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Review Paper

What are the Protective Factors to Reduce the Incidence and Severity of Pain After Open Heart Surgery? A Scoping Review

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ABSTRACT

Background: Pain following open cardiac surgery is a common and debilitating complication that negatively impacts patients' quality of life. Although extensive research has focused on risk factors, protective factors that may reduce the incidence or severity of pain have received less attention. The aim of this scoping review was to identify and categorize protective factors against pain after open cardiac surgery and to elucidate their mechanisms of action.

Materials and Methods: This scoping review was conducted in accordance with the PRISMA-ScR guidelines. A systematic search was performed in PubMed, Scopus, Web of Science, and Cochrane Library for studies published from 2010 to February 2026. Studies investigating factors associated with reduced incidence or severity of pain following open heart surgery were included. Data extraction was carried out independently by two authors, and the identified factors were reported.

Results: Of the 847 articles identified, 27 studies met the inclusion criteria. Protective factors were classified into five main categories: (1) Psychological factors, (2) prehabilitation interventions, (3) factors associated with acute pain management (4) lifestyle factors, and (5) social support. The underlying mechanisms of action included modulation of inflammation, reduction of central sensitization, enhancement of descending inhibitory pain pathways, and improvement in coping strategies.

Conclusion: This study offers a new perspective on post-cardiac surgery pain management, emphasizing protective factors and novel biotechnological approaches. Integrated multimodal interventions may reduce suffering, prevent chronic pain, and improve quality of life. Future trials should validate biotechnological strategies and explore underlying bio-psychosocial and molecular mechanisms.

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Introduction

Open heart surgery is considered one of the most common and invasive surgical interventions, performed annually on millions of patients with coronary artery and valvular heart diseases. Despite remarkable advances in surgical techniques, anesthesia, and postoperative care, post-surgical pain remains a significant clinical challenge [1]. According to a 2025 meta-analysis, the global prevalence of post–open heart surgery pain syndrome is approximately 34.4% [2]. According to a 2025 meta-analysis, the global prevalence of post-cardiac surgery pain syndrome is approximately 34.4%. Separately, another study reported the incidence of chronic pain at 28.7% and chronic neuropathic pain at 14.7% [3].

According to the definition set by the International Association for the Study of Pain (IASP), chronic post-surgical pain (CPSP) refers to pain that arises following a surgical procedure, persists for at least three months, cannot be explained by other causes, such as infection or disease recurrence, and leads to significant functional or psychological impairment [4]. Based on a pathophysiological classification, this complex, multidimensional pain is categorized into neuropathic, somatic (musculoskeletal), visceral, and chronic types [5]. These pains can have a profound impact on patients' quality of life, functional recovery, psychological health, and return to daily activities [6]. Studies have reported a trend toward a decreasing age at the time of this surgery. Although this trend is partly attributable to advances in technology and earlier diagnosis, it underscores the need for greater attention [7, 8]. Most studies to date have focused on identifying risk factors associated with the occurrence and severity of pain following cardiac surgery. For instance, a 2026 study by Domain et al. reported that factors, such as the intensity of acute pain in the early postoperative days, psychological distress, younger age, female sex, low body mass index, and pre-existing chronic pain were among the strongest predictors of chronic pain after cardiac and thoracic surgery [1]. A systematic review by Guimarães et al. not only highlighted an increase in the reporting of persistent postoperative pain during the first six months but also acknowledged the role of inadequate acute pain management as a major risk factor [9]. Notably, considering only risk factors without integrating prevention and protection-related factors remains a gap in the literatures.

What factors cause some patients to experience milder pain under almost identical conditions? Identifying these protective factors could directly inform the design of preventive interventions and targeted rehabilitation programs, representing an important step toward preserving and improving patients' quality of life. Limited studies suggest the existence of such protective factors. For instance, Cursio et al. demonstrated that psychological resilience is associated with reduced pain at 30 days following cardiac surgery, with patients exhibiting low resilience reporting higher pain levels. Additionally, another study investigated the potential association between resilience-related biomarkers and post-surgical recovery, reporting that resilient individuals show better recovery trajectories after surgery [10, 11]. A recent narrative review by Leivaditis et al. emphasized the importance of social support and preoperative psychological readiness, demonstrating that psychosocial interventions can reduce reported pain by up to 33% [6].

Although a limited number of studies have identified psychological factors as influential, our search did not identify any scoping review that has systematically identified and categorized the protective factors against postoperative pain in patients undergoing open-heart surgery. A scoping review was selected as the appropriate methodology for the present study, as this type of review is considered ideal for mapping broad and heterogeneous bodies of literature, identifying knowledge gaps, and categorizing key concepts across diverse and multidisciplinary fields [12, 13]. Accordingly, the aim of this study was to identify, categorize, and elucidate the mechanisms of protective factors against the incidence and severity of pain following open-heart surgery using a scoping review methodology.

Materials and Methods

The present scoping review was conducted in accordance with the PRISMA-ScR (preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews) guidelines and based on the methodological framework of the Joanna Briggs Institute (JBI) for scoping reviews [12]. The study steps included formulating the research question, defining the search strategy, establishing the inclusion and exclusion criteria, study selection, data extraction, narrative synthesis of the data, and categorization and reporting of the results.

Research questions

The fundamental questions of this review were three, as listed below:

1. What are the protective factors against the occurrence or severity of pain after open-heart surgery?

2. How are these factors categorized?

3. What is the possible mechanism of action of each of these factors in reducing pain?

Search strategy

A systematic search was conducted across four major electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library (CENTRAL), covering the period from January 1, 2010, to March 30, 2026. The search keywords were defined based on the PEO (population, exposure, and outcome) framework. The final search syntax, comprising Boolean operators (AND, OR, NOT) to combine relevant terms, is presented in Table 1. Additionally, the reference lists of relevant review studies, the PROSPERO registry of clinical trials, and Iranian thesis databases (Iran Doc and SID) were searched to identify further eligible studies.

Population: Adult patients (aged >18 years) undergoing any type of open cardiac surgery, including coronary artery bypass grafting (CABG), valvular heart surgery, or combined procedures (CABG + valve surgery).

Exposure: Pharmacological or non-pharmacological pain-protective strategies, including but not limited to nerve blocks, systemic or regional drug administration, and multimodal analgesic techniques.

Outcomes: Assessment of pain intensity (using the questioner), reduction in postoperative opioid consumption, decrease in pain-related complications, and improvement in patient satisfaction.

