.[15,16] Esketamine, an enantiomer of ketamine, has a strong affinity with the *N*-methyl-d-aspartate receptor. It plays the analgesic role by noncompetitively inhibiting the *N*-methyl-d-aspartate receptor, shortening the opening time of the receptor channel, and reducing the opening frequency of the receptor channel to block the transmission of glutamate.[17] In addition, esketamine antagonizes central or peripheral nociception and reduces opioid tolerance.[18]

For patients with normal arterial pressure/normal heart rate, both analgesic pump regimens are suitable. In the oral regimen, different treatment options were selected according to the degree of pain. Regardless of the severity of the pain, the addition of pregabalin was recommended in surgical procedures that involved the intercostal nerve.

Outcomes

The effectiveness of ADP was evaluated in terms of pain scores using an NRS, with 11 levels of pain severity. Scores from 0 to 10 were used to represent pain severity, with 0 being no pain and 10 being unbearably severe pain. The pain intensity of patients was reported on days 1, 3, and 5. In addition, the average consumption of opioids in analgesic pumps was used as an additional indicator to evaluate effectiveness. Data on adverse events that occurred after the use of analgesics were collected to evaluate the safety.

Statistical Analysis

Data collected retrospectively before the administration of analgesic drugs were compared with the data collected after the administration. Continuous variables were expressed as mean and SD and compared using 2-sided sample *t* test after ensuring that the data were normally distributed. Nonparametric rank-sum test was

Table 1
Demographic characteristics of patients before and after implementation of the analgesic drug pathway.

Variable	Before (n = 193)	After (n = 218)	*P* value
Gender*			
Male	129 (66.8)	141 (64.7)	NS
Female	64 (33.2)	77 (35.3)	
Age, y†	63.00 (54.00, 68.00)	63.00 (55.00, 70.00)	NS
BMI‡	25.29 ± 3.79	25.28 ± 3.45	NS
Basic diseases*			
Diabetes	31 (16.1)	43 (19.7)	NS
Hypertension	89 (46.1)	112 (51.4)	NS
Hypercholesterolemia	1 (0.5)	1 (0.5)	NS
Cerebrovascular disease	25 (13.0)	25 (11.5)	NS
COPD	1 (0.5)	1 (0.5)	NS
Mental illness	4 (2.1)	4 (1.8)	NS
Heart diseases*			
Coronary heart disease	7 (3.6)	3 (1.4)	NS
Atrial fibrillation	4 (2.1)	1 (0.5)	NS
Myocardial infarction	2 (1.0)	0 (0.0)	NS
Past history*			
Smoking	60 (31.1)	64 (29.4)	NS
History of cardiac surgery	15 (7.8)	22 (10.1)	NS
History of noncardiac surgery	55 (28.5)	59 (27.1)	NS
Aspirin after surgery*	82 (42.5)	103 (47.2)	NS

BMI = body mass index; COPD = chronic obstructive pulmonary disease; NS = not significant.
* Values are presented as n (%).
† Values are presented as median (25th percentile, 75th percentile).
‡ Values are presented as mean (SD).

used for data without normal distribution. Comparisons between categorical variables were evaluated using the χ^2 test, and the bilateral significance values were evaluated as percentages. Continuous outcomes such as dose of sufentanil and butorphanol were transformed to binary outcomes based on median value. Binary logistic regression models were performed to compare binary outcomes between study groups. Adjusted odds ratio (OR) and 95% CI were calculated. The repeated measures were analyzed by using a generalized estimation equation (GEE) model to estimate the group effect, time effect, and interaction between group effect and time effect. Adjusted coefficient and 95% CI were calculated. These models were adjusted for relevant covariates, including age, diabetes, hypertension, heart disease, use of aspirin, and other basic morbidity (eg, hypercholesterolemia, cerebrovascular disease, chronic obstructive pulmonary disease, and mental illness). Opioid analgesic consumption and incidence of adverse effects were statistically analyzed using SPSS version 21 software (IBM SPSS Statistics for Windows, Armonk, New York), and a P value $< .05$ was considered statistically significant.

