Chronic Pain after Cardiac Surgery in Patients with Different Methods of Postoperative Analgesia

Vykintė Kleibaitė[1], Milda Švagždienė[2]
[1]*Lithuanian University of Health Sciences, Faculty of Nursing, Lithuania;*
[2]*Lithuanian University of Health Sciences, Faculty of Medicine, Clinic of Anesthesiology, Lithuania*

Key Words: *postoperative pain, chronic, persistent, early postoperative period, heart surgery, systemic analgesia, multimodal analgesia, epidural analgesia.*

Summary. *The aim of this study was to analyze trends for developing chronic postoperative pain in the early postoperative period by comparing the effect of two different methods of analgesia after cardiac surgery.*

Design. A single-centre, prospective randomized controlled trial, with an open-label design was performed in patients undergoing open heart surgeries with cardiopulmonary bypass. Surgeries included coronary artery bypass grafting, heart valve replacement or combined surgery.

Methods. Patients were divided into two groups (group I and group II) in relation to the type of analgesia during and after the surgery. Group I received systemic analgesia, while group II had multimodal analgesia. The study was performed at the Hospital of Lithuanian University of Health Sciences Kauno klinikos, Department of Cardiothoracic and Vascular Surgery from September, 2019, until January, 2020.

Results. In total, 122 patients participated in the study. Chronic pain was found to develop in less than one third of the patients (29.5%, n = 36). Group I had slightly higher rates of pain level, although different analgesia methods did not affect the rate of chronic pain. The patients over 75 years of age, obese and overweight were at least 3.5 times more likely to develop chronic pain than the patients younger than 50 years and those with normal weight. There was no significant difference between patients' gender or type of surgery and the development of chronic postoperative pain.

Introduction

Heart surgery, such as coronary artery bypass grafting (CABG) and heart valve replacement (HVR), ranks among the most frequently performed interventions worldwide (1). Pain levels after cardiac surgery are often severe, undertreated and prolonged. The development of chronic pain is considered a major complication after surgery. Chronic (or persistent) postoperative pain (CPOP) has been defined by the International Association for the Study of Pain as a clinical discomfort that lasts more than 3 months post-surgery without other causes of pain such as chronic infection or pain from a chronic condition preceding the surgery (2). According to the International Classification of Diseases, persistent postoperative pain has greater intensity or different pain characteristics than preoperative pain and is a continuum of acute postoperative pain that may develop after an asymptomatic period (3, 4).

Postoperative pain (POP) is one of the most common postoperative complications that is experienced by up to 80% of patients. The problematic nature of POP is still a relevant and under-investigated topic in the works of foreign and Lithuanian researchers (5). Sufficient POP management improves patients' quality of life and their recovery time and reduces the cost of treatment (5–7).

Pain after cardiac surgery is caused by several factors: sternotomy, sternal/rib retraction, pericardiotomy, internal mammary artery harvesting, saphenous vein harvesting, surgical manipulation of the parietal pleura, chest tube insertion and other musculoskeletal trauma during surgery. The effects of undertreated pain during early postoperative period (EPP) may lead to an increase of anxiety, emotional discomfort and sleep disturbance. The influence of pain on physiology can cause cardiovascular dysfunction, thromboembolic complications, pulmonary dysfunction and, in some cases, may be associated with pulmonary atelectasis and pneumonia (5, 6, 8). Current evidence suggests that poorly treated acute postoperative pain not only influences patient well-being, but also increases the risk for development of chronic pain (9, 10). The rates of chronic postoperative pain in patients after heart surgery range between 21% and 55% (11).

Effective POP management has been problematic for health professionals who manage pain. Hence, previous researchers have devoted time and resources to discover measures that would improve pain management. Even though studies continue to report inadequate POP management (12–15), in the first decade of the 21st century, postoperative pain

Correspondence to Vykintė Kleibaitė, Lithuanian University of Health Sciences, Mickevičiaus 9, LT-44307 Kaunas, Lithuania
E-mail: v.kleibaite@gmail.com

was still not successfully managed in one third to half of patients (5, 16).