Articles published in English or Persian were considered. Inclusion criteria included randomized controlled trials, cohort studies, case-control studies, cross-sectional studies, and review articles that reported at least one factor associated with a reduced incidence or severity of postoperative pain. Studies that focused exclusively on risk factors without addressing protective factors were excluded. Additionally, conference abstracts and animal studies were not included (Figure 1).

Study selection and data extraction

The screening process was conducted independently by two reviewers across three stages: Title, abstract, and full-text review. Disagreements were resolved through discussion and consensus with a third reviewer via Google Meet. The following data were extracted from the final set of included studies: Bibliographic information (first author, publication year, and country), study design and sample size, type of cardiac surgery, protective intervention, pain assessment tool, key findings related to pain reduction, and the proposed mechanism of action.

Data synthesis

Given the exploratory nature of this scoping review, which constituted the primary rationale for selecting the methodology of the present study and the heterogeneity of the included studies, a narrative synthesis was employed. Extracted protective factors were grouped into main categories based on conceptual similarity. Subsequently, the putative evidence-based mechanisms of action were elucidated from the literature [12].

Results

Of the 847 articles initially identified, after removing duplicates using End-Note reference management software and applying a multi-step screening process, 38 studies met the inclusion criteria for the present review. Ultimately, 27 studies were selected for the final analysis. These comprised 5 clinical trials, 10 systematic or narrative reviews, 7 cohort studies, 2 descriptive-analytical studies, 2 animal studies, and 1 qualitative study. Approximately 54% of the included studies (n=13) employed the visual analog scale (VAS). Most studies were conducted in Europe, followed by Asia and the Americas. The characteristics of the included studies are summarized in Table 2.

Categorization of protective factors

Based on a review of the literature, the results were reclassified into five main categories under the heading of protective factors and their mechanisms of action, which will be discussed in detail below.

Category 1: Psychological factors

Psychological resilience

One of the most important protective psychological factors is resilience. Resilience refers to the ability to maintain positive adaptation and return to one's baseline level of functioning in the face of a stressful or threatening event. Curcio et al. reported that in a study of 402 patients undergoing cardiac surgery, resilience was associated with a significant reduction in pain at 30 days post-surgery. Accordingly, patients with lower resilience reported higher levels of pain. Resilience was also posi-

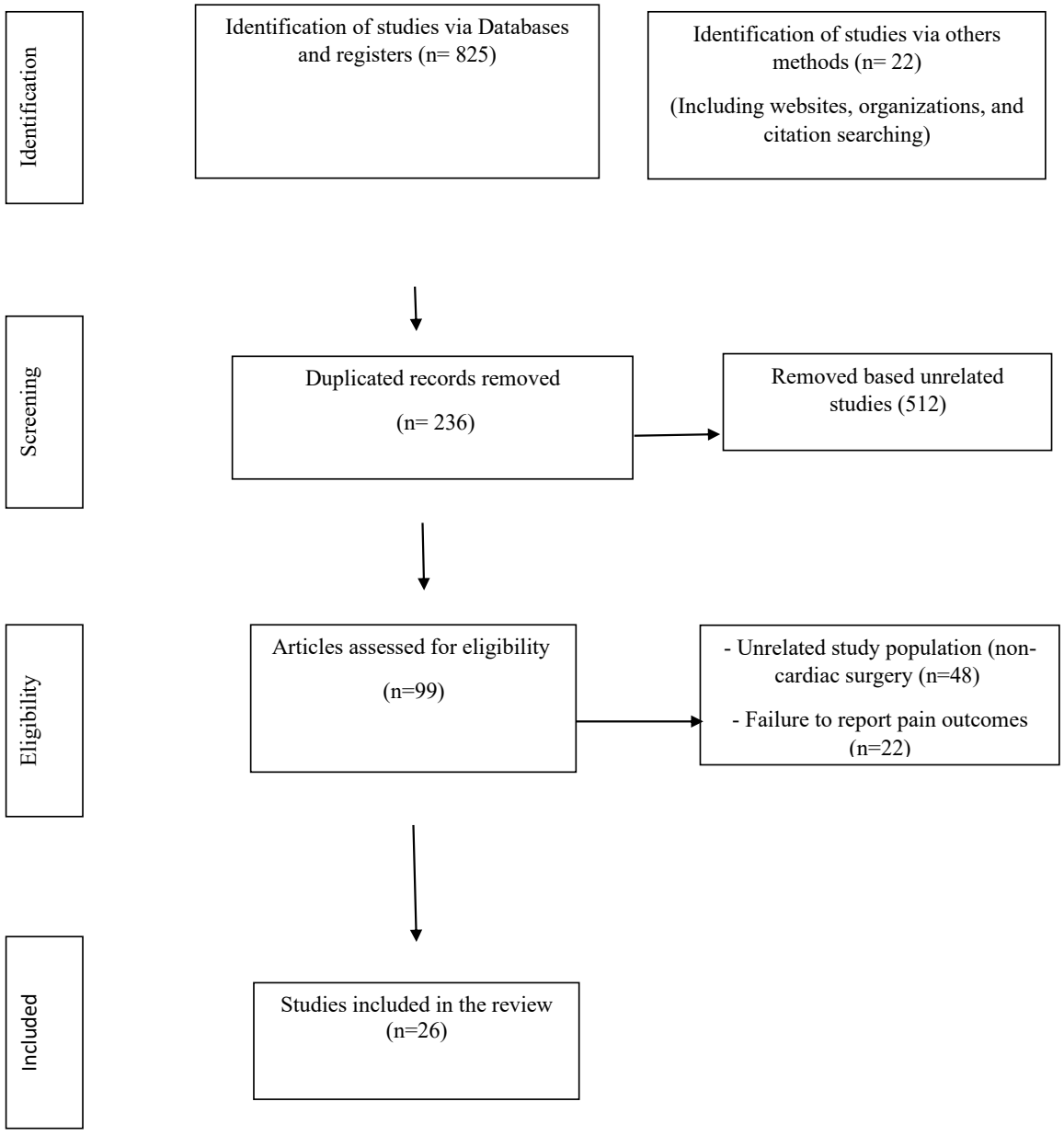


Figure 1. PRISMA flow diagram of the study

tively correlated with variables, such as quality of life, social support, and lower levels of anxiety and depression [11].

