



OPEN The effect of peri-operative pain neuroscience education on pain and recovery in adult patients receiving laparoscopic inguinal hernia repair

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To optimize the efficacy of analgesia for patients receiving laparoscopic inguinal hernia repair, peri-operative pain neuroscience education (PNE) as a pain-specific cognitive therapy was incorporated into multi-modal analgesia. A randomized controlled trial was conducted to compare conventional analgesia (group CA) and the addition of pain neuroscience education into it (group PNE) in patients receiving laparoscopic inguinal hernia repair. Characteristics of peri-operative pain was evaluated with Douleur Neuropathique 4 questionnaire (DN-4), central sensitization inventory (CSI), pain catastrophizing scale (PCS) post-operatively and pressure pain threshold. Post-operative quality of recovery was measured with EuroQol five dimensions questionnaire (EQ-5D-5L). The incidence of chronic post-operative pain was also recorded. A total of 184 patients consented to participate in this study and finished follow-up. Compared with those receiving conventional analgesia (group CA, $N=91$), patients in group PNE ($N=93$) reported reduced incidence of moderate-to-severe pain and less dosages of opioid during hospitalization ($p < 0.05$). Catastrophizing, sensitization related to pain were reduced in group PNE ($p < 0.05$). Quality of recovery was improved till 1 month after surgery ($p < 0.05$). The addition of pain neuroscience education improved analgesic effect and quality of recovery for patients undergoing laparoscopic inguinal hernia repair. It also helped reduce sensitization and catastrophic of acute surgical pain. This psychologically-oriented analgesic approach merits future research and application for these patients.

Keywords Post-surgical pain, Analgesia, Pain neuroscience education, Hernia repair, Laparoscopy, Recovery

Inguinal hernia repair ranks as one of the most frequently performed abdominal surgical interventions, with patients frequently reporting chronic pain and groin discomfort attributable to the hernial condition¹. The role of analgesia in peri-operative care is paramount for overall patient satisfaction and clinical outcomes post-operatively². Ineffective post-operative pain management can precipitate a myriad of adverse outcomes, such as delayed gastrointestinal functionality as well as cardio-pulmonary complications³. The utility of peri-operative multi-modal analgesia is incontrovertible in attenuating surgical pain and associated stress responses^{4,5}. Despite the conceptual maturation of “multi-modal analgesia” over the past two decades, a significant fraction of patients undergoing hernia repair continue to experience moderate-to-severe pain in both pre- and post-operative settings^{6,7}.

An inguinal hernia manifests as the egress of abdominal organs through a defect in the inguinal area, leading to the formation of a palpable external mass colloquially termed as a “hernia”^{8,9}. Currently, surgical intervention has involved from traditional hernia repair to tension-free hernia repair. whereas the latter, exemplified by methods like the Lichtenstein technique, offers advantages such as reduced post-operative recurrence and concomitant complications^{10,11}. Laparoscopic inguinal hernia repair has emerged as the linchpin of tension-free repair strategies. This category encompasses techniques like trans-abdominal preperitoneal hernioplasty (TAPP), totally extraperitoneal hernioplasty (TEP), intra-abdominal patch implantation (IPOM), as well as

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robot-assisted procedures^{12,13}. Nevertheless, even minimally invasive approaches are not entirely devoid of challenges pertaining to peri-operative moderate-to-severe pain and its persistence^{14,15}.

Understanding the