An examination of the literature shows some reasons for inadequate POP management, such as effect of culture, inappropriate attitude of health personnel, patients, and their families, inadequate knowledge of health professionals, and lack of multidisciplinary approach to pain management (17, 18). Studies have further explored these key barriers; for example, health professionals' barriers for POP management pain assessment, prejudice and bias toward patients, and inability to empathize and establish rapport (19, 20). Nurses have been found to contribute to the ineffective management of POP pain. According to Coulling (2005), doctors and nurses made their own judgments about the patient's pain instead of relying on the patient's self-report of pain (21). Studies have attributed most of the barriers associated with ineffective pain management to the nurse, perhaps because the nurse is the only health professional who spends 24 hours per day with the patient. Thus, the nurse plays a key role in the management of POP because it is the responsibility of the nurse to assess pain and provide a timely intervention.

Systemic analgesia (with opioids and non-opioids) is still considered to be the basis (even the gold-standard) of postoperative pain therapy. However, it is well known that the parenteral application of opioids is associated with a high rate of side effects (22, 23). Regional blocks with local anaesthetics and opioids are key components of effective multimodal analgesia. To achieve effective analgesia with parenteral opioids, much higher doses are necessary when compared with the epidural route (e.g., morphine 50–100 mg via intravenous patient-controlled analgesia versus 5 mg via an epidural catheter). The advantageous effects of epidural anaesthesia compared with parenteral opioids were also confirmed in a current meta-analysis (24). This combination leads not only to a decrease in the dose and consequently the side-effects of each drug; there is also a synergy in which the local anaesthetic facilitates the transfer of the opioid into the cerebrospinal fluid and increases the affinity of the opioid receptor for the opioid (24).

The aim of this study was to compare the effect of two different types of analgesia (systemic and multimodal (combined with regional)) after heart surgery on the development of postoperative chronic pain.

Material and Methods

Study Design. A single-centre, prospective randomized controlled trial with an open-label design was performed. The study was performed at the Hospital of Lithuanian University of Health Sciences Kauno klinikos, Department of Cardiothoracic and Vascular Surgery from September of 2019 until January of 2020. The study was divided into two stages: early postoperative period (postoperative days 1–3) and follow-up period (3 months after surgery). During the EPP, acute pain levels were recorded. During the follow-up period, the patients were contacted by phone to assess the onset of chronic postoperative pain.

Participants. The patients were enrolled on the day before heart surgery and the written informed consent was obtained. The patients underwent open heart surgery with cardiopulmonary bypass (CPB) and were monitored 3 days after their surgery with the questionnaire of their pain level completed. Then, in order to investigate chronic postoperative pain, they were contacted by phone 3 months after the surgery.

Patient inclusion criteria were the following: age of 18–85 years, elective heart surgery with CPB, type of the heart surgery such as CABG, HVR and combined surgery (HVR and CABG). Exclusion criteria were emergency surgery, redo (repeated) operation, complicated postoperative course, history of persistent pain before the surgery, difficulty to communicate with the patient and incomplete data collection during whole six month period.

During the three-month period, 234 patients underwent heart surgery with CPB. A total of 122 patients matched the inclusion criteria and were enrolled in the study. The patients were divided into two groups according to the type of analgesia they were given: group I received systemic analgesia according to the schedule in Table 1 and group II received combined multimodal analgesia (regional epidural analgesia combined with systemic analgesia). A continuous infusion using an automatic syringe pump (APS) was given through the catheter. Bupivacaine 50 mg to 10 mL and Fentanyl 200 μg (4 mL) were diluted to 40 mL with 0.9% NaCl solution and administered into the epidural catheter at the rate of 5 to 6 mL/h. The rate of infusion into the epidural was only changed if the side effects occurred (e.g., numbness of hand(s), fingers).

In both groups, POP intensity was assessed on the VAS scale at rest and during motion (cough). The nature and localization of pain were also assessed. Three months after surgery, the patients were contacted by the phone and the data about CPOP development was collected.

EPP pain was assessed at 7 time points: right after extubation, 8 hours, 12 hours, 18 hours after the surgery, 1 day, 2 days and 3 days after the surgery. Chronic pain was assessed three months after the surgery interviewing patients by phone.