Positive attitude

Studies have shown that optimism and a positive attitude can serve as effective coping resources to reduce pain intensity. The review by Leivaditis et al. found that patients' positive attitudes lead to the adoption of more effective coping strategies when facing pain [6]. Furthermore, a phenomenological study highlighted the complex interplay between patient attitude, coping, and self-care, which can influence how patients perceive their role in pain management. These factors contribute to the development of the patient's role in pain management, forming an integrated feedback loop. The patient's attitude facilitates their ability to cope with pain and engage in pain assessment and management. Conversely, their coping ability and willingness to participate in treatment decisions shape the development of their attitude [14]. In their study, Khan et al. found that, based on multiple regression analysis, postoperative pain intensity was associated with higher levels of preoperative pain catastrophizing. In their final report, they concluded that pain catastrophizing can predict the severity of postoperative pain in cardiac surgery patients, independent of

the presence of anxiety, depression, or preoperative pain intensity [15]. This evidence supports the argument that preoperative psychological preparation may effectively reduce perceived pain intensity. These findings suggest that pain is not merely a physical phenomenon; rather, the patient's preoperative psychological state plays a significant role in the chronification of pain.

Preoperative psychological readiness

A systematic review of clinical trials reported that preoperative psychosocial interventions reduce postoperative pain by up to 33%, shorten hospital length of stay, improve treatment adherence, and enhance long-term quality of life. Preoperative educational and counseling interventions decrease postoperative pain by alleviating anxiety and increasing patients' perceived control over the treatment process [6]. Psychological resilience acts through modulation of the hypothalamic-pituitary-adrenal (HPA) axis, attenuation of the inflammatory response to surgical stress, and activation of descending inhibitory pain pathways in the brain [11, 16]. Additionally, resilient individuals may manage negative emotions—such as fear, stress, and anxiety—through emotional regulation, which in turn contributes to reduced pain perception in patients.

Category 2: Prehabilitation interventions

Prehabilitation refers to a set of interventions implemented prior to surgery to optimize a patient's physical and psychological readiness [17]. In this context, interventions may include educational, exercise-based, nutritional, and multimodal approaches [18].

Exercise training

A review study reported that exercise training (aerobic, resistance, and respiratory exercises) represents the most common prehabilitation modality, utilized in 84.7% of studies [17]. Although reported pain outcomes were heterogeneous, 82% of studies demonstrated improvement in at least one postoperative outcome. Furthermore, a randomized clinical trial reported that performing exercise training—three 60-minute sessions per week, tailored to the patient's condition—improved psychological metrics following surgery [19].

Nutritional interventions

A clinical trial reported that daily intake of 30 mL of extra virgin olive oil, initiated the day before surgery and continued for 30 days postoperatively, was associated with a significant reduction in mean postoperative pain scores compared to the control group [20]. Furthermore, a review study noted that although direct evidence regarding the effects on pain is limited, improvements in nutritional status may alleviate pain by reducing inflammation and accelerating tissue repair through enhanced blood supply [21].

Category 3: Factors associated with acute pain management

Optimal pain control within the first 48–72 hours

Inadequate acute pain management is a fundamental contributor to the development and persistence of chronic pain. A scoping review by Bonilla et al emphasizes that acute pain intensity during the initial days following surgery is the strongest and most consistent predictor of chronic pain. Conversely, optimal acute pain control can serve as a powerful protective factor. The impact of surgical technique and anesthetic method is less definitive than that of bio-psychosocial factors [1]. The use of high-dose remifentanil is particularly notable and concerning. Remifentanil is a potent, short-acting opioid. Administering high doses can induce opioid-induced hyperalgesia—a phenomenon in which, instead of alleviating pain, the nervous system is sensitized, leading to increased pain perception. Furthermore, the requirement for high-dose infusion in the early postoperative period likely reflects a multifactorial etiology and greater clinical severity of the patient's condition.

Multimodal approach to pain management

Three key mechanisms contribute to the initiation and persistence of pain: Peripheral and central sensitization resulting from peripheral neural injury, neuroplastic changes that predispose the nervous system to a heightened state of excitability, and inflammatory pathways that trigger neural cascades. Regional anesthesia techniques, such as parasternal blocks, erector spinae plane (ESP) blocks, and intercostal nerve blocks play a crucial role in mitigating acute pain and preventing its chronification. As described by Dast et al., these techniques interrupt pain signals at their source, thereby preventing central sensitization [5].

Multimodal approach to pain management

The use of a multimodal approach incorporating drugs with different mechanisms of action (anti-inflammatory drugs, gabapentinoids, and acetaminophen) along with regional techniques has been described as the most ef-

fective strategy for acute pain control [5]. In this way, acetaminophen and gabapentin primarily contribute to improved pain management by reducing the need for opioids and modulating central neural pathways. Since opioids themselves increase inflammation and postoperative ileus (intestinal paralysis), reducing their consumption indirectly aids in controlling inflammation and its associated complications [22]. Complementary methods, including music therapy, massage, breathing and relaxation exercises, guided imagery, lavender inhalation, acupuncture, cryotherapy, and transcutaneous electrical nerve stimulation were evaluated in a systematic review. The review reported that patients who received these non-pharmacological pain interventions alongside pharmacological treatments experienced three times less pain than those who received drug therapy alone [23].

Emerging biotechnological approaches in pain management

From a pharmaceutical biotechnology perspective, emerging strategies beyond traditional non-pharmacological approaches are under development. For instance, targeted inhibition of the systemic inflammatory response using protease inhibitors, such as ulinastatin, in combination with aprotinin, in patients undergoing cardiac surgery with cardiopulmonary bypass has been shown to significantly reduce IL-6 and TNF-α levels and decrease mechanical ventilation time and postoperative complications [24]. Furthermore, targeted drug delivery to the inflammatory microenvironment using bioresponsive nanoparticles containing non-steroidal anti-inflammatory drugs (e.g. HES-flurbiprofen nanoparticles) can accumulate at the surgical incision site and inhibit hyperalgesia without systemic immunosuppression [25]. In parallel, intrinsic anti-inflammatory nanomedicines based on mesoporous silica nanoparticles containing local anesthetics (e.g. levobupivacaine) and coated with liposomes containing ginsenoside Rg3, by inhibiting macrophage activation, simultaneously produce long-acting anesthesia and anti-inflammatory properties [26]. These biotechnological approaches complement the physiological mechanisms described above and offer a new perspective for multimodal pain management following cardiac surgery.

