

Risk Factors of Chronic Postoperative Pain After Inguinal Hernia Repair and the Relationship Between Preoperative Depression-Anxiety: Observational Study

İnguinal Herni Onarımı Sonrası Kronik Postoperatif Ağrının Risk Faktörleri ve Preoperatif Depresyon-Anksiyete İlişkisi: Gözlemsel Çalışma

^{id} Derya BAYRAM^a, ^{id} Dostali ALİYEYEV^b, ^{id} İbrahim AŞIK^c

^aMardin Training and Research Hospital, Clinic of Neurology, Mardin, Türkiye

^bTOBB University of Economics and Technology Faculty of Medicine Hospital, Department of Anesthesiology and Reanimation, Ankara, Türkiye

^cAnkara University Faculty of Medicine İbn-i Sina Hospital, Department of Anesthesiology and Reanimation, Division of Algology, Ankara, Türkiye

ABSTRACT Objective: To determine the incidence and risk factors associated with chronic postoperative pain after inguinal hernia repair and to observe the relationship between preoperative depression/anxiety and chronic postoperative pain. **Material and Methods:** Between June 2021 and December 2022, two hundred and sixty patients who underwent inguinal hernia repair were enrolled in the study. Preoperative chronic pain and chronic postoperative pain were assessed with visual analogue scale, and the patients' results were recorded in the third and sixth months. Depression and anxiety assessments were made using the Beck Depression and Beck Anxiety Inventory before the operation. Preoperative, intraoperative, and postoperative details were recorded and the relationship with chronic postoperative pain was statistically analysed. **Results:** Pain persisted in 22.3% of the patients at the postoperative 3rd month and 12.3% of the patients at the 6th month. Preoperative pain was present in 56.53% of the patients, and chronic pain developed in 39.4%. A statistically significant relationship was found between preoperative chronic pain, postoperative analgesic use, duration of pain, female gender, reoperation, postoperative complication, and chronic postoperative pain ($p<0.001$). Chronic postoperative pain developed in 21 of 24 patients who underwent recurrent operations. The pain was in neuropathic character in 53.4% of the patients. A significant correlation was observed between preoperative anxiety/depression and chronic pain ($p<0.001$). **Conclusion:** Preoperative pain, the severity of postoperative acute pain, and reoperation should be questioned preoperatively, and adequate pain palliation should be provided to prevent chronic postoperative pain. In addition, the psychological state significantly affects the development of chronic postoperative pain.

ÖZET Amaç: Amaç, inguinal herni onarımı sonrası postoperatif kronik ağrı ile ilişkili insidans ve risk faktörlerini belirlemek ve preoperatif depresyon/anksiyete ile postoperatif kronik ağrı arasındaki ilişkiyi incelemektir. **Gereç ve Yöntemler:** Haziran 2021-Aralık 2022 tarihleri arasında inguinal herni onarımı yapılan 260 hasta çalışmaya alındı. Preoperatif kronik ağrı ve postoperatif kronik ağrı görsel analog skala skoru değerlendirildi ve hastaların operasyon sonrası 3 ve 6. aylardaki sonuçları kaydedildi. Ameliyat öncesi depresyon ve anksiyete değerlendirmeleri Beck Depresyon Envanteri ve Beck Anksiyete Envanteri kullanılarak yapıldı. Ameliyat öncesi, ameliyat sonrası ve ameliyat sonrası detaylar kaydedildi ve kronik postoperatif ağrı ile ilişkisi istatistiksel olarak analiz edildi. **Bulgular:** Postoperatif 3. ayda hastaların %22,3'ünde, 6. ayda ise hastaların %12,3'ünde ağrı devam etti. Hastaların %56,53'ünde preoperatif ağrı mevcuttu ve bu hastaların %39,4'ünde kronik ağrı gelişti. Preoperatif kronik ağrı, postoperatif analjezik kullanımı, ağrı süresi, kadın cinsiyet, reoperasyon, postoperatif komplikasyon ve postoperatif kronik ağrı arasında istatistiksel olarak anlamlı bir ilişki bulundu ($p<0,001$). Rekürren operasyon geçiren 24 hastanın 21'inde postoperatif kronik ağrı gelişti. Hastaların %53,4'ünde ağrı nöropatik karakterdeydi. Ameliyat öncesi anksiyete/depresyon ile kronik ağrı arasında anlamlı bir ilişki gözlemlendi ($p<0,001$). **Sonuç:** Preoperatif ağrı, postoperatif akut ağrının şiddeti ve reoperasyon preoperatif dönemde sorgulanmalı ve postoperatif kronik ağrıyı önlemek için yeterli ağrı palyasyonu sağlanmalıdır. Ek olarak, preoperatif psikolojik durum postoperatif kronik ağrı gelişiminde önemli bir etkiye sahiptir.