Results

CPOP was found to develop in less than one third of the cardiac surgery patients that received

different types of postsurgical analgesia (29.5%, n = 36). The study enrolled 122 patients including 70 (57.4%) men and 52 (42.6%) women. The sociodemographic and clinical characteristics of the patients are presented in the Table 2.

The Influence of Sociodemographic and Clinical Characteristics on CPOP Development. The influence of socio-demographic and clinical characteristics on the development of CPOP in patients after cardiac surgery were evaluated. Multivariate logistic regression showed that the patients over 75 years old had nearly 3.5 times higher incidence of CPOP (OR = 3.46) compared with the patients under age of 50 years ($P < 0.05$). In overweight patients, the likelihood of CPOP increased almost fourfold (OR = 3.89) and in obese patients by more than three and a half times (OR = 3.67) if compared with normal weight patients ($P < 0.05$) (Table 3). No significant differences were found between gender or type of surgery and CPOP development.

EPP Pain Dynamics in Patients with Systemic and Modal Analgesia. When assessing the intensity of pain during EPP, we found that 18 hours after surgery postoperative pain intensity at rest was significantly higher in group I than in group II ($P < 0.05$, Mann-Whitney U test). Although the other results were not statistically significant, the tendency was observed that group II had a lower pain level from day 0 (day of surgery) throughout day 3 (72 hours after surgery) (Fig. 1).

When assessing the pain intensity of patients during movement (coughing), we found that the pain intensity at different time points after surgery was similar in group I and group II. As well as pain at rest, pain during movement had a tendency to be higher in group I, although the difference was not statistically significant (Fig. 2).

The Influence of Different Methods of Analgesia on Developing CPOP. Multivariate logistic regression showed that the patients with different analgesic methods had similar development of CPOP ($P > 0.05$) (Fig. 3).

Table 1. The scheme for applying systemic analgesia

Medications	Method of Administration	Timing
1. Opioids		
Morphine	20 mg i/v	2 mL/h speed – ASP
Morphine or Petidine	10 mg i/m or 50 mg i/m	8:30 – 20:30
2. Paracetamol	1000 mg i/v	6:00 – 12:00 – 18:00 – 24:00
3. NSAIDs		
Diclofenac	75 mg i/v or i/m	10:00 – 22:00
Ketonal	100 mg i/v	12:00 – 24:00
Ketanov	30 mg i/v	7:00 – 15:00 – 23:00

ASP, automatic syringe pump.

Table 2. Sociodemographic and clinical characteristics of the participants

Features		Systemic Analgesia (n = 98) n (%)	Multimodal Analgesia (n = 24) n (%)	Total (n = 122) n (%)
Gender	Male Female	57 (58.2) 41 (41.8)	13 (54.2) 11 (45.8)	70 (57.4) 52 (42.6)
Age (in ears)	< 50 50–74 ⩾ 75	12 (12.2) 51 (52.0) 35 (35.7)	– 18 (75.0) 6 (25.0)	12 (9.8) 69 (56.6) 41 (33,6)
Body Mass Index	Normal Overweight Obese	18 (18.4) 34 (34.7) 46 (46.9)	2 (8.3) 9 (37.5) 13 (54.2)	20 (16.4) 43 (35.2) 59 (48.4)
Surgery	CABG HVR CABG+HVR	68 (69.4) 17 (17.3) 13 (13.3)	18 (75.0) 5 (20.8) 1 (4.2)	86 (70.5) 22 (18.0) 14 (11.5)

CABG, coronary artery bypass graft surgery; HVR, heart valve replacement.

Table 3. Dependence of CPOP Development on sociodemographic and clinical characteristics (multivariate logistic regression)

Features		OR	95 % CI	*P*
Gender	Male	1		
	Female	1.38	0.57–3.32	0.472
Age in years	< 50	1		
	50–74	1.39	0.80–2.50	0.258
	⩾ 75	3.46	1.18–11.17	**0.032**
Body Mass Index	Normal	1		
	Overweight	3.89	1.07–14.1	**0.039**
	Obese	3.67	1.05–12.8	**0.043**
Surgery	CABG	1		
	HVR	0.71	0.20–2.51	0.596
	CABG+HVR	0.40	0.07–2.13	0.280

OR, odds ratio; CI, confidence interval; CABG, coronary artery bypass graft surgery; HVR, heart valve replacement.