Category 4: Lifestyle

Preoperative functional status and well-being

Optimal preoperative functional status and a sense of well-being positively influence patient outcomes. This finding suggests that lifestyle factors and subjective comfort may act as protective or risk factors [27]. Another important factor is the role of sex/gender in adopting healthy behaviors and lifestyle patterns. According to the literature, women generally maintain healthier lifestyles, both in terms of preventive behaviors and treatment adherence [28, 29].

Non-use of tobacco and alcohol

According to the 2024 Stambagh study, there was no clear association between mild-to-moderate preoperative alcohol consumption and early postoperative pain or opioid use in patients undergoing CABG [30]. However, another study reported that cigarette smoking was associated with impaired healing of leg and sternal wounds in these patients [31]. Additionally, a comparable study found that a longer duration of smoking cessation prior to surgery was associated with fewer hemodynamic changes and lower postoperative pain scores [32].

Sociodemographic characteristics

A systematic review provided a comprehensive analysis of demographic factors and reported that racial and ethnic differences influence pain perception. Specifically, Black/African American patients reported more severe postoperative pain compared to White patients. Furthermore, White patients were more likely than Black, Hispanic, and Asian patients to receive opioid prescriptions for pain management. The review also highlighted the role of sex and socioeconomic status, noting that individuals with lower socioeconomic status, as well as women, reported higher levels of postoperative pain [33]. Although low body mass index (BMI) has been identified as a risk factor in the Bonilla study [1], the Nishioka study reported that low BMI was associated with an increased risk of pneumonia, whereas high BMI was associated with an increased risk of saphenous vein graft infection and mediastinitis. Therefore, it can be concluded that a normal BMI may serve as a protective factor against both mortality and morbidity. Obesity is associated with increased systemic inflammation and a reduced response to analgesics, which may explain the relationship between BMI and pain [34]. Exercise reduces pain sensitivity through the release of endorphins, reduction of pro-inflammatory cytokines, and improvement in immune function. Additionally, by promoting normal body weight, exercise may further contribute to pain reduction [17].

Table 1. Definition of search keywords based on the PEO framework

Synonym	Original	Keywords
CABG patients, heart surgery patients, coronary surgery, valve surgery patients, thoracic surgery	Cardiac surgery	Population/ Patients
Protection, pre-emptive analgesia	Protective factors	Exposure
Pain, intensity, severity, reduced pain	Postoperative pain	Outcome

CABG: Coronary artery bypass grafting; PEO: Patient, exposure, outcome.

Category 5: Social support

Family and caregiver support

In a qualitative study, patients reported that family support played an important role in their recovery process [35]. Family involvement in treatment and rehabilitation helps reduce patient pain by decreasing anxiety and improving treatment adherence [6]. However, another study found that perceived social support was not a significant predictor of postoperative pain intensity or postoperative opioid requirements; rather, biological and psychological factors were more likely to influence patients' pain perception [36].

Clinician support

Clinician support is best achieved through a patient-centered approach to treatment. In this model, patients who are actively involved in decisions regarding their own care report a greater sense of control and lower pain levels [6]. Patient engagement and informed choice, facilitated through preoperative education, significantly improve treatment adherence and outcomes related to surgical-site pain. The authors recommended that preoperative education be integrated into pain management protocols as a cost-effective non-pharmacological strategy. Modifying patients' beliefs and attitudes through education plays a key role in enhancing the postoperative pain experience [37]. Furthermore, effective communication with the healthcare team is of particular importance. Clear and empathetic communication with physicians and nurses increases patient trust, leading to better pain reporting and more effective pain management [6]. In addition, patient satisfaction with nurses' pain management was identified as another factor contributing to reduced pain perception among patients [38].

Based on the findings of the present study, an integrated biopsychosocial protective model for pain management in patients undergoing open-heart surgery can be proposed across the preoperative, intraoperative, and postoperative phases. In each phase, three core domains are addressed: Biological (e.g. prehabilitation, anesthesia technique, acute pain control), psychological (e.g. mental preparation, resilience enhancement, cognitive coping), and social (e.g. family support, social network strengthening, peer groups)

Mechanisms of action

Reduction of the inflammatory response

In the immediate aftermath of tissue injury, pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) are released and serve two key roles. Initially, they act as alarm signals, and subsequently, by recruiting immune cells to the damaged tissue, they help establish the conditions necessary for tissue repair. Later, IL-10 becomes active and facilitates the repair process, creating an environment that supports healing without chronic pain [17, 39]. Therefore, if proinflammatory cytokines continue to be produced for an extended period or if IL-10 levels are insufficient, chronic inflammation can develop, which may transition into persistent pain lasting more than three months. Consequently, an appropriate pain management strategy is not to completely suppress inflammation but rather to help the body restore this balance more quickly [40]. Exercise, proper nutrition, psychological resilience, and effective management of acute pain all contribute to reducing proinflammatory cytokine levels while increasing IL-10. This accelerates the resolution of the inflammatory phase and shifts the body into a repair-oriented state, thereby improving pain management outcomes [41]. A well-balanced diet promotes the growth of beneficial gut bacteria, which produce short-chain fatty acids. Once absorbed into the bloodstream, these compounds reduce systemic inflammation and help modulate the pain response [42].

Prevention of central sensitization

Acute pain management and regional anesthesia can be utilized in pain management by preventing central sensitization [5].