Keywords: Hernia; inguinal; postoperative pain; depression; anxiety

Anahtar Kelimeler: Herni; inguinal; postoperatif ağrı; depresyon; anksiyete

TO CITE THIS ARTICLE:

Bayram D, Aliyev D, Aşık İ. Risk factors of chronic postoperative pain after inguinal hernia repair and the relationship between preoperative depression-anxiety: Observational study. Türkiye Klinikleri J Med Sci. 2024;44(4):149-57.

Correspondence: Derya BAYRAM

Mardin Training and Research Hospital, Clinic of Neurology, Mardin, Türkiye
E-mail: deryak_30@hotmail.com



Peer review under responsibility of Türkiye Klinikleri Journal of Medical Sciences.

Received: 15 Mar 2024

Received in revised form: 24 Apr 2024

Accepted: 13 May 2024

Available online: 21 May 2024

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Chronic postoperative pain (CPP) is known as pain lasting longer than three months, associated with the surgical field, and impairing the quality of life despite the healing of the surgical wound.^{1,2} The incidence of CPP after inguinal hernia repair is 11% and it is reported to be moderate-to-severe at a rate of 6%.³ It limits activities of daily living, causes anxiety and depression, and increases the use of analgesics.⁴

While postsurgical pain is mostly considered to be neuropathic pain, nociceptive pain may be associated with inflammation, muscle or ligament strain, perineural fibrosis, mesh, or scar tissue around the fixation material. It was thought that especially changes in sensory processing might increase the risk of chronic pain in patients with preoperative chronic pain.⁵ In recent years, studies investigating the role of psychological factors, especially depression and anxiety in CPP have been published and reported that there were physiological similarities between chronic pain and depression.^{6,7}

The present study aimed to analyse the incidence of CPP, contributing risk factors in patients who underwent inguinal hernia surgery, and the relationship between preoperative depression/anxiety and CPP.

MATERIAL AND METHODS

This prospective, observational study was performed in accordance with the Helsinki Declaration criteria (2013), after the approval of the ethics committee of Ankara University Faculty of Medicine (date: June 17, 2021, no: I6-399-21). The patients (n=272) between the ages of 18 to 65 who underwent inguinal hernia repair between June 2021 and December 2022 were enrolled in the study. Since 12 patients did not respond at 6 months postoperatively, the study was continued with 260 patients. Written informed consent was obtained from each patient. The patients were informed about the visual analogue scale (VAS: 0=no pain, 10=severe pain) to evaluate the severity of pain before and after the operation at the 24th hours, 3rd months, and 6th months. Patients with alcohol dependence, previous

extensive lower abdominal surgery, impaired cognitive function, a history of malignancy, and radiotherapy were excluded from the study.

Demographic information and phone numbers of the patients were recorded. The smoking status, existing comorbid diseases, presence of preoperative pain, if any, severity, and duration of pain were noted. In addition, the type of inguinal hernia (direct/indirect/combo) and anesthesia (general, spinal, local), surgery (laparoscopic or open), and postoperative complication were recorded. The preoperative depression and anxiety status of the patients were evaluated with the Beck Depression and Anxiety Inventory, respectively, and the effects of preoperative anxiety and depression on postsurgical chronic pain were analysed.^{8,9} The items in the Beck Depression Inventory are mainly based on behaviours and symptoms specific to depression and are described in a series of sentences, and each sentence is numbered from 0 to 3. It consists of twenty-one items and the items are listed from mild to severe form. Beck Anxiety Inventory consists of 21 items, each describing a common symptom of anxiety. The patients are asked to rate how much they have been bothered by each symptom over the past week on a 4-point scale. Pain characterization was evaluated with Douleur Neuropathique 4 Questions (DN4).¹⁰ The questionnaire contains 7 items relating to symptoms (sensations of burning, electric shock, painful cold, tingling etc.) and 3 items relating to physical examination with each element scored as present (1) or absent (0). A score of at least 4/10 in this questionnaire was indicative of neuropathic pain.

Pain with a VAS score of ≥ 3 three months after surgery was considered chronic pain. In addition, the study examined the association between the number of comorbidities and development of chronic pain.