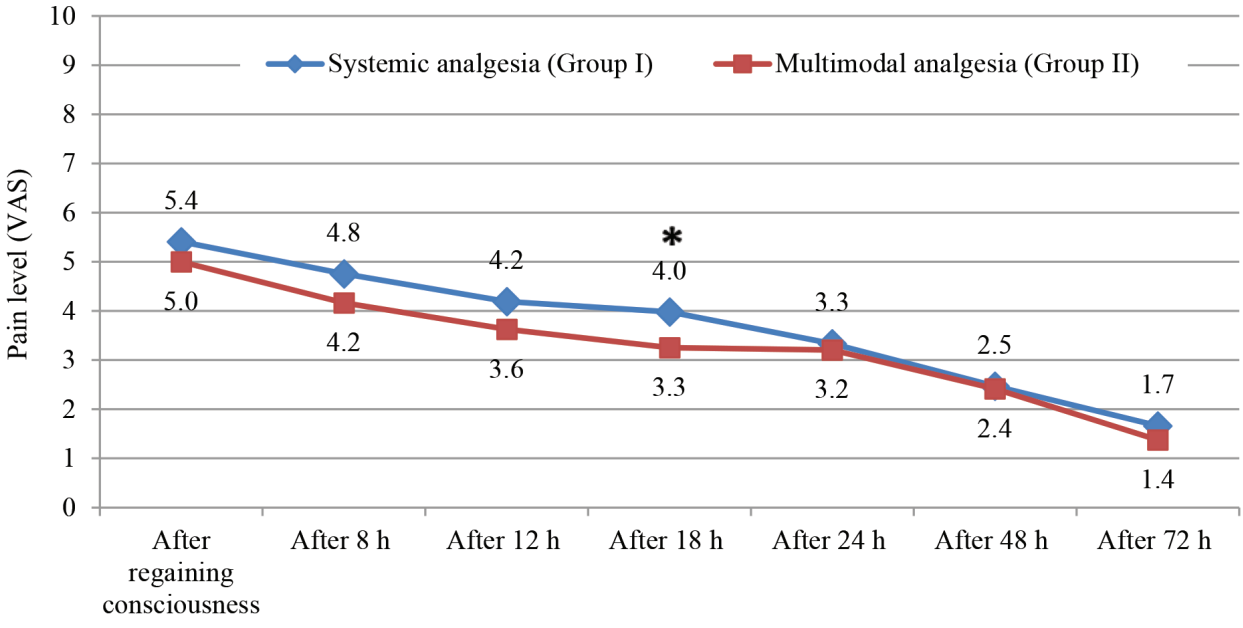

Fig. 1. Pain dynamics in patients with systemic and multimodal analgesia at rest position (mean scores on a 10-point scale)
*$P < 0.05$ compared with multimodal analgesia (Mann-Whitney U test).

Discussion

Our study showed that the rate of CPOP was 29.5% 3 months after heart surgery. This number is similar to the ones that were found in previous similar studies. The number varied from 11% to 45% (25–29). Thus, a different type of analgesia did not have a statistically significant impact on the EPP pain levels and the development of CPOP in our study ($P > 0.05$), while it was found in a few similar studies (30–31).

The study results also showed the relationship of sociodemographic and clinical characteristics with the development of CPOP. The main factors for development of CPOP were age over 75 years, overweight and obesity. The data on the age influence for CPOP development are controversial. Most of the studies found that the younger age was the influencing factor (11, 25, 26, 28, 29). Guimaraes-Pereira et al. (2016) say that the reason why younger age is associated with a greater likelihood to develop chronic pain is because younger aged patients usually feel higher acute postoperative pain; meanwhile, a greater likelihood of chronic postoperative pain was associated with a higher worst pain intensity during EEP (26).