Table 2. Characteristics of the studies included in the analysis

Author(s), Year	Country	Type of Study	Sample Size	Instruments	Result(s)
Bonilla et al. 2026 [1]	Ecuador	Scoping review	7559 studies	VAS, NRS, ELS	Successful management of acute pain acts as a strong protective factor.
Leivaditis et al. 2025 [6]	Germany	Narrative review	76 studies	VAS, NRS, self-report	Psychosocial interventions reduce postoperative pain by up to 33%.
Curcio 2020 [47]	USA	Prospective	402	VAS, NRS	Psychological factors, such as resilience and social support play a role.
Walton et al. 2024 [14]	Canada	Qualitative	6	Interview	Optimism, realistic expectations, and interpersonal dynamics in cardiovascular care play a role.
Jia et al. 2024 [25]	China	Animal study	n=3 per group	HES-flurbiprofen nanoparticles	The nanoparticles self-assemble in water, improving flurbiprofen's solubility and half-life. Preoperative administration resulted in accumulation at the incision site, effectively inhibiting hyperalgesia and alleviating inflammation in rats.
Qiao et al. 2024 [26]	China	Animal study	n=5 per group	Local anesthetics for pain reduction	The nanomedicine provides sustained anesthetic release and intrinsic anti-inflammatory effects by inhibiting macrophage activation. LMSN-bupi demonstrated significantly prolonged analgesic effects and attenuated inflammatory responses compared to traditional liposome-decorated nanoparticles (TMSN-bupi)
Ma et al. 2023 [24]	China	Retrospective clinical study	86 patients	Pain pump usage	The combination significantly reduced postoperative IL-6, TNF-α, WBC count, and neutrophil percentage. It also lowered dopamine requirements, shortened mechanical ventilation duration, and reduced complications compared to the control group. TNF-α, cTnI, and treatment regimen were independent risk factors for prognosis
Khan et al. 2012 [15]	UK	Prospective cohort	102	VAS, NRS	Patients with higher levels of catastrophic thinking about pain experienced more severe postoperative pain.
Giusti et al. 2021 [16]	Italy	Systematic review	8322	Different tools	Psychological predictors, notably anxiety, depression, and pain catastrophizing, significantly influence postoperative pain outcomes.
Sosa et al. 2026 [17]	USA	Systematic review	153 randomized clinical trials (RCTs)	Different tools	Pre-rehabilitation interventions serve as a beneficial strategy for the physiological and psychological preparation of patients, leading to improved recovery and reduced postoperative pain.
Akbari 2025 [18]	Iran	Review		Unknown	Preoperative education effectively reduces patient anxiety and enhances pain management after surgery.
Akbari et al. 2025 [19]	Iran	RCT	60	SCL-90-R	Reduction in pain following cardiac surgery through cardiac rehabilitation is mediated by improvements in psychological indicators such as decreased anxiety and depression.
Bahrami et al. 2025 [20]	Iran	RCT	110	VAS, BSFS	Positive effects of olive oil consumption on pain reduction have been observed, supporting the inclusion of olive oil in the dietary regimen as part of a comprehensive pain management approach.
Hill et al. 2018 [21]	Germany	Review		Different tools	A proper nutritional support strategy, particularly early enteral nutrition, mitigates the inflammatory response induced by cardiopulmonary bypass by preventing bacterial translocation into the bloodstream. Given that inflammation is a key determinant of postoperative pain severity, its management through nutritional intervention may indirectly reduce pain intensity following cardiac surgery.
Yıldız et al. 2024 [23]	Turkish	Systematic review	3097	Different tools	The integration of non-pharmacological approaches with pharmacological strategies enhances pain control and improves overall patient outcomes after surgery
Dolu et al. 2024 [27]	Turkish	Prospective cohort	50	Cardiac symptom survey	Patient comfort during procedures is directly related to the effective reduction of pain.

Author(s), Year	Country	Type of Study	Sample Size	Instruments	Result(s)
Lautert et al. 2025 [28]	Brazil	Descriptive	26	McGill pain questionnaire, VAS	This study did not report a direct association between lifestyle factors and pain.
Thurston et al. 2023 [33]	USA	Systematic review	32	VAS, NRS	Race, sex (female), and socioeconomic status are influential factors in pain perception.
Nishioka et al. 2020 [34]	Japan	Retrospective	96058	Side effects and mortality	Low body mass index was associated with an increased likelihood of pneumonia, whereas elevated BMI was correlated with saphenous vein graft site infection and mediastinitis.
Stombaugh et al. 2024 [30]	USA	Retrospective cohort	1338	NRS	No clear association was observed between mild-to-moderate preoperative alcohol and opioid use and early postoperative pain.
Nazir et al. 2021 [32]	Pakistan	Prospective cohort	256	VAS, NRS	Smoking cessation lasting more than 4 weeks before elective surgery improves cardiovascular stability and tissue oxygenation, which directly reduces the severity of early postoperative pain. Conversely, patients who quit less than 2-4 weeks prior may experience increased pain sensitivity due to airway hyperreactivity and catecholamine fluctuations.
Sharif-Kashani et al. 2016 [31]	Iran	RCT	810	Side effects of surgery	Cigarette smoking is associated with an increased incidence of impaired lower extremity wound healing, particularly necrosis and wound edge dehiscence, following coronary artery bypass grafting (CABG) surgery.
Ibrahim et al. 2025 [48]	UK	Systematic review on qualitative	266	Not applicable due to the nature of the study design	Patients acknowledged that family support played a role in reducing their pain.
Khalid et al. 2022 [37]	Pakistan	RCT	80	Questionnaire	Pre-procedural education led to greater acceptance of the patient's clinical condition, improved pain management, and reduced fear of opioid dependence.
Wenze et al. 2025 [36]	Germany	RCT	217	VAS, NRS	Social support did not demonstrate a direct effect on reducing acute postoperative pain.
Karabulut et al. 2015 [38]	Australian	Descriptive-analytical	70	VAS, comfort level assessed alongside	Timely management of prescribed medications by the healthcare team can play a role in pain reduction.

Abbreviations: VAS: Visual pain scale; BSFS: Bristol stool form scale; NRS: Numeric rating scale; SCL-90-R: Symptom checklist-90-revised; MPQ: McGill pain; ELS: Engaged living scale.

Enhancement of descending inhibitory pathways

Resilience, positive attitude, and social support are associated with mechanisms that activate descending pain inhibitory pathways within the central nervous system [16].

Improvement of coping strategies

Psychological preparedness and pre- and postoperative education enhance the patient's ability to adopt appropriate pain-related coping behaviors [14].

Biotechnological mechanisms

Apart from physiological approaches, biotechnological interventions confer their protective function by employing certain molecular processes. Protease inhibitors, such as ulinastatin and aprotinin mitigate central sensitization by inhibiting NLRP3 inflammasome activity and the downstream IL-1β maturation process [24]. Bioresponsive nanoparticles (HES-flurbiprofen) exert selective COX-2 inhibition only at incision sites, whereas levobupivacaine-loaded mesoporous silica nanoparticles coated with ginsenoside Rg3 target macrophage M [25, 26].

Collectively, the aforementioned factors exert their effects across a temporal continuum from the preoperative to the postoperative period, engaging in complex interactions that ultimately influence the patient's perception of pain.