Patients underwent open anterior surgical repair or laparoscopic surgery with macroporous, monofilament polypropylene mesh of dimension 15 cm×10 cm or 11 cm×6 cm under general anesthesia or spinal anesthesia. Local anaesthetic infiltration was applied to some of the patients. In the postop-

erative period, the patients were followed up for the presence, severity, character, and localization of the pain. Neuropathic pain was caused by a primary lesion or disease in the peripheral or central somatosensory nervous systems and it has been described as a burning, stinging, throbbing, aching, etc. sensation. Somatic pain was carried along the sensory fibers which is usually discrete and intense.

Postoperative follow-up was done at the 24th hours, third and 6 months face-to-face at the hospital. If required, patients were given either peroral paracetamol or tramadol for pain management.

According to the result of chi-square test power analysis with 95% confidence (1- α), 85% test power (1- β), $w=0.185$ effect size, research should be conducted on 262 cases based on the study Karaman et al.⁴ Statistical analysis was performed using SPSS version 22.0 software (IBM, Chicago, Illinois, United States). Data were presented as mean \pm SD and minimum-maximum or number and percentage (n, %) as appropriate. The chi-square test was used

to analyse the categorical variables. Non-normally distributed continuous variables were displayed as median (interquartile range). Kruskal-Wallis and Mann-Whitney U test was used. Correlation coefficients and statistical significance for the relationships between variables were calculated with the Spearman correlation analysis. The level of statistical significance was accepted as $p<0.05$.

RESULTS

Analysis was performed on 260 patients who fully answered the questionnaire in the third and sixth months. Detailed demographic information is shown in Table 1.

The number of patients with $VAS\geq 3$ pain at the surgical site at 3 months postoperatively was 58 (22.3%). In the remaining patients, the pain was either absent or at a level that could not affect the quality of life. After 6 months of follow-up, 32 (12.3%) patients reported inguinal pain with an in-

TABLE 1: Patients characteristics by chronic pain.

		Total patients numbers	Chronic pain (in 3 rd months)	No chronic pain (in the 3 rd months)	p value
Total patients numbers (%)			58 (22.3)	202 (77.7)	
Age, year (%)	<40	28	10 (35.7)	18 (64.3)	0.091
	40-60	96	16 (16.7)	80 (83.3)	
	>60	136	32 (23.5)	104 (76.5)	
Sex (%)	Female	24	11 (45.8)	13 (54.2)	0.004
	Male	236	47 (19.9)	189 (80.1)	
Smoking status (%)	Current	73	16 (21.9)	57 (78.1)	0.941
	Never	146	32 (21.9)	114 (78.1)	
	Former	41	10 (24.4)	31 (75.6)	
ASA class (%)	1	168	34 (20.2)	134 (79.8)	0.251
	2	52	11 (21.2)	41 (78.8)	
	3	34	10 (29.4)	24 (70.6)	
	4	6	3 (50)	3 (50)	
Postoperative analgesia	Yes	140	57 (40.7)	83 (59.3)	<0.001
	No	120	1 (0.8)	119 (99.2)	
Other simultaneous operation	Yes	13	5 (38.5)	8 (61.5)	0.151
	No	247	53 (21.5)	194 (78.5)	
BMI (interquartile range)		25.7 (23.7-28.0)	25.7 (23.5-28.3)	25.7 (23.8-28.0)	0.874

ASA: The American Society of Anesthesiologists; BMI: Body mass index; Categorical data was shown as a number (percentage). Non-normally distributed continuous variables were displayed as median (interquartile range). $p<0.05$: significant (shown in bold).

tensity ranging from grades 3 to 6. The mean VAS value in the first 24 hours after surgery was 3.76 ± 1.12 in patients with CPP and 1.12 ± 1.27 in patients without chronic pain ($p < 0.05$). Preoperative pain was reported in 56.53% of the patients, and 39.4% of them developed chronic pain. In addition, a significant correlation was found between postoperative acute pain and CPP at the 3rd and 6th months (VAS24/VAS3 Correlation Coefficient: 0.765, $p < 0.001$ and VAS24/VAS6 Correlation Coefficient: 0.652, $p < 0.001$).

