Submitted: 24 March, 2021 Accepted: 12 April, 2021 Published: 08 November, 2021 DOI:10.22514/sv.2021.102

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ORIGINAL RESEARCH

Postoperative chronic pain incidence and etiology in coronary artery bypass graft surgery: a prospective study

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Abstract

Introduction: Post-operative chronic pain (POCP), after updated by Werner-Kongsgaard, is defined as the pain developed after the surgical procedure or increased in intensity after the procedure, as the continuation of acute postoperative pain, localized in the surgical area, lasted at least 3 months, and other causes of pain excluded. In our study, we aimed to prospectively examine the prevalence of POCP and risk factors in the first three months after coronary artery bypass graft surgery (CABGS).
Methods: Between June 2019 and December 2020, a numerical rating scale (NRS) was announced by the study team to evaluate the preoperative pain levels of patients undergoing CABGS in a university hospital. When patients came for the control on the 15th postoperative day, physical examinations were performed, pain status was evaluated, and followed up by phone for three months (30, 60 and 90 days postoperatively). The study, which started with 158 patients, was completed with 110 patients.
Results: The patients were divided into two groups as the patients with pain (those with POCP) and the painless group (those without POCP). While there were 39 patients (35.5%) in the group of patients with pain, 71 patients (64.5%) were in the painless group. The proportion of female patients in the group of patients with pain was significantly higher than the painless group ($p < 0.05$).
Conclusions: As a result of our study, postoperative chronic pain is seen in one of every three patients after cardiac surgery. We observed that the risk increased in female patients and in patients with severe preoperative anxiety.

Keywords

Coronary artery bypass surgery; Postoperative chronic pain; Cardiac surgery

1. Introduction

Post-operative chronic pain (POCP), after updated by Werner-Kongsgaard, is defined as the pain developed after the surgical procedure or increased in intensity after the procedure, as the continuation of acute postoperative pain, localized in the surgical area, lasted at least 3 months, and other causes of pain (for example, in infection or ongoing malignancy in oncological surgery) is excluded [1]. While the cause of POCP remains uncertain, it is thought that it may be caused by neuropathic pain, visceral pain, somatic pain or mixed pain [2].

It has been suggested that factors including surgical factors such as surgery type, incision type, duration of operation, use of electrocautery, patient age, gender, weight, genetic characteristics, presence of some systemic diseases, socioeconomic status, psychological factors, unable to provide effective analgesia in the postoperative period and opioids being preferred in the treatment may cause POCP, but its etiology is still not fully known [2–5].

After open heart surgery (OHS), POCP may be caused by thoracic pain at the sternotomy site or leg pain due to saphenous graft removal. However, myocardial ischemia, sternal instability and mediastinitis are important differential diagnoses [6]. The prevalence of POCP after OHS varies widely in different populations such that the observed numbers range from 11% to 56%. In addition, the number of patients reporting severe pain is quite consistently less than 10% [5, 7].

POCP has serious economic costs besides reducing the physical and mental functions of the patient. In a study by Guertin *et al*. [8], it was observed that the cost to the patient peaked one year after surgery in patients with POCP after OHS. The reason for this was the loss of work in the patient and the time allocated for receiving and providing care. Considering the incidence of POCP up to 56%, it will be understood that it may cause serious economic burden.

POCP continues to be an underrecognized complication. Despite the scientific advances made in the field of pain pathophysiology and treatment, patients still suffer long-term pain after surgery. In our study, we aimed to prospectively examine the prevalence of POCP and risk factors in the first three months after coronary artery bypass graft surgery (CABGS).