In our study, we found that obesity and overweight in patients almost fourfold (OR 3.67 and 3.89) increased the risk to develop CPOP compared with the normal body weight. These results corre-

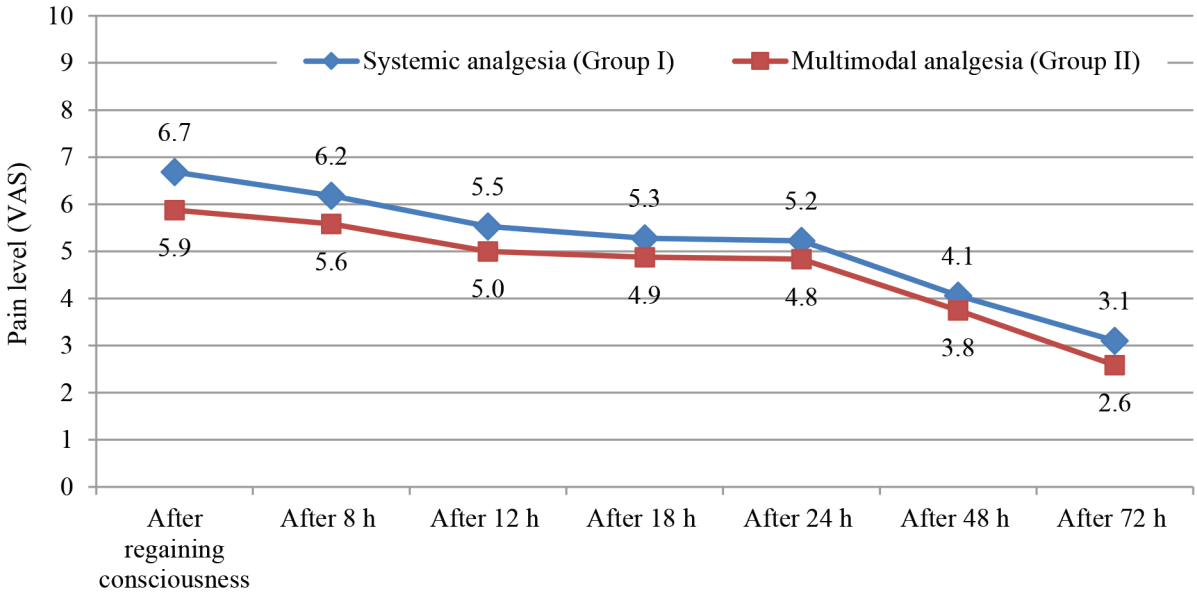

Fig. 2. Pain dynamics in patients with systemic and multimodal analgesia during movement (coughing) (mean scores on a 10-point scale)
$P > 0.05$ (Mann-Whitney U test).