The mean Beck Depression Inventory score was 16.16 ± 7.15 and, Beck Anxiety Inventory score was 12.79 ± 6.85 . The results of the study revealed that there was a statistically significant correlation between preoperative depression/anxiety and CPP ($p = 0.022$ and $p = 0.034$ at 3rd months and $p < 0.001$ at 6th months, respectively) (Table 2). Chronic pain developed in 38 out of 120 patients with moderate-to-severe depression and in 28 out of 140 patients with moderate-to-severe anxiety.

Patients with hypertension, diabetes mellitus, hyperlipidaemia, coronary artery disease, chronic obstructive pulmonary disease, hypothyroidism, chronic renal failure were recorded to investigate the effect of patients' chronic diseases numbers on the development of chronic pain. The results revealed that the number of existing chronic diseases did not affect the development of chronic pain at 3rd and 6th months, as shown in Table 3.

Preoperative pain, duration of preoperative pain, female gender, the severity of postoperative pain, postoperative complications, and recurrent inguinal operations had significant effect on developing CPP (Table 1, Table 2, Table 4).

It was found that 21 out of 24 patients who underwent recurrent inguinal repair developed CPP, and this difference was statistically significant compared to patients who underwent surgery for the first time ($p < 0.001$). In addition, complications were also a significant risk factor for CPP ($p = 0.006$ and 0.001 , at 3rd and 6th months, respectively).

TABLE 2: Effect of preoperative factors on VAS scores at 24th hours, 3rd and 6th months.

Parameters	Postoperative VAS at 24 th hours		Postoperative VAS at 3 rd months		Postoperative VAS at 6 th months	
	Correlation coefficient	p value	Correlation coefficient	p value	Correlation coefficient	p value
VAS 0	0.941	<0.001	0.766	<0.001	0.648	<0.001
Duration of inguinal hernia	0.083	0.185	0.000	0.994	0.022	0.729
Duration of pain	0.703	<0.001	0.663	<0.001	0.566	<0.001
Beck Depression Inventory			0.300	0.022	0.427	<0.001
Beck Anxiety Inventory			0.278	0.034	0.514	<0.001
VAS at 24 th hours			0.765	<0.001	0.652	<0.001
VAS at 3 rd months					0.819	<0.001

VAS: Visual analogue scale; Spearman's correlation test was used; $p < 0.05$: significant (shown in bold).

TABLE 3: The effect of the number of existing diseases on chronic pain.

Number of patients' diseases (n)	VAS at 3 rd months	p value	VAS at 6 th months	p value
0 (119)	1 (0-2)		0 (0-2)	
1 (96)	1 (0-2)		0 (0-2)	
2 (32)	0 (0-2)	0.258	0 (0-1)	0.311
3 (12)	1 (0-2)		0 (0-2)	
4 (1)	3 (3-3)		3 (3-3)	

VAS: Visual analogue scale; Mann-Whitney U test was used, $p < 0.05$: significant.

TABLE 4: Effect of perioperative factors on VAS scores at 3rd and 6th months.

		Total patients	VAS at 3 rd months	p value	VAS at 6 th months	p value
Surgery	Laparoscopic	170	0.5 (0-2)	0.503	0 (0-2)	0.184
	Open	90	1 (0-2)		0 (0-2)	
Laterality	Unilateral	177	0 (0-2)	0.286	0 (0-2)	0.813
	Bilateral	83	1 (0-3)		0 (0-2)	
Anesthesia	General	229	1 (0-2)	0.305	0 (0-2)	0.487
	Spinal	31	2 (0-2)		0 (0-2)	
Postoperative local infiltration	No	111	1 (0-3)	0.688	0 (0-2)	0.352
	Yes	149	1 (0-2)		0 (0-2)	
Inguinal hernia	First repair	236	0 (0-2)	<0.001	0 (0-1)	<0.001
	Recurrence	24	3 (3-4)		3 (3-3)	
Mesh size	15 cmx10 cm	220	1 (0-2)	0.944	0 (0-2)	0.928
	11 cmx6 cm	40	0 (0-3)		0 (0-2)	
Hernia type	Direct	111	0 (0-2)	0.102	0 (0-1)	0.134
	Indirect	134	1 (0-3)		0 (0-2)	
	Direct+Indirect	15	2 (0-2)		2 (0-2)	
Postoperative complication	Yes	5	3 (2-4)	0.006	3 (2-3)	0.001
	No	255	1 (0-2)		0 (0-2)	

VAS: Visual analogue scale; Non-normally distributed continuous variables were displayed as median (interquartile range); Kruskal-Wallis and Mann-Whitney U test was used; p<0.05: significant (shown in bold).