2. Materials and methods

After approval of the ethics committee (B.08.06. YOK 2.I.U.E 50.0.00/14), the numerical rating scale (NRS) was explained to patients undergoing CABGS between June 2019 and December 2020 in a university hospital by the study team to evaluate their pain levels before surgery. NRS is a pain rating scale that evaluates pain according to between 0 and 10 points. Zero means no pain and 10 means maximum pain. The patient demographic information, physical characteristics, addiction status, previous diseases, medications used and psychological characteristics included in the form we prepared were recorded before the surgery. In the anesthesia planning of our institution, the patients who were planned to have open heart surgery, vascular access was established with a 20 G cannula half an hour before being taken to the operating room, 0.03 mg/kg midazolam (IV) was administered as premedication and then taken to the operating table. Standard anesthesia induction is applied to all patients with the IV administration of midazolam 0.2 mg/kg, fentanyl 10 μg/kg, rocuronium 1 mg/kg. Total intravenous anesthesia was applied with propofol 25–40 μg/kg/min, fentanyl 4 μg/kg/hour and rocuronium 10 mg/hour infusion for anesthesia maintenance.

In our study, all patients were operated using conventional on-pump coronary artery bypass method. Median sternotomy was performed in all patients by the surgical team. All patients were taken to the postoperative intensive care unit after surgery. Postoperative multimodal analgesia protocol was applied. In the postoperative analgesia treatment, all patients were administered intravenous 100 mg tramadol and 1000 mg paracetamol 4 times a day for three postoperative days. Pain treatment was applied by oral paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) administration for three to seven days postoperatively and at discharge.

Information about the surgery, surgical features and the anesthesia method applied, sedative and anesthetic drugs used during the surgery, the methods applied for pain treatment, the complications arose during the surgery and the patient's postoperative early pain status were recorded in the form documents by the anesthesiologist. When the patients came for control on the 15th postoperative day, they were physically examined, their pain status was evaluated, and they were followed up with a phone call for three months (30, 60, and 90 days after surgery). The phone call was made by a physician working in another department of the university and NRS was evaluated. According to NRS, pain scores were grouped in three severity as painless (NRS = 0), mild (NRS = 1–3), moderate pain (NRS = 4–6) and severe pain (NRS = 7–10). Pain is defined as persistent postoperative pain if it meets the following three criteria: (1) first occurrence after surgery, (2) pain felt before surgery (e.g., Angina pain) or not related to other causes (e.g., Infection), and (3) pain was felt at least for 3 months. Patients who met all three criteria were asked to rate the intensity of their average pain in the last seven days using the NRS.

2.1 Inclusion criteria

Participants met all participation criteria.

(1) Being over the age of 18 years.

(2) Undergoing CABGS through median sternotomy.

(3) Signing the informed consent form.

(4) To be at a cognitive level to understand and answer the questions in the questionnaire form.

2.2 Exclusion criteria

Patients meeting any of the following criteria were excluded.

(1) Undergoing heart valve surgery, combined cardiac and non-cardiac surgery

(2) Patients underwent emergency surgery.

(3) Pregnancy.

(4) Not being at a cognitive level to understand and answer the questions in the prepared questionnaire.

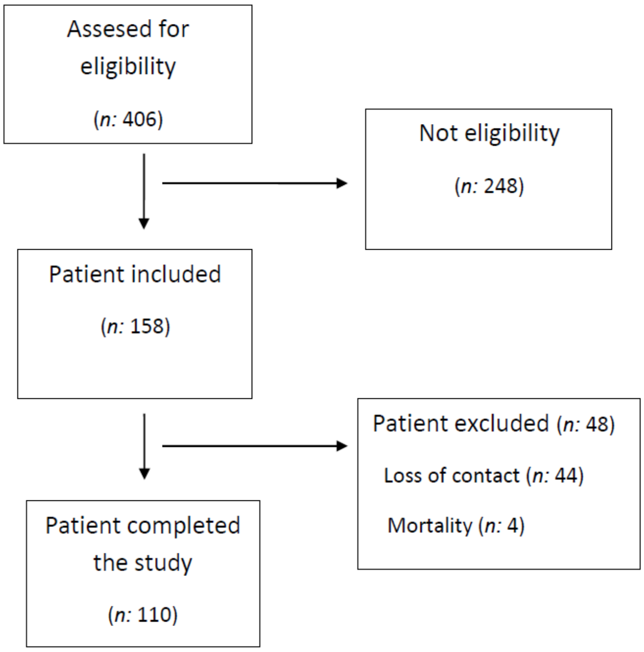

FIGURE 1. Flow chart of the cohort.