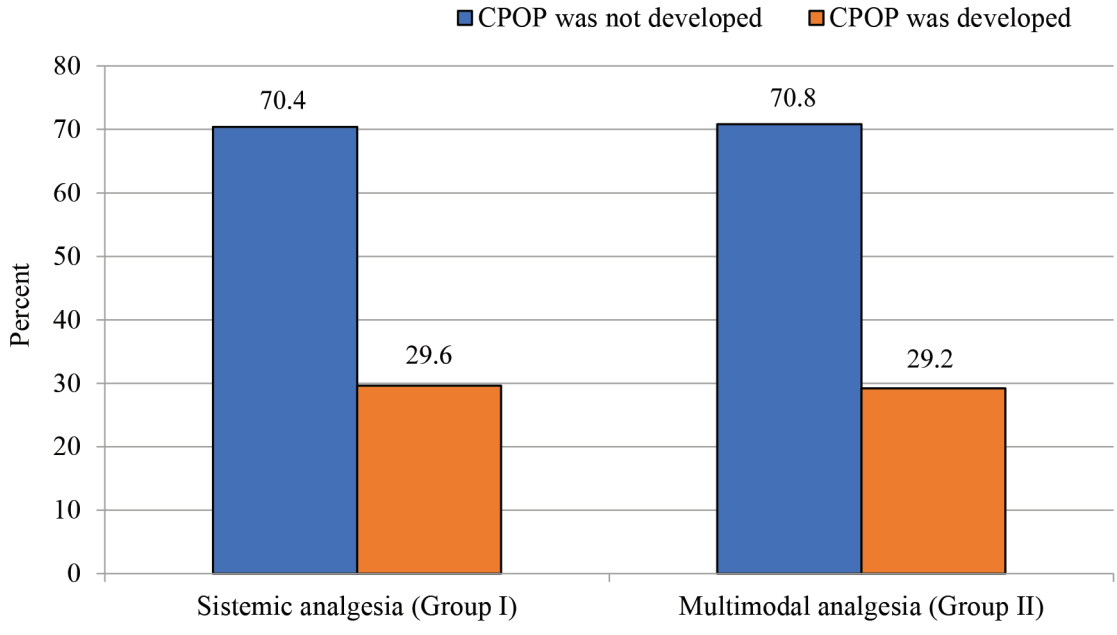

Fig. 3. The relationship between analgesia and chronic postoperative pain
$\chi^2 = 0.1$, $P = 0.967$.

spond with other studies reporting that the higher body mass index (BMI) is a significant factor for CPOP development. Heart surgery in patients with a higher BMI is technically more complicated, with prolonged retraction and more probable nerve damage, and thus a higher incidence of CPOP (25, 26, 28, 29, 32).

No statistically significant relations were found between gender or type of surgery and CPOP development after heart surgery. Studies of other researchers provide different results on gender as a CPOP influencing factor: in some studies, such influence was determined (26, 28, 29), while in others it was not (25). Most authors found the female

gender more prone to develop CPOP (26, 28, 29).

The EPP pain dynamics in both study groups (patients with systemic analgesia and with multimodal analgesia) revealed that postoperative pain intensity 18 hours after surgery at rest was significantly higher in patients with systemic analgesia compared with patients with multimodal analgesia. We discovered the tendency that the group II (multimodal analgesia) patients were having lower pain level scores throughout all 7 EPP assessment time points than the group I (systemic analgesia) patients. Rafiq et al. (2014) in their study with heart surgery patients also described alike results when comparing traditional (opiate based) analgesia with multimodal analgesia. The authors reported that almost at all evaluation points multimodal analgesia patients described lower pain scores and scored significantly lower on average pain sensation from day 0 (day of surgery) throughout day 3 (30).

We aimed to establish the influence of applying two different analgesic techniques during the EPP on development of CPOP. Multivariate logistic regression showed that the patients with different analgesic methods had a similar rate of CPOP. Although there were a few studies performed to compare the effects of preoperatively or postoperatively initiated thoracic epidural anaesthesia (TEA) versus intravenous opioids, the findings were controversial. Senturk et al. (2005) found that the preoperative initiation of TEA was associated with a significant improvement in both acute and chronic post thoracotomy pain (33). Reuben et al. (2007) provided the data that preventive multimodal analgesic techniques may play a role in reducing the prevalence of certain chronic postoperative pain syndromes (34).

The appropriate timing of analgesic intervention in the perioperative period is an important factor to understand. In order to effectively prevent the development of central neuroplasticity, it is necessary to administer analgesia during the preoperative, intraoperative, and postoperative periods (34).

Aziato et al. (2014) state that a person who plays a key role in the postsurgical pain management is an intensive care unit (ICU) nurse. It is because a nurse is the person who spends 24 hours with patients after their heart surgeries, assesses their needs, including pain, and provides a timely intervention. Therefore, they attribute most barriers associated with ineffective pain management to the nurse. In the same study, nurses described their perceptions of POP, which indicated that pain was a subjective individual experience. Nurses also responded to their patients' POP by administering analgesics and offering psychological care and other nonpharmacologic interventions. This study shows that there is a major need for nurses to be well educated in postoperative pain assessment and management.

Our study relevantly contributes to a better understanding of CPOP after cardiac surgeries. Although some studies have already focused on CPOP after heart surgeries, this study adds new knowledge to the field and helps to get closer near finally finding the "golden standard" of treating postsurgical pain and preventing the chronic postsurgical pain development in patients. Also, there are very few studies that concentrate on CPOP depending on the different types of perioperative and postoperative analgesia, so future large-scale randomized, controlled trials are necessary to better understand the problem of chronic pain after cardiac surgeries.