Results

Baseline characteristics

A total of 328 patients from September to November 2021 (before the implementation of the ADP) and 359 patients from September to November 2022 (after the implementation of the ADP) were screened. After applying the exclusion criteria, 193 patients before the implementation of the ADP and 218 patients after the implementation of the ADP were enrolled. Most men in both the before-ADP (n = 129 [66.8%]) and after-ADP (n = 141 [64.7%]) study groups, and hypertension was the most common basic disease observed (before-ADP group, n = 89 [46.1%] and after-ADP group, n = 112 [51.4%]). Overall, the baseline data were comparable between the 2 groups (Table 1). The number of patients who received opioid + dexmedetomidine and opioid + esketamine was 148 and 70, respectively, and were included in the analgesic pump regimen. We also analyzed the surgery data before and after implementation of the ADP and observed no significant differences (Table 2).

Binary outcomes

Based on multivariate logistic regression models, we found that the after-ADP group was associated with decreased risk of use of butorphanol ≥6 days (OR = 0.03; 95% CI, 0.02–0.08) as well as nausea and vomiting (OR = 0.50; 95% CI, 0.28–0.90) (Table 3).

GEE model

After considering the 3 time points and adjusting for covariates, the GEE model suggested that there was significant decline in pain scores ($\beta = -0.713$; 95% CI, −0.750 to −0.676; $P < .001$). The after-ADP group had significantly lower pain scores than the before-ADP group ($\beta = -1.286$; 95% CI, −1.568 to −1.004; $P < .001$). The interaction effect suggests that the difference in pain score did not change over time ($\beta = -0.040$; 95% CI, −0.114 to 0.034; $P = .291$) (Table 4).

Effectiveness

NRS scores and the corresponding number of patients before and after the implementation of the ADP are shown in Table 5. Compared with before ADP implementation, the pain scores of cardiovascular surgery patients on the first, third, and fifth day after ADP implementation showed a downward trend, but the difference was significant only in patients with mild pain and severe pain. Pain scores were higher on the first day after ADP surgery and decreased on the third and fifth days after surgery. According to the recorded pain scores, most patients undergoing cardiovascular surgery had moderate pain on the first day after surgery, and then more patients showed mild pain as the length of hospital stay increased. Regarding the consumption of opioids in analgesic pumps, a significant reduction in the dose of butorphanol (6.0 mg [range, 6.0–11.0] vs 2.0 [range, 0.0–6.0]; $P = .000$) and sufentanil (7.0 μg [range, 6.0–9.0] vs 7.0 [range, 6.0–8.0]; $P = .041$) was observed after the implementation of ADP in patients who underwent cardiovascular surgery (Table 6).

Table 2
Surgical data of patients before and after implementation of the analgesic drug pathway.

Variable	Before (n = 193)	After (n = 218)	*P* value
Type of incision*			
Median sternotomy			
CABG	73 (37.8)	85 (39.0)	NS
Valve replacement/repair surgery	44 (22.8)	59 (27.1)	NS
CABG + valve replacement/repair surgery	9 (4.7)	18 (8.3)	NS
Others	58 (30.0)	66 (30.3)	NS
Lateral thoracotomy			
Small incision surgery	9 (4.7)	10 (4.6)	NS

CABG = coronary artery bypass graft; NS = not significant.
* Values are presented as n (%).

Table 3
The consumption of opioids in the analgesia pump and the incidence of adverse reactions compared before and after the implementation of the analgesic drug pathway.