2.3 Statistical analysis

Mean, standard deviation, median, lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov-Smirnov Test. Mann-Whitney U Test was used to analyze quantitative independent data. Chi-Square Test was used in the analysis of qualitative independent data, and Fischer Test was used when the conditions were not met. SPSS 27.0 program was used in the analyses.

TABLE 1. Comparison of demographic data between groups.

		Painless group			Group of patients with pain			p
		Mean ± SD/n-%		Median	Mean ± SD/n-%		Median	
Age		61.4 ± 9.6		60	60.2 ± 11.8		64	0.597^{m}
Gender	Male	59	83.1%		17	43.6%		**0.000^{X^2}**
	Female	12	16.9%		22	56.4%		
BMI		27.7 ± 3.0		27	27.7 ± 2.9		27.7	0.490^{m}
Living with	Family	66	93.0%		35	89.7%		0.556^{X^2}
	Alone	5	7.0%		4	10.30%		
Socioecomonic status	Poor	1	1.4%		3	7.7%		0.900^{X^2}
	Fair	12	16.9%		3	7.7%		
	Good	58	81.7%		31	79.5%		
	Very good	0	0.0%		2	5.1%		
Social support	Forlorn	0	0.0%		1	2.6%		0.355^{X^2}
	Usual	71	100.0%		38	97.4%		
Smoking status	No	22	31.0%		20	51.3%		**0.036^{m}**
	Yes	49	69.0%		19	48.7%		
Cigarette pack/year		28.1 ± 17.2		30	25.9 ± 162		27.5	0.919^{X^2}
Alcohol use	Never	52	73.2%		34	87.2%		0.238^{X^2}
	Occasionally	8	11.3%		2	5.1%		
	Addicted	11	15.5%		3	7.7%		
Drug use	No	71	100.0%		39	100.0%		1.000^{X^2}
	Yes	0	0.0%		0	0.0%		
Systemic disease	No	19	26.8%		13	33.3%		0.468^{X^2}
	Yes	52	73.2%		26	66.7%		
Diabetes mellitus		28	39.4%		18	46.2%		0.494^{X^2}
Hypertension		43	60.6%		21	53.8%		0.494^{X^2}
Other systemic diseases		18	25.4%		11	28.2%		0.745^{X^2}
Use of analgesic	Never	40	56.3%		18	46.2%		0.306^{X^2}
	Occasionally	4	5.6%		1	2.6%		
	Always	27	38.0%		20	51.3%		
Use of antipsychotics	Never	68	95.8%		39	100.0%		0.551^{X^2}
	Occasionally	1	1.4%		0	0.0%		
	Always	2	2.8%		0	0.0%		
Use of antidepressants	Never	64	90.1%		34	87.2%		0.634^{X^2}
	Occasionally	2	2.8%		2	5.1%		
	Always	5	7.0%		3	7.7%		
Congenital anomaly	No	71	100.0%		39	100.0%		1.000^{X^2}

BMI, Body massindex; ^{m} Mann-Whitney U test/ $^{X^2}$ Chi-Square test.

3. Results

A total of 158 patients who underwent CABGS operation in our study. As 44 patients could not be reached postoperatively and four patients died in the postoperative period, they were excluded from the study (Fig. 1). The study continued with a total of 110 patients. Of all patients 76 (69.1%) patients were male. The ages of the patients varied between 40 and 81 (mean = 61.0 ± 10.4). Body mass index (BMI) of the patients was 27.7 ± 2.9 kg/m^2. The patients mostly lived with their families (91.8%). While most patients' socioeconomic status was good (89%), only one of our patients was homeless and receiving social support. None of our patients had congenital anomalies.