Discussion

The present scoping review systematically reported protective factors against the incidence and severity of pain after cardiac surgery. Based on the literature review, the protective factors for post-cardiac surgery pain can be presented within an integrated, five-tiered protective model encompassing psychological factors, prehabilitation, acute pain management, lifestyle, and social support. These findings are fully consistent with the biopsy-

chosocial model of pain described in the literature [16, 43, 44]. Previous studies have primarily focused on risk factors. The scoping review by Bonilla et al. reported risk factors, such as acute pain severity, psychological distress, younger age, and female sex [1]. In contrast to the systematic review by Guimarães et al., which reported risk factors associated with the prevalence of chronic pain, the present study focused on protective factors and their mechanisms of action [45].

The primary findings related to psychological factors, with psychological resilience emerging as the most significant protective factor, are consistent with the observations of Curcio et al. [11]. This finding holds substantial clinical relevance, as resilience is a modifiable skill that can be enhanced through targeted interventions. The second category encompassed pre-rehabilitation factors, representing an emerging strategy with high potential for impact. Sosa et al. highlighted the role of multimodal interventions, although pain-related outcomes were reported heterogeneously across these studies [17], underscoring the multifactorial nature of the determinants involved.

Optimal control of acute pain, as demonstrated in the third-floor cohort, was identified as the strongest protective factor against the development of chronic pain, which is consistent with the findings of several studies [1, 5, 9]. This finding suggests that focusing on pain management within the first few hours after surgery represents one of the most effective protective strategies.

Beyond these factors, studies have reported that novel biotechnological approaches offer different ways to optimize acute postoperative pain management. As illustrated in our results, strategies, such as protease inhibitors (e.g. ulinastatin with aprotinin), bioresponsive NSAID-containing nanoparticles, and anesthetic nanomedicines (e.g. levobupivacaine with ginsenoside Rg3) have shown the potential to reduce systemic inflammation, inhibit hyperalgesia, and provide long-lasting analgesia without immunosuppression [24-26]. These findings underscore the importance of biotechnology-based interventions. However, further evidence in this area is required to inform the design of high-quality interventions in cardiac surgery populations, as studies involving human subjects have been limited.

In the fourth domain of lifestyle—encompassing health behaviors and subjective well-being—significant findings emerged. The results of this study align with constructs from the bio psychosocial model, highlighting the decisive role of lifestyle and social support in the experience of pain following cardiac surgery. Biological factors, such as BMI, influence patients' pain perception through mechanisms involving systemic inflammation or altered analgesic response. Conversely, a normal BMI was identified as a protective factor [1]. A healthy lifestyle and a preoperative subjective perception of well-being—which itself may be shaped by gender—emerged as protective factors against adverse postoperative outcomes [14]. Lifestyle factors, including alcohol consumption and substance abuse, were also considered in the analyses. Smoking cessation contributes to faster recovery by reducing impairment of wound healing [31]. However, mild alcohol consumption was not significantly associated with acute postoperative pain [30]. Further studies appear to be warranted in this regard.

At the social level, social support and self-efficacy theory explain the mechanisms through which interpersonal interactions influence pain perception. According to these theories, receiving family support and engaging patients actively in treatment decisions—through preoperative education [37], and empathetic communication with the healthcare team—enhance perceived control and self-efficacy while reducing anxiety, ultimately leading to lower reported pain and more effective pain management [46].

The findings of the present study underscore the necessity of adopting a holistic approach to pain management before, during, and after cardiac surgery, with particular emphasis on improving psychological well-being and strengthening the patient's support network.

Limitations

This study has several novel aspects, including being among the limited scoping reviews that examine protective factors in the context of pain perception in patients undergoing cardiac surgery. Furthermore, it represents a paradigm shift from a disease-oriented approach (i.e. asking why patients experience pain) to a health-oriented approach (i.e. identifying protective pain-related factors) to design health-focused interventions.

The limitations of the present study include linguistic restrictions (Persian–English), incomplete reporting of pain-related outcomes in the primary studies, heterogeneity across studies, and publication bias (stemming from journals' reluctance to publish negative or null findings). Additionally, due to the inherent nature of a scoping review, no formal quality assessment of the included studies was conducted. Therefore, caution is advised when interpreting and applying the findings of this study.

Conclusion

The present study provides a new perspective on the management and prevention of pain after cardiac surgery, with a special focus on the protective roles and pathways of action, including novel biotechnological approaches. Designing integrated and multimodal interventions—combining conventional protective factors with novel biotechnological strategies, such as targeted anti-inflammatory agents and nanomedicines—could be an important step toward reducing patient suffering, facilitating timely discharge, preventing chronic pain, reducing hospital admissions, and improving quality of life. Future studies should focus on designing clinical trials to enhance these protective factors, validating biotechnological interventions, developing combinatorial predictive models, and conducting more detailed investigations into the underlying biological, psychosocial, and molecular mechanisms.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of Semnan University of Medical Sciences, Semnan, Iran (Code: IR.SEMUMS.REC.1404.216).

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Authors contribution's

Conceptualization and study design: Mohammad Forozeshfard; Methodolohy, investigation and data collection, and data analysis: Ilia Zamani Hajiabadi and Keshvar Samadaeegelehkolaee. Writing the original draft: Mohammad Forozeshfard, Shahrzad Izadi, Kamran Ghods, and Ilia Zamani Hajiabadi. Supervision: Mohammad Forozeshfard and Kamran Ghods; Final approval: All authors.

Conflict of interests

The authors declared no conflict of interests.

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References

[1] Bonilla Sierra P, Celi MA, Suárez Burneo C. Predisposing factors for chronic post-surgical pain after thoracic surgery: A scoping review with quantitative synthesis. J Pain Res. 2026; 19:557361. [DOI:10.2147/JPR.S557361] [PMID] [PMCID]

[2] Roozegar MA, Erfani A, Vasigh A. Global prevalence post-sternotomy pain syndrome (PSPS) after cardiac surgery: Systematic reviews and meta-analyse. Arch Anesthesiol Crit Care. 2025; 11(2):231-6. [DOI:10.18502/aacc.v11i2.17968]

[3] Girgin S, Gölboyu BE. Incidence of chronic neuropathic pain after open-heart surgery: A retrospective cohort analysis. GKD Anest Yoğ Bak Dern Derg. 2023; 29(1):1-6. [DOI:10.14744/GKDAD.2023.29052]

[4] Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: The IASP classification of chronic pain for the international classification of diseases (ICD-11). Pain. 2019; 160(1):19-27. [DOI:10.1097/j.pain.0000000000001384] [PMID]