Outcome	Before* (n = 193)	After* (n = 218)	*P* value	Adjusted odds ratio‡ (95% CI)	*P* value
Sufentanil ≥7 d	122 (63.21)	128 (58.72)	.351	0.809 (0.535-1.223)	.314
Butorphanol ≥6 d	186 (96.37)	106 (48.62)	< .001	0.034 (0.015-0.076)	< .001
Nausea and vomiting	34 (17.6)	22 (10.1)	.026	0.503 (0.281-0.900)	.021
Constipation	16 (8.3)	9 (4.1)	.078	–	–
Hypotension	8 (4.1)	4 (1.8)	.241	–	–
Fast heart rate	5 (2.6)	2 (0.9)	.261	–	–
Respiratory inhibition	8 (4.1)	1 (0.5)	.015	–	–
Dizziness and headaches	10 (5.2)	3 (1.4)	.044	–	–

* Values are presented as n (%).
‡ Adjusted odds ratio cannot be calculated due to insufficient number of outcomes. Odds ratios were adjusted for age, diabetes, hypertension, heart disease, use of aspirin and other basic morbidity.

Table 4
Generalized estimation equation models of in pain score between study groups.

Day	Before* (n = 193)	After* (n = 218)	Crude model			Adjusted model†		
			Group effect‡	Time effect‡	Group × time interaction‡	Group effect‡	Time effect‡	Group × time interaction‡
1	5.51 ± 1.91	4.43 ± 1.96	−1.264 (−1.547 to −0.981), < .001	−0.713 (−0.750 to −0.676), < .001	−0.040 (−0.114 to 0.034), .291	−1.286 −1.568 to −1.004), < .001	−0.713 (−0.750 to −0.676), < .001	−0.040 (−0.114 to 0.034), .291
3	4.13 ± 1.54	2.67 ± 1.72						
5	2.74 ± 1.35	1.50 ± 1.21						

* Values are presented as mean ± SD.
† Model was adjusted for age, diabetes, hypertension, heart disease, use of aspirin, and other basic morbidity.
‡ Values are presented as β (95% CI), *P* value.

Table 5
Pain score and number of patients before and after the implementation of the analgesic drug pathway.

Pain level	Day 1			Day 3			Day 5		
	n (%)	Pain score*	*P* value	n (%)	Pain score*	*P* value	n (%)	Pain score*	*P* value
Mild									
Before	26 (13.47)	2.92 ± 0.27	< .001	82 (42.49)	2.90 ± 0.30	0.000	127 (65.80)	2.17 ± 0.48	< .001
After	70 (32.11)	2.23 ± 0.54		138 (63.30)	2.03 ± 0.73		159 (72.94)	1.38 ± 0.57	
Moderate									
Before	117 (60.62)	4.92 ± 0.75	NS	91 (47.15)	4.68 ± 0.79	NS	53 (27.46)	4.26 ± 0.52	NS
After	112 (51.38)	4.79 ± 0.85		53 (41.41)	4.45 ± 0.67		26 (11.93)	4.15 ± 0.46	
Severe									
Before	50 (25.91)	8.22 ± 1.02	.001	18 (9.33)	7.44 ± 0.71	NS	4 (2.07)	NA	
After	36 (16.51)	7.58 ± 0.73		9 (7.03)	7.22 ± 0.44		0 (0.00)		

NA = not applicable; NS = not significant.
* Values are presented as mean ± SD.

Table 6
Consumption of opioids in analgesic pumps before and after implementation of the analgesic drug pathway.

Variable	Before* (n = 193)	After* (n = 218)	*P* value
Sufentanil (50 μg:1 mL, intravenous infusion pump)	7.0 (6.0, 9.0)	7.0 (6.0, 8.0)	.041
Butorphanol (1 mg:1 mL, intravenous infusion pump)	6.0 (6.0, 11.0)	2.0 (0.0, 6.0)	.000

* Values are presented as median (25th percentile, 75th percentile).

Table 7
Incidence of adverse events in patients before and after implementation of the analgesic drug pathway.