While the smoking rate was 61.8%, the average amount of use was 27.5 ± 16.8 pack/year. While 86 (78.2%) patients did not use alcohol, 10 (9.1%) patients occasionally consumed alcohol, and 14 (12.7%) patients were alcohol addicts. We had

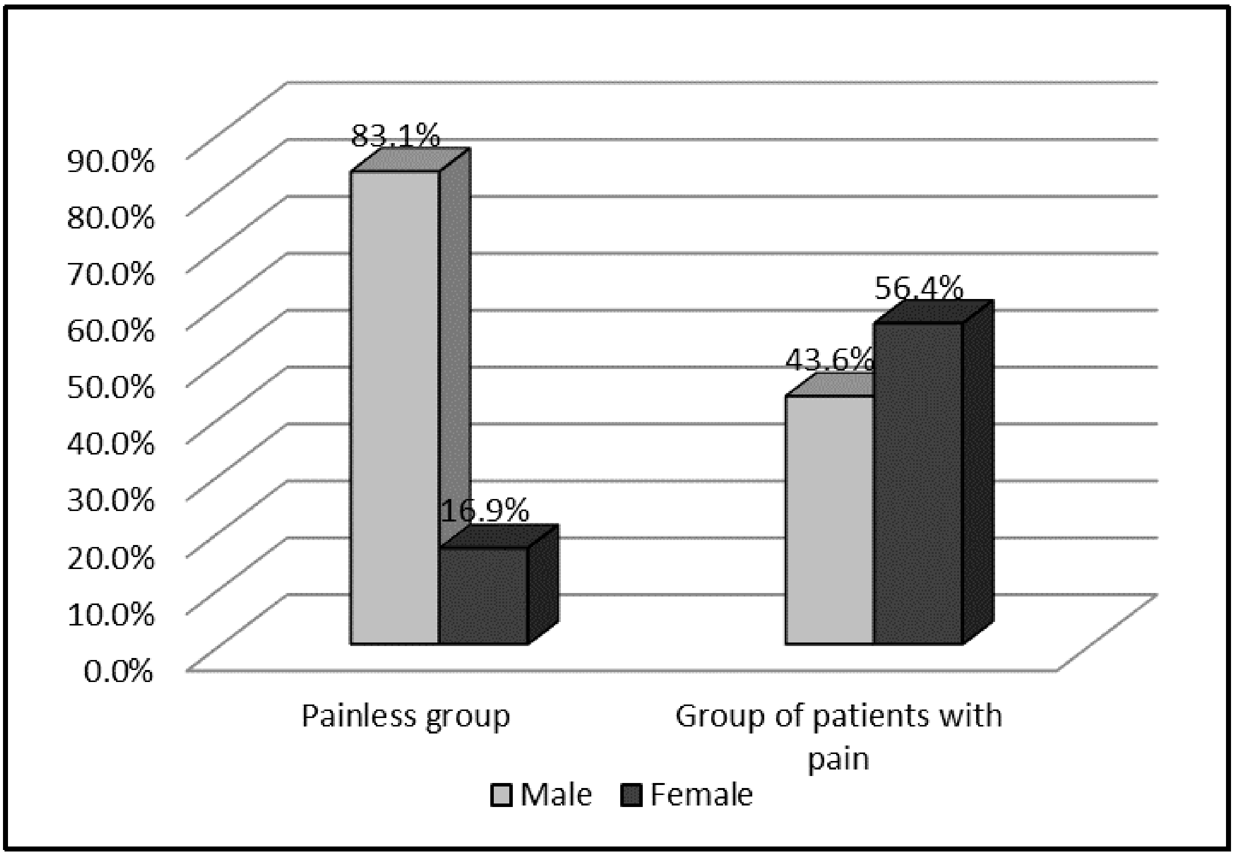

FIGURE 2. Gender relationship between groups.

no patients using drugs. Diabetes (41.8%) and hypertension (58.2%) were the most common systemic diseases. Our mean duration of operation was 4.8 ± 0.8 hours. While 52.7% of the patients had no history of preoperative analgesic drug use, 4.5% were using analgesic drugs in the occasionally and 42.7% were using analgesic drugs continuously. In the preoperative use of antidepressants, four patients (3.6%) stated that they used antidepressants occasionally, while eight patients (7.3%) were using antidepressants continuously.