Conclusions

Chronic postoperative pain is common after cardiac surgery. This study showed that almost every third patient after heart surgery experienced this complication. Chronic postoperative pain was affected by patient's age and weight although the type of analgesia did not influence pain development. Patients that received multimodal analgesia after their heart surgery showed a tendency to feel lower pain during early postoperative period than patients with multimodal analgesia.

We emphasize the importance of measuring postsurgical pain constantly during early postoperative period and start treating postoperative pain as soon as possible, thus preventing the development of chronic pain. However, our study reveals that postsurgical pain management is still a big challenge for a medical team. This may lead to the conclusion that surgical and intensive care nurses do not get efficient education and necessary empowerment on pain management.

A significant part in postoperative pain management and chronic pain prevention could be appointed to advanced practice nurses (APN) in anaesthesia ant intensive care units. APN should be trained not only to monitor the pain level, but also to assess medication doses, administration methods and even to create an individual postoperative analgesia plan. Moreover, a big step forward in prevention of chronic pain would be follow-up programmes for postsurgical patients. A periodic contact between a patient and an APN nurse would enable delivering appropriate care for patients with pain problems and educating them even after they are discharged from hospital.

Statement of Conflict of Interest

The authors state no conflict of interest.

Acknowledgments

We would like to extend special thanks to the nurses of the Department of Intensive Care Unit for Cardiothoracic and Vascular Surgery who contributed us in helping to collect the data in this study.