Spinal anesthesia was applied to 11.9% of these patients, and general anesthesia was applied to 88.07%. There was no significant effect of anesthesia type on the development of CPP (p=0.487) as shown in Table 4.

Mesh was used in all patients and mesh size didn't affect the development of CPP. The most common mesh size was 15 cmx10 cm.

Thirty-one (53.4%) patients had neuropathic pain according to DN4 in the 3rd months. Among these, burning pain was reported by 16 patients (27.6%), stinging pain by 7 patients (12.1%), throbbing pain by 2 patients (3.4%), and stabbing pain by 6 patients (10.3%). Additionally, somatic pain was reported by 27 patients in the third months.

During the third month, 202 patients experienced mild preoperative pain, while 57 patients experienced moderate pain. By the sixth month, the number of patients with mild preoperative pain increased to 230, while 33 patients still experienced moderate pain.

DISCUSSION

In this study, we compared patients with and without CPP and found notable differences in some preoperative factors and postoperative outcomes between the two groups. The study revealed that the incidence of CPP was 22.3% in the third month after surgery, and it decreased to 12.30% in the sixth month. This suggests that a shorter follow-up period was associated with a higher rate of chronic pain, and that CPP spontaneously subsided over time. We observed that preoperative pain was recorded in 56.53% of the patients, and chronic pain developed in 39.4% of them. Based on the study, preoperative pain, duration of preoperative pain, female gender, the severity of postoperative pain, postoperative complications, and recurrent inguinal operations were all identified as risk factors for CPP. In addition psychological factors had a significant effect on the development of CPP after inguinal hernia repair.

Various studies have been conducted to investigate the risk factors associated with the develop-

ment of CPP after inguinal hernia surgery. According to Forester et al., some of the high-risk factors for CPP included younger age, female gender, use of multifilament polyester mesh, a history of recurrent inguinal hernia surgery on the same side, preoperative high pain intensity, higher American Society of Anesthesiologists class, and urinary catheter.¹¹ In contrast, our study found no correlation between age and the incidence of CPP, which is consistent with the findings of Manangi et al.¹² Furthermore, our study did not find any association between body mass index (BMI) and the development of chronic pain, although Karaman et al. reported a higher incidence of CPP in obese patients than in normal-weight patients.⁴ However, they did not find a statistically significant relationship between BMI and CPP.

Smoking showed no significant effect on the development of CPP in our study, whereas some studies have shown that changes in the neuronal level caused by smoking in the nervous system contribute to the development of CPP.¹³ These changes persist for a long time and predispose to the development of CPP more than active smokers.¹⁴

There are different surgical methods available for repairing inguinal hernias. These approaches include open repair using sutures or mesh, and laparoscopic repair. Using a mesh or laparoscopic repair has been shown to reduce the risk of chronic pain following inguinal hernia repair.¹⁵ Laparoscopic repair was also known to reduce the risk of acute pain and numbness, and allowed patients to resume their daily activities more quickly.¹⁶ This could be explained by laparoscopic method minimizes tissue damage and reduces the risk of nerve damage. However, some studies have found no significant difference between the open and laparoscopic techniques for the development of CPP.¹⁷ Additionally, the current study showed that open surgery and laparoscopic approaches were not statistically significant in the risk of developing CPP (Table 4). While the skin incision causes damage to the cutaneous and subcutaneous structures, fixation of the mesh may cause damage to the nerves in the operation area.

The most common type of pain experienced after surgery is somatic pain, which occurs due to damage caused to the inguinal tubercle or deep muscle layers. Neuropathic and visceral pain syndromes have also been identified. Injury to the somatic sacral or sympathetic nerves might result in visceral pain.¹⁵ It has been suggested that chronic noxious input from the inguinal region causes neuroplastic changes in the spinal cord followed by a postoperative hyperpathic area.¹⁸ Additionally, postoperative inflammation or mesh response, followed by neural involvement may contribute to this. In this study, 31 patients reported chronic neuropathic pain, while 27 patients reported somatic pain in the 6th months. Neuropathic pain usually occurs in the sensory distribution of the ilioinguinal, iliohypogastric, or genitofemoral nerves. Knowledge of the anatomy of cutaneous nerves is necessary to prevent nerve injury.¹⁵

The neuronal changes caused by postoperative acute pain in the central and peripheral nervous system have shown a significant effect on the development of CPP.¹⁹ The relationship between early postoperative acute pain and CPP was statistically significant in our study ($p < 0.001$) and we found that CPP was higher in patients requiring postoperative analgesia. We attributed this result to acute postoperative pain and associated opioid use as predictors of CPP.²⁰