The patients were divided into two groups as the patients with pain (those with POCP) and the painless group (those without POCP). While there were 39 patients (35.5%) in the group of patients with pain, 71 patients (64.5%) were in the painless group. In the NSR query of those with pain, 33 (84.6%) patients had mild pain, five (12.8%) patients had moderate pain, and only one (1.6%) patient had severe pain. There was no significant difference between the ages and BMI values of the group of patients with pain and painless groups in the intergroup evaluation of demographic data ($p > 0.05$). The proportion of female patients in the group of patients with pain was significantly higher than the painless group ($p < 0.05$; Table 1; Fig. 2).

Remarkably, the rate of smoking was significantly lower in the group of patients with pain than in the painless group ($p < 0.05$). The amount of cigarette consumption, alcohol and drug use rates were similar between the groups ($p > 0.05$). There was no significant difference between the rates of diabetes, hypertension and other systemic diseases in both groups ($p > 0.05$). In addition, the rate of living alone, socioeconomic status, social support rate, analgesic, antipsychotic and antidepressant usage rate did not differ between the groups ($p > 0.05$; Table 1).

While the total number of bypass grafts were significantly higher in the painless group ($p = 0.02$), operation times were similar between groups ($p = 0.243$). No relationship was found between the use of internal mammary artery during CABGS and chronic pain ($p = 0.895$). Preoperative pain and preoperative pain disease rates were similar between groups ($p > 0.05$). Preoperative anxiety rate was significantly higher in the group of patients with pain compared to the painless group ($p < 0.05$; Table 2; Fig. 3).

Although it was not our primary goal, further analysis was made due to the curiosity of the stress factors associated with COVID-19 pandemic on psychology and pain perception. No statistically significant relationship was found between the chronic pain rates and preoperative anxiety levels of 54 patients before the pandemic and 26 patients (before and after 10 March 2020) ($p > 0.05$) (Table 3).

4. Discussion

CABGS is a pain-sensitive operation as it requires interventions such as a median sternotomy, intervention of intrathoracic muscles and organs, and saphenous vein graft removal. Although the cause of POCP after CABGS is not known exactly, it may be due to the manipulation and retraction of the sternum, as well as the use of electrocautery to separate the internal mammary artery (IMA) from the chest wall, and consequently, nerve damage that leads to intercostal neuralgia [9].