References

1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics – 2012 update: a report from the American Heart Association. Circulation 2012;125:e2-220.
2. Macrae WA, Davies HT. Chronic postsurgical pain. Epidemiology of Pain. Crombie IK, Croft PR, Linton SJ, LeResche L, Korff MV, editors. Seattle: IASP Press; 1999. p. 125-42.
3. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R. A classification of chronic pain for ICD-11. Pain 2015;156:1003-7.
4. Richebé P, Capdevila X, Rivat C. Persistent Postsurgical Pain: Pathophysiology and Preventative Pharmacologic Considerations. Anesthesiology 2018 Sep;129(3):590-607.
5. Piščalkienė V. Pooperacinio skausmo ypatumai pagal operacijos pobūdį bei sociodemografines pacientų grupių charakteristikas. (Peculiarities of post operation pains according to surgery type and sociodemographic characteristics of patients groups.) Sveikatos mokslai 2011;21(5):152-7.
6. Piščalkienė V. Pooperacinio skausmo raiška ir nemedikamentinių priemonių taikymo galimybės. (Expression of postoperative pain and options non-pharmacological pain management.) Mokslo taikomieji tyrimai Lietuvos kolegijose 2015;11(1):58-63.
7. Piščalkienė V, Stasiūnaitė E. Priešoperacinio nerimo raiška ir jo mažinimo galimybės. (Pre-operational anxiety expression and reduction options.) Sveikatos mokslai 2014; 24(6):166-71.
8. Gerbershagen HJ, Pogatzki-Zahn E, Aduckathil S, Kappen TH, van Wijck AJM, Kalkman CJ, et al. Procedure-specific risk factor analysis for the development of severe postoperative pain. Anesthesiology 2014 May;120(5):1237-45.
9. Chandrakantan A, Glass PSA. Multimodal therapies for postoperative nausea and vomiting, and pain. Br J Anaesth 2011 Dec;107 Suppl 1:i27-40.
10. Mazzeffi M, Khelemsky Y. Poststernotomy pain: a clinical review. J Cardiothorac Vasc Anesth 2011;25:1163-78.
11. Cogan J. Pain management after cardiac surgery. Semin Cardiothorac Vasc Anesth 2010 Sep;14(3):201-4.
12. Clegg-Lamptey JNA, Hodasi WM. An audit of aspects of informed consent and pain relief in general surgical units of Korle-Bu teaching hospital. Ghana Med J 2005;39(2):63-7.
13. Dahl JL, Gordon D, Ward S, Skemp M, Wochos S, Schurr M. Institutionalizing pain management: the Post-operative Pain Management Quality Improvement Project. J Pain 2003;4(7):361-71.
14. Manias E, Botti M, Bucknall T. Patients' decision-making strategies for managing postoperative pain. J Pain 2006; 7(6):428-37.
15. Qu S, Sherwood GD, McNeill JA, Zheng L. Postoperative pain management outcome in Chinese inpatients. West J Nurs Res 2008;30(8):975-90.
16. Málek J, Ševčík P, Bejšovec D, Gabrhelík T, Hnilicová M, Křikava I, et al. Postoperative pain management. 3rd ed. Praha: Mladá fronta a. s., Mezi Vodami 1952/9; 2017.
17. Carr ECJ. Refusing analgesics: using continuous improvement to improve pain management on a surgical ward. J Clin Nurs 2002;11(6):743-52.
18. Mac Lellan K. Management of pain: a practical approach for health care professional. Nelson Thomes; 2006.
19. Manias E, Botti M, Bucknall T. Observation of pain assessment and management – the complexities of clinical practice. J Clini Nurs 2002;11(6):724-33.
20. Rejeh N, Ahmadi F, Mohammadi E, Kazemnejad A, Anoosheh M. Nurses' experiences and perceptions of influencing barriers to postoperative pain management. Scand J Caring Sci 2009;23(2):274-81.
21. Coulling S. Nurses' and doctors' knowledge of pain after surgery. Nurs Stand 2005;19(34):41-9.
22. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg 1993;77:1048-56.
23. Dahl JB, Rosenberg J, Dirkes WE, Mogensen T, Kehlet H. Prevention of postoperative pain by balanced analgesia. Br J Anaesth 1990;64:518-20.
24. Senturk M. Acute and chronic pain after thoracotomies. Curr Opin Anaesthesiol 2005 Feb;18(1):1-4.
25. Gjeilo KH, Klepstad P, Wahba A, Lydersen S, Stenseth R. Chronic pain after cardiac surgery: a prospective study. Acta Anaesthesiol Scand 2010;54(1):70-8.
26. Guimaraes-Pereira L, Farinha F, Azevedo L, Abelha F, Castro-Lopes J. Persistent Postoperative Pain after Cardiac Surgery: Incidence, Characterization, Associated Factors and its impact in Quality of Life. Eur J Pain 2016 Oct;20(9): 1433-42.
27. Lee W, Yan YY, Jensen MP, Shun S-Ch, Lin Y-K, Tsai T-P, et al. Predictors and patterns of chronic pain three months after cardiac surgery in Taiwan. Pain Med 2010; 11(12):1849-58.
28. Choinière M, Watt-Watson J, Charles J, Baskett RJF, Bussières JS, Carrier M, et al. Prevalence of and risk factors for persistent postoperative nonanginal pain after cardiac surgery: a 2-year prospective multicentre study. CMAJ 2014; Apr 15;186(7):E213-23.
29. van Gulik L, Janssen LI, Ahlers SJ, Bruins P, Driessen AHG, van Boven WJ, et al. Risk factors for chronic thoracic pain after cardiac surgery via sternotomy. Eur J Cardiothorac Surg 2011;40(6):1309-13.
30. Rafiq S, Steinbrüchel DA, Wanscher MJ, Andersen LW, Navne A, Lilleoer NB, et al. Multimodal analgesia versus traditional opiate based analgesia after cardiac surgery, a randomized controlled trial. J Cardiothorac Surg 2014 Mar 20;9:52.
31. Fortier S, Hanna HA, Bernard A, Girard C. Comparison between systemic analgesia, continuous wound catheter analgesia and continuous thoracic paravertebral block: a randomised, controlled trial of postthoracotomy pain management. Eur J Anaesthesiol 2012 Nov;29(11):524-30.
32. Adrejaitienė J. Pooperacinio skausmo malšinimo aktualijos širdies chirurgijoje. (New trends in the treatment of postoperative pain in cardiac surgery.) Lietuvos chirurgija (Lithuanian Surgery) 2010;8(1):6-22.
33. Senturk M, Ozcan PE, Talu GK, Kiyan E, Camci E, Ozyalcin S, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. Anesth Analg 2002 Jan;94(1):11-5.
34. Reuben SS, Buvanendran A. Preventing the development of chronic pain after orthopaedic surgery with preventive multimodal analgesic techniques. J Bone Joint Surg Am 2007 Jun;89(6):1343-58.

Received May 2020
Accepted June 2020