[5] Dost B, Karapinar YE, Karakaya D, Demir ZA, Baris S, Koksal E, et al. Chronic postsurgical pain after cardiac surgery: A narrative review. Saudi J Anaesth. 2025; 19(2):181-9. [DOI:10.4103/sja.sja_829_24] [PMID]

[6] Leivaditis V, Sepetis A, Mulita F, Mitsos S, Baikoussis NG, Koletsis E, et al. Patient-centered cardiac surgery: Psychosocial challenges, evidence-based interventions, and future horizons. Healthcare. 2025; 13(22):2957. [DOI:10.3390/healthcare13222957] [PMID] [PMCID]

[7] Sela O, Gelman S, Gordon A, Farkash A, Pevni D, Kakoush M, et al. Trends in patient characteristics and cardiothoracic surgeries over 14 years (2010-2023): A single center experience. J Clin Med. 2024; 13(21):6467. [DOI:10.3390/jcm13216467] [PMID] [PMCID]

[8] Bui R, Macnojia A, Li T, Hasoon J, Khalifa A, Nguyen A. A review of chronic post-sternotomy pain syndrome. Curr Pain Headache Rep. 2026; 30(1):41. [DOI:10.1007/s11916-026-01483-7] [PMID]

[9] Guimarães-Pereira L, Reis P, Abelha F, Azevedo LF, Castro-Lopes JM. Persistent postoperative pain after cardiac surgery: A systematic review with meta-analysis regarding incidence and pain intensity. Pain. 2017; 158(10):1869-85. [DOI:10.1097/j.pain.0000000000000997] [PMID]

[10] Graham D, Becerril-Martinez G. Surgical resilience: A review of resilience biomarkers and surgical recovery. Surgeon. 2014; 12(6):334-44. [DOI:10.1016/j.surge.2014.03.006] [PMID]

[11] Curcio N, Turner ED, Leonard K, Bennett MM, Warren AM, Edgerton JR. The role of resilience and spirituality in recovery following cardiac surgery. Proc (Bayl Univ Med Cent). 2022; 35(4):420-7. [DOI:10.1080/08998280.2022.2043985] [PMID] [PMCID]

[12] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med. 2018; 169(7):467-73. [DOI:10.7326/M18-0850] [PMID]

[13] Samadaee Gelehkolaee K, Azin SA, Nedjat S, Zamani Hajiabadi A, Maasoumi R. Reaching consensus: A scoping review on school-based comprehensive sexuality education programs (CSE). Práxis Educacional. 2020; 16(37):345-60. [DOI:10.22481/praxisedu.v16i37.6175]

[14] Walton LL, Duff E, Arora RC, McMillan DE. The role of the cardiac surgery patient in pain management: The patient perspective. Clin Nurs Res. 2024; 33(7):538-44. [DOI:10.1177/10547738241273232] [PMID] [PMCID]

[15] Khan RS, Skapinakis P, Ahmed K, Stefanou DC, Ashrafian H, Darzi A, et al. The association between preoperative pain catastrophizing and postoperative pain intensity in cardiac surgery patients. Pain Med. 2012; 13(6):820-7. [DOI:10.1111/j.1526-4637.2012.01386.x] [PMID]

[16] Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic post-surgical pain: A systematic review and meta-analysis. Pain. 2021; 162(1):10-30. [DOI:10.1097/j.pain.0000000000001999] [PMID]

[17] Sosa EA, Henick A, Binda DD, Joseph C, Kim S, Mathew D, et al. Integrating pain prehabilitation into surgical pathways: Current modalities, outcomes, and research gaps. Curr Pain Headache Rep. 2026; 30(1):30. [DOI:10.1007/s11916-025-01464-2] [PMID] [PMCID]

[18] Akbari A. The effects of preoperative education on post-operative outcomes in cardiac surgery patients [bachelor's thesis]. Tampere: Tampere University of Applied Sciences; 2025. [Link]

[19] Akbari A, Babaie M, Sadeghi G, Yadollahifar S, Jervani MA. Cardiac rehabilitation and psychological symptoms in patients undergoing coronary artery bypass graft surgery: A randomized clinical trial. Evid Based Care. 2025; 15(2):18-27. [Link]

[20] Bahrami R, Ebadi A, Saeid Y, Farzam SS, Gomrokchian E, Moayed MS. Impact of olive oil consumption on surgical outcomes in patients undergoing open heart surgery: A randomized clinical trial. J Complement Integr Med. 2025; 22(3):522-9. [DOI:10.1515/jcim-2024-0256] [PMID]

[21] Hill A, Nesterova E, Lomivorotov V, Efremov S, Goetzenich A, Benstoem C, et al. Current evidence about nutrition support in cardiac surgery patients-what do we know? Nutrients. 2018; 10(5):597. [DOI:10.3390/nu10050597] [PMID] [PMCID]

[22] Kianian S, Bansal J, Lee C, Zhang K, Bergese SD. Perioperative multimodal analgesia: A review of efficacy and safety of the treatment options. Anesthesiol Perioper Sci. 2024; 2(1):9. [DOI:10.1007/s44254-023-00043-1]

[23] Yıldız T, Oyuktaş M, Avcu Ç. The effect of non-pharmacological methods on pain in patients undergoing open heart surgery: A systematic review and meta-analysis. Turk Gogus Kalp Damar Cerrahisi Derg. 2024; 32(3):291-306. [DOI:10.5606/tgkdc.dergisi.2024.25603] [PMID] [PMCID]

[24] Ma E, Chen W, Zhang C, Liu C, Lan J, Yan X. Ulinastatin in combination with aprotinin improves systemic inflammation in patients undergoing cardiac surgery with cardiopulmonary bypass. Am J Transl Res. 2023; 15(11):6505-13. [PMID]

[25] Jia J, Zhang M, Zheng J, Zhang J, Fang T, Sun T, et al. Bioresponsive hydroxyethyl starch-flurbiprofen nanoparticles targeted to inflammatory microenvironments for post-operative pain management. J Drug Deliv Sci Technol. 2024; 100:106079. [DOI:10.1016/j.jddst.2024.106079]

[26] Qiao B, Yao J, Fan Ya, Zhang N, Feng M, Zhao J, et al. Intrinsic anti-inflammatory nanomedicines for enhanced pain management. Front Bioengin Biotechnol. 2024; 12:1514245. [DOI:10.3389/fbioe.2024.1514245] [PMID] [PMCID]