Variable	Before* (n = 193)	After* (n = 218)	*P* value
Digestive system			
Nausea and vomiting	34 (17.6)	22 (10.1)	.026
Constipation	16 (8.3)	9 (4.1)	NS
Cardiovascular system			
Hypotension	8 (4.1)	4 (1.8)	NS
Fast heart rate	5 (2.6)	2 (0.9)	NS
Respiratory system			
Respiratory inhibition	8 (4.1)	1 (0.5)	.027
Nervous system			
Dizziness and headaches	10 (5.2)	3 (1.4)	.028

NS = not significant.
* Values are presented as n (%).

Safety

Several common adverse reactions influencing the digestive system, cardiovascular system, respiratory system, and nervous system and their occurrence before and after administering the ADP were analyzed. A significant reduction in the incidence of nausea and vomiting ($P = .026$), respiratory inhibition ($P = .027$), and dizziness and headache ($P = .028$) was observed after the implementation of the ADP in patients who underwent cardiovascular surgery. No significant differences were observed in terms of respiratory inhibition, hypotension, and fast heart rate before and after the implementation of the ADP (Table 7).

Discussion

Moderate to severe pain was experienced by 75% of patients following cardiovascular surgery. Studies from Norway and the United States reported postoperative pain within 2 weeks following cardiovascular surgery in 77% to 85% of patients.[19,20] A median duration of 5 days and 6 days was reported in patients undergoing bypass and valvular surgeries, respectively.[21] A prospective inquiry of acute and chronic poststernotomy pain evaluations show severe pain at rest in 49% of patients and during coughing and movement in 78% and 62% of patients, respectively.[22] In cardiovascular surgery, the intensity of pain does not change significantly during the first 2 postoperative days but gradually subsides from the third day.[23] The most commonly reported sites of pain are chest (discomfort of noncardiac origin), mediastinal, pleural drain-placement sites, back, and the gluteal region. Patients also had pain in the shoulders and lower legs because of increased motor activity and spasticity of shoulder muscles.[24–26] Before implementation of the ADP, postoperative pain was managed by single or multiple opioids, which was expensive and associated with a high incidence of adverse events and prolonged hospital stay. Moreover, the long-term use of opioids can lead to severe dependence and demand for opioids leading to opioid abuse.[27–29] Taking these factors into consideration, both guidelines on the management of postoperative pain and the literature recommend a multimodal analgesia approach for pain management.[10,13] On the basis of the recommendations on multimodal analgesia, our study suggested the use of 2 analgesic pump protocols using opioids in combination with dexmedetomidine or esketamine for postoperative pain management in patients undergoing cardiovascular surgery. In both protocols, drugs with different mechanisms of action are used in combination with opioids for postoperative analgesia. It is expected to reduce the adverse reactions caused by the combination of single or multiple opioids.

Dexmedetomidine relieves postoperative anxiety and reduces the incidence of opioid-related adverse events, and the use of dexmedetomidine is not associated with any significant respiratory inhibition.[30] Opioid receptor agonist-based patient-controlled intravenous analgesia combined with dexmedetomidine has also been recommended for traumatic and painful open surgical procedures.[31] Studies have shown that the combination of dexmedetomidine and an opioid in analgesic pumps has a synergistic effect that greatly reduces the amount of opioids required.[32] Dexmedetomidine with opioids also reduces postoperative pain scores as well as the incidence of nausea and vomiting and other adverse events such as hypotension and drowsiness.[33] In addition, it reduces the length of hospital stay and improves patient satisfaction.[30]

The US guidelines for postoperative pain management recommend ketamine as part of multimodal analgesia, mainly for pain management after major surgical procedures such as thoracotomy and coronary artery bypass grafting (weak recommendation, moderate-quality evidence).[13] Esketamine has a stronger analgesic effect compared with ketamine, with significantly lower incidence of adverse events such as nausea and vomiting. Furthermore, it reduces the respiratory depression caused by opioids and has fast metabolism and high clearance rates.[34,35] The cost of analgesic drugs (sufentanil + butorphanol/pentazocine/dezocine) before the implementation of the ADP cost somewhere between 160 to 230 Chinese Yuan (~$22–$32). Meanwhile, after ADP implementation, the cost of opioid + dexmedetomidine or opioid + esketamine was as little as 8 Chinese Yuan (~$1.1) for fentanyl + dexmedetomidine to a maximum of 142 Chinese Yuan (~$19.8) for sufentanil + esketamine.