This study observed more chronic pain in patients with recurrent hernia repair than in patients with primary inguinal hernia repair. Mesh implantation was considered as the gold standard in inguinal hernia repair because it reduced the risk of recurrence although the use of foreign material might induce a stronger inflammatory reaction.¹² There has been no consensus on the contribution of mesh weight, pore size, or other mesh characteristics to the development of CPP. While some authors stated that the risk of recurrence increased with the use of low weight mesh, others have found no difference between the use of low-weight mesh and heavy-weight mesh in recurrence and risk of perioperative complications but found less chronic pain with low-weight mesh.²¹⁻²³ It's also reported that the

size of the pore determines the extent of the inflammatory response, and the small pores cause a dense scar plate that develops around the entire mesh.²⁴ In this study, macroporous, monofilament polypropylene mesh was used in all patients, so we were not able to investigate the role of mesh character on CPP, however, the CPP rate was not statistically significant in patients with a mesh of different sizes.

It has been observed that among different types of anesthesia, the use of regional anesthesia carried a higher risk of pain. Moreover, Joshi et al. have recommended the use of local anaesthetic infiltration even when the patient is being operated on under general anesthesia.²⁵ In our cases, general anesthesia technique was used in 88.01% of cases, and there was no significant difference in the development of CPP between general anesthesia and spinal anesthesia. However, randomized studies with a larger sample size are necessary to obtain more reliable data since the spinal anesthesia group had a small sample size. In addition, patients with and without local infiltration did not show a significant difference in chronic pain.

For pain lasting more than one year after the operation, laparoscopic retroperitoneal triple neurectomy (the ilioinguinal, iliohypogastric, and genital branches of genitofemoral nerves) is indicated.²⁶ Campanelli et al. used the surgical approach and they couldn't get success with a few patients and suggested that pain palliation may not be achieved in every patient due to differences in personality and pain tolerance.²⁷

Pain has been defined as an experience consisting of sensory, motivational, and emotional components.²⁸ In addition, it was reported that there were physiological similarities between chronic pain and depression.⁷ Noradrenaline and serotonin, which play a role in the pathophysiology of depression, also modulate pain stimuli in the limbic system and periaqueductal areas.⁷ Antidepressants acting through these neurotransmitters also have analgesic effects. However, it has been noted that patients with severe anxiety have a lower pain threshold and the activation of astrocytes by anxi-

ety in the anterior cingulate cortex might result in chronic pain.⁶ Our results showed that the psychological state of the patients played an important role in the development of CPP ($p < 0.001$). Chronic pain developed in 38 of 120 patients with moderate-to-severe depression and in 28 of 140 patients with moderate-to-severe anxiety symptoms.

There were limiting factors in the present study. Since the centre where the study was conducted in a teaching hospital, the surgical procedure was performed by different operators, which could have led to slight variations in the surgical techniques used. A larger sample size and longer follow-up might be needed before any certain conclusion. However, the evaluation of demographic, surgical, and psychological factors together makes this study special.

CONCLUSION

This prospective study highlighted that the incidence of CPP after inguinal hernia repair was 22.3% in 3rd months and 12.3% in 6th months. Preoperative pain, female gender, the intensity of postoperative acute pain, duration of preoperative pain, postoperative complication, patients' preoperative psychological state and recurrent operations were risk factors for the development of CPP. It's suggested that patients and physicians should be aware of the role of depression and anxiety and it was important to question the presence of pain in the preoperative and postoperative early periods to provide good analgesia.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Derya Bayram, Dostali Aliyev; **Design:** Derya Bayram, Dostali Aliyev, İbrahim Aşık; **Control/Supervision:** Derya Bayram, İbrahim Aşık; **Data Collection and/or Processing:** Derya Bayram, Dostali Aliyev, İbrahim Aşık; **Analysis and/or Interpretation:** Derya Bayram, Dostali

Aliyev; **Literature Review:** Derya Bayram, Dostali Aliyev; **Writing the Article:** Derya Bayram, Dostali Aliyev, İbrahim Aşık; **Critical Review:** Derya Bayram, Dostali Aliyev; **References and Fundings:** Derya Bayram, Dostali Aliyev, İbrahim Aşık; **Materials:** Derya Bayram, Dostali Aliyev, İbrahim Aşık.

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