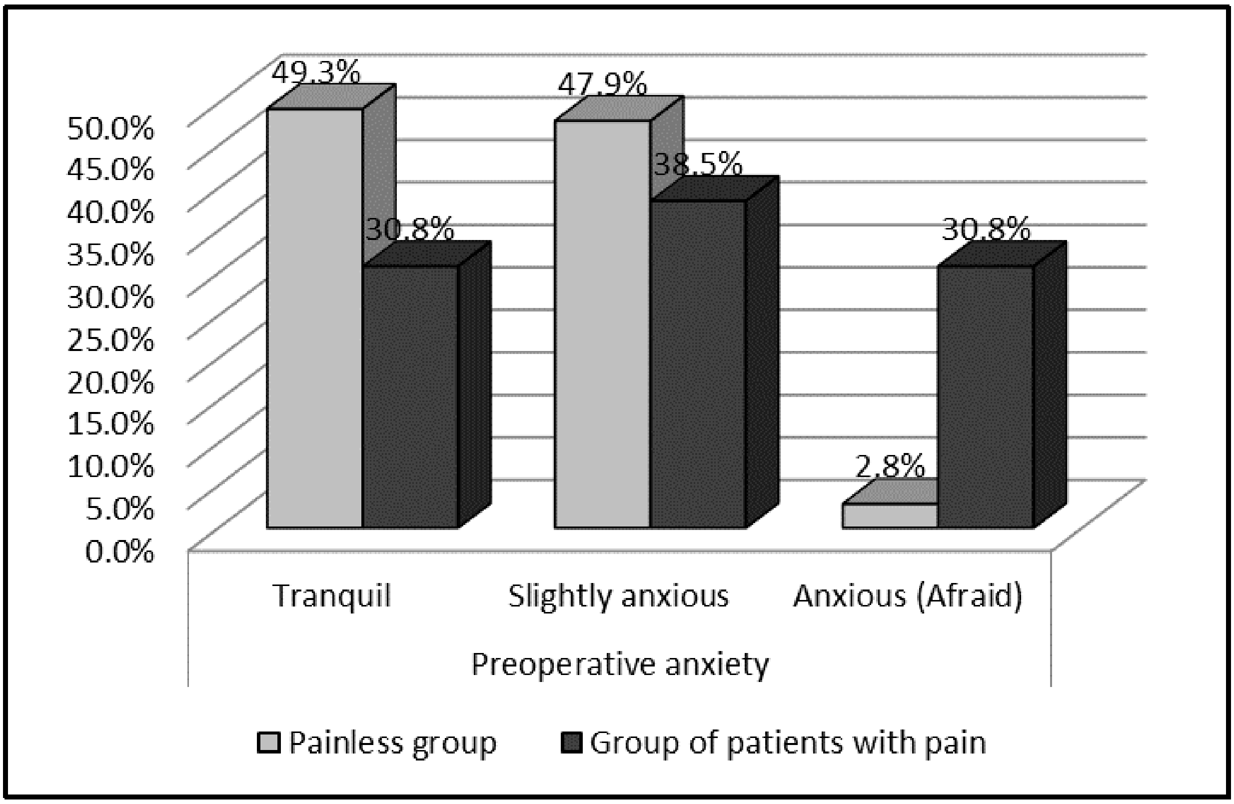

FIGURE 3. Comparison of preoperative anxiety levels between groups.

TABLE 2. Comparison of anxiety levels and preoperative pain between groups.

		Painless group			Group of patients with pain			p
		Mean ± SD/n-%		Median	Mean ± SD/n-%		Median	
History of surgery	No	31	43.7%		23	59.0%		0.124^{X^2}
	Yes	40	56.3%		16	41.0%		
Operation time		4.9 ± 0.8		5.0	4.6 ± 0.7		4.9	0.243^{m}
Total number of bypass greft		2.9 ± 1.0		3.0	2.4 ± 0.7		3.0	0.02^{m}
IMA use	No	16	22.5%		10	25.6%		0.895^{X^2}
	Yes	55	77.5%		29	74.4%		
Preoperative pain	No	52	73.2%		28	71.8%		0.871^{X^2}
	Yes	19	26.8%		11	28.2%		
Preoperative painful disease	No	63	88.7%		39	97.4%		0.111^{X^2}
	Yes	8	11.3%		0	0.0%		
Preoperative anxiety	Tranquil	35	49.3%		12	30.8%		0.000^{X^2}
	Slightly anxious	34	47.9%		15	38.5%		
	Anxious (Afraid)	2	2.8%		12	30.8%		

^{m} Mann-Whitney U test/ $^{X^2}$ Chi-Square test.
IMA, Internal mammary artery.

In a study conducted by Meyerson *et al.*, in patients who underwent OHS in 2001, it was observed that 28% of patients who underwent sternotomy had POCP in the surgical area. They reported that 13% of these patients experienced moderate pain and 4% severe pain [10]. In more recent studies on POCP after OHC, the POCP rate ranged from 16% to 44% [11–13]. It is noteworthy that despite the scientific advances in the last 20 years, POCP rates have not changed. Our POCP rate after CABGS was 35%. While most of our patients with POCP had mild pain, 12.8% had moderate and 1.6% had severe pain. In our study, our POCP rates were close to the average values of similar studies, but unlike most studies, the rate of severe pain was lower. In the study of Choinière *et al.* [12], in which longer-term follow-up of POCP was performed, they reported that the prevalence rates of POCP at three, six and 12 months following cardiac surgery were 40%, 22% and 17%,

TABLE 3. The effect of the pandemic on chronic pain and preoperative anxiety.