Considering the above factors, we recommend dexmedetomidine or esketamine combined with opioids in analgesic pump regimens for postoperative analgesia. The combination showed significant benefits in both effectiveness and safety in postoperative patients who underwent cardiovascular surgery. Similar to the positive outcomes discussed, the cost involved for postoperative pain management also was reduced considerably with a multimodal ADP approach, which is highly welcoming.

Small incision surgery damages the intercostal nerve resulting in nerve pain for which pregabalin can be prescribed. Pregabalin is a gamma-aminobutyric acid receptor blocker that can inhibit the excessive excitation of neurons, reduces neuropathic pain, and has a good analgesic effect. Therefore, it should be considered as the first choice for the treatment of neuropathic pain. Also, it reduces the incidence of adverse events.[36] It does not bind to plasma proteins and is almost not metabolized in the body.[37] These features make pregabalin an ideal drug for prophylactic analgesia and cardiovascular surgery involving the intercostal nerve and it use showed beneficial outcomes in our study.

Limitations

A limitation of our study is that the results were based on single-center observations. No studies have been done to determine the effectiveness and applicability of ADP in other centers. Besides, the study collectively reported ADP outcomes in patients undergoing cardiovascular surgery and did not differentiate between lateral and sternal thoracotomies. Effectiveness of the ADP required continuous monitoring and drug combinations/doses needed to be revised to keep up with updates of guidelines and new evidence from clinical studies. A multicenter study investigating the efficiency of ADP for a longer time should be undertaken. Finally, this study did not consider the length of postoperative hospital stay as an evaluation indicator because care after coronary artery bypass grafting pertaining to hospital stay in China is different to that in Western countries. Herein, length of hospital stay includes preoperative duration of patient admission, wait time for surgery due to the large volume of patients, and lack of infrastructure in community hospitals to accept patients after coronary

artery bypass graft surgery that results in extended hospital stay until patients are deemed fit to lead their daily lives.

Conclusions

To the best of our knowledge, this is the first study to demonstrate the effectiveness and safety of postoperative analgesic routes in patients undergoing cardiovascular surgery. The establishment of the ADP greatly benefitted patients who underwent cardiovascular surgery in terms of reduced postoperative pain scores and opioid consumption. The incidence of adverse events was also significantly reduced. Hence, the ADP could be an effective treatment modality for clinical management of pain in cardiovascular surgery.

Declaration of competing interest

The authors have indicated that there are no conflicts of interest regarding the content of this article.

Acknowledgments

The authors thank C. R. Swathirajan, PhD, and Ramandeep Singh, PhD, Indegene Pvt Ltd, for providing editorial support.

This work was funded by grants from the China Health Promotion Foundation to Dr Li (funding/grant No. XM_2020_011_0245_09).

Dr Yue was responsible for conceptualization, data curation, formal analysis, funding acquisition, methodology, supervision, validation, and writing (original draft, review, and editing). Dr Ji was responsible for conceptualization, data curation, formal analysis, funding acquisition, methodology, supervision, validation, and writing (original draft, review, and editing). Dr Wang was responsible for data curation, formal analysis, methodology, software, and writing (original draft, review, and editing). Dr Cheng was responsible for data curation, formal analysis, investigation, methodology, and visualization. Mr Wang was responsible for conceptualization, methodology, project administration, resources, and writing (original draft, review, and editing). Mr Qu was responsible for conceptualization, investigation, project administration, resources, software, visualization, and writing (original draft, review, and editing). Mr Li was responsible for conceptualization, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing (review and editing).

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