[27] Dolu İ, Demirtaş H, Çelik S. A prospective study on activities of daily living, comfort, body image, and cardiac symptoms in coronary artery bypass patients. Pain Manag Nurs. 2024; 25(5):518-28. [DOI:10.1016/j.pmn.2024.04.014] [PMID]

[28] Lautert RP, Gaedke MÂ, Reckziegel MB. Lifestyle and pain perception of adults in the pre-cardiac surgery period. Saúde Coletiva. 2025; 15(98):16770. [Link]

[29] Hosseini J, Gelehkolaee KS, Hajebrahimi S, Salehi-pourmehr H, Shariatpanahi S, Sadeghi-Ghyassi F, et al. A systematic synthesis of national policies and practice initiatives in men's health worldwide. World Med Health Policy. 2025; 17(4):806-13.[DOI:10.1002/wmh3.70042]

[30] Stombaugh DK, Singh K, Malek A, Kleiman A, Walters S, Zaaqoq A, et al. Preoperative alcohol use, postoperative pain, and opioid use after coronary artery bypass surgery. J Cardiothor Vasc Anesth. 2024; 38(4):957-63. [DOI:10.1053/j.jvca.2024.01.010] [PMID]

[31] Sharif-Kashani B, Shahabi P, Mandegar MH, Saliminejad L, Bikdeli B, Behzadnia N, et al. Smoking and wound complications after coronary artery bypass grafting. J Surg Res. 2016; 200(2):743-8. [DOI:10.1016/j.jss.2015.09.017] [PMID]

[32] Nazir M, Afshan G, Ejaz M, Raza A. Duration of cessation of smoking before elective surgery: Impact on intraoperative hemodynamics and early postoperative pain in developing country. Open J Anesthesiol. 2021; 11(9):288. [DOI:10.4236/ojanes.2021.119028]

[33] Thurston KL, Zhang SJ, Wilbanks BA, Billings R, Aroke EN. A systematic review of race, sex, and socioeconomic status differences in postoperative pain and pain management. J Perianesth Nurs. 2023; 38(3):504-15. [DOI:10.1016/j.jopan.2022.09.004] [PMID]

[34] Nishioka N, Ichihara N, Bando K, Motomura N, Koyama N, Miyata H, et al. Body mass index as a tool for optimizing surgical care in coronary artery bypass grafting through understanding risks of specific complications. J Thorac Cardiovasc Surg. 2020; 160(2):409-20.e14. [DOI:10.1016/j.jtcvs.2019.07.048] [PMID]

[35] Kaya H, Lumprom O, Schofield P, Carey MC, Latour JM. Patient experiences after open heart surgery: A qualitative systematic review. Florence Nightingale J Nurs. 2025; 33:e24294. [DOI:10.5152/FNJN.2025.24294] [PMCID]

[36] Wenzel P, Gründahl M, Fischer M, Hein G, Fuchtmann F, Schnabel K, et al. Influence of social support on perioperative pain: a secondary sub-sample analysis of a prospective observational trial. Eur J Pain. 2025; 29(8):e70094. [DOI:10.1002/ejp.70094] [PMID] [PMCID]

[37] Khalid A, Kausar S, Sadiqa A, Abid A, Jabeen S. Relevance of preoperative pain education to the cardiac patients on their response to postoperative pain therapy: Preoperative pain education to the cardiac patients. Pak BioMed J. 2022; 147-51. [DOI:10.54393/pbmj.v5i1.248]

[38] Karabulut N, Aktas YY, Gurcayır D, Yılmaz D, Gokmen V. Patient satisfaction with their pain management and comfort level after open heart surgery. Aust J Adv Nurs. 2015; 32(3):16-24. [DOI:10.37464/2015.323.1576]

[39] Cocea AC, Stoica CI. Interactions and trends of interleukins, PAI-1, CRP, and TNF-α in inflammatory responses during the perioperative period of joint arthroplasty: Implications for pain management-A narrative review. J Pers Med. 2024; 14(5):537. [DOI:10.3390/jpm14050537] [PMID] [PMCID]

[40] Ebersberger A, Schaible HG. Do cytokines play a role in the transition from acute to chronic musculoskeletal pain? Pharmacol Res. 2025; 212:107585. [DOI:10.1016/j.phrs.2025.107585] [PMID]

[41] Tsai KL, Huang PC, Wang LK, Hung CH, Chen YW. Incline treadmill exercise suppresses pain hypersensitivity associated with the modulation of pro-inflammatory cytokines and anti-inflammatory cytokine in rats with peripheral nerve injury. Neurosci Lett. 2017; 643:27-31. [DOI:10.1016/j.neulet.2017.02.021] [PMID]

[42] Wang Y, Cao Z, Gao Y, Shao P, Gao S, Dong M, et al. Nutritional interventions for osteoarthritis: Targeting the metabolism-inflammation-oxidative stress axis-clinical evidence and translational practice. Front Nutr. 2025; 12:1661136. [DOI:10.3389/fnut.2025.1661136] [PMID] [PMCID]

[43] Hadlandsmyth K, Conrad M, Steffensmeier KS, Van Tiem J, Obrecht A, Cullen JJ, et al. Enhancing the biopsychosocial approach to perioperative care: A pilot randomized trial of the perioperative pain self-management (PePS) intervention. Ann Surg. 2022; 275(1):pe8-14. [DOI:10.1097/SLA.0000000000004671]

[44] Dismore L, van Wersch A, Murty AN, Swainston K. A qualitative study with orthopaedic surgeons on pain catastrophizing and surgical outcomes: Shifting from a medical towards a biopsychosocial model of surgery. Br J Pain. 2022; 16(1):14-22. [DOI:10.1177/20494637211004658] [PMID] [PMCID]

[45] Guimarães-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; 20(9):1433-42. [DOI:10.1002/ejp.866] [PMID]

[46] Mubita WM, Richardson C, Briggs M. Patient satisfaction with pain relief following major abdominal surgery is influenced by good communication, pain relief and empathic caring: A qualitative interview study. Br J Pain. 2020; 14(1):14-22. [DOI:10.1177/2049463719854471] [PMID] [PMCID]

[47] Curcio NE. The role of resilience in cardiovascular surgery recovery [doctoral dissertation].Dallas: University of Texas Southwestern Medical Center; 2020. [Link]

[48] Ibrahim MK, Haria A, Mehta NV, Degani MS. Antimicrobial potential of quaternary phosphonium salt compounds: A review. Future Med Chem. 2023; 15(22):2113-41. [DOI:10.4155/fmc-2023-0188] [PMID]

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