		Pre-pandemic CABGS		Post-pandemic CABGS		*p*
		n	%	n	%	
Preoperative anxiety	Tranquil	35	43.8%	12	40.0%	0.939^{X^2}
	Slightly anxious	35	43.8%	14	46.7%	
	Anxious (Afraid)	10	12.5%	4	13.3%	
POCP	No	54	67.5%	17	56.7%	0.290^{X^2}
	Yes	26	32.5%	13	43.3%	

POCP, Postoperative chronic pain; CABGS, Coronary artery bypass graft surgery; $^{X^2}$ *Chi-Square test.*

respectively. Gjeilo *et al*. [14] showed that the prevalence of POCP was 11% at 12 months and 3.8% at five years. This study showed that POCP decreased over time, but it could still continue for a long period of five years.

The relationship between POCP and demographic data is contradictory in studies. In the study of Choinière *et al*. [12], younger age was reported to be a risk factor for POCP development. Apart from this, many studies have not found a relationship between POCP and age [7, 15]. In our study, we did not find a significant relationship between age and acc. While a positive relationship was found between body mass index (BMI) and POCP in the study of Van Gulik *et al*. [7], most studies did not find a relationship between BMI and POCP [7, 14]. Similar to these studies, we found no relationship between BMI and POCP in our study. Again, as in similar studies, systemic diseases had no effect on POCP [9]. Although the specific etiological basis underlying gender differences is unknown, it has emerged that hormonal and genetic factors contribute, but more studies are needed on the underlying mechanisms. In the study of Gerbersen *et al*. [16], it was observed that women reported similarly higher POCP in different types of surgery. In another study, authors found that, for each of their different anatomical regions, more women than men reported pain, and women had significantly higher complaints of common chronic pain [17]. This is similar in CABGS. In a study where Routledge *et al*. [18], they examined POCP after CABGS and they found that POCP, which can last up to one year, is more in female patients compared to men. In our study, parallel to these studies, the rate of POCP in female patients was higher than in male patients.

The ability of preoperative non-anginal pain to predict subsequent pain has a significant impact on patients' POCP risk. The reason for this may be related to the person's perception of pain. In our study, we found no significant difference in the POCP rate in patients with preoperative pain. Van Gulik *et al*. [7] found a serious relationship between postoperative acute postoperative pain intensity and POCP. For this reason, attempts to reduce acute pain are important in preventing POCP after OHS. After cardiac surgery, evidence to support any prophylactic analgesic regimen is either lacking or limited. We applied a standard analgesia regimen consisting of paracetamol and opioid to all patients in the early postoperative period and afterwards. We wanted to reduce acute pain as much as possible and to have minimal effect on chronic pain.

Unlike most surgeries, patients who will undergo cardiac surgery will undergo surgery with a serious fear of death. This is due to both the context of the surgery and the implications that society places on heart diseases. It has been shown that the relation of pre-operatively increased anxiety with POCP is an important risk factor independent of its effect on acute postoperative pain [12]. In our study, when preoperative anxiety was questioned, the POCP rates of patients who stated that they had a high anxiety rate, namely 'fear', were significantly higher than those without chronic pain. While this result supports other studies, it also shows how important the elimination of preoperative anxiety is also in preventing POCP.

Not only in the preoperative state of anxiety, but many patients suffering postoperative pain may feel that something is wrong or the surgeon has made a mistake. Actually, this is not the case, educating patients and doctors about the POCP problem will help in solving the problems. Patients with POCP have more behavioral disorders, distress, poor response to treatments, and doubt about the success of future treatments.

In a study in women who had breast cancer surgery, Tasmuth and colleagues found increased levels of anxiety and depression before surgery compared to healthy women. While anxiety levels returned to normal in all patients one year after surgery, depression remained at a higher level in those with chronic pain [19]. This study shows that anxiety and depression can be both a triggering cause of POCP and a result of POCP.

Another finding that attracted our attention in our study was that the chronic pain rates of smokers were significantly lower than those who did not. Although it is now known that smoking has serious fatal damages, it has been observed that nicotine exerts analgesic effects through one or more nicotinic acetylcholine receptor (nAChR) subtypes in some experimental studies with animals and humans [20–23]. However, the clinical studies examined show that the effects of smoking on chronic pain are not clear. In addition to studies showing that the frequency of chronic painful conditions has increased in smokers, different studies show that among those with chronic pain, smokers complain of greater pain intensity and an increasing number of painful areas [24]. Some studies state that there is no relationship between chronic pain and smoking [25].

Besides the etiology of POCP, treatments for prevention remain unclear. Although the use of gabapentin and pregabalin is prominent in pharmacological studies aimed at preventing limited numbers of POCP, the results are contradictory, and intraoperative ketamine use is promising. Although it is not clear that nerve damage was the cause of chronic pain, nerve-sparing surgical techniques were tried [26, 27]. Future studies are needed to prevent POCP.

While our study was at the data collection stage, the COVID-19 pandemic that affected the whole world occurred. After the appearance of the first cases of COVID-19 on 10 March 2020 in Turkey, there was no significant difference between patients undergoing OHC before the pandemic and after the pandemic when we evaluated preoperative anxiety levels and POCP rates of the preoperative anxiety levels. In Italy, where the course of the pandemic is intense, high preoperative anxiety levels were found in non-emergency neurosurgery patients during the COVID-19 pandemic [28]. This difference may be due to geographic location or different types of operations. Therefore, more studies are needed on this topic.

5. Limitations

While many prospective studies on POCP after CABGS are not present in the literature, the prospective nature of our study is a valuable contribution for the literature. Neurophysiological examinations and quantitative sensory tests could not be performed to evaluate the presence of sensory abnormalities (e.g., hyperesthesia, hypoesthesia) in the operation area in the preoperative and postoperative period. The pain levels of the patients were determined through the verbal evaluation test subjectively. Another limitation of our study is that since the patients were evaluated for a period of three months, although we have detected the occurrence of POCP, we could not track how long the POCP lasted.

6. Conclusions

As a result of our study, postoperative chronic pain is seen in one of every three patients after cardiac surgery. We observed that the risk increased in female patients and in patients with severe preoperative anxiety. Although POCP significantly reduces the comfort of life physically, psychologically and economically, sufficient effort is not made to prevent or treat it. In the future, we recommend that more comprehensive studies be conducted with POCP after CABGS.

AUTHOR CONTRIBUTIONS

HYA, YO searched the literature and prepared the methodology. In the preoperative period, YO, MAY, AFP, AOY provided the evaluation of the patients and the filling of the prepared forms. AOY and IH examined the patients in the postoperative period and were called by phone. AFP and MAY made the statistical analysis of the data. HYA and APS contributed to the writing of the article. All authors read and approved the final version of the article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the Istanbul University-Cerrahpasa Ethical committee (B.08.06. YOK 2.I.U.E 50.0.00/14).

ACKNOWLEDGMENT

Thanks to Nancy Anderson for her contribution to the translation of our article.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Hulya Yilmaz Ak, Yasemin Ozsahin, Mehmet Ali Yesiltas, Ismail Haberal, Ahmet Ozan Koyuncu, Ali Ferit Pekel, *et al*. Postoperative chronic pain incidence and etiology in coronary artery bypass graft surgery: a prospective study. Signa Vitae. 2021;17(6):82-89. doi:10.22514/sv.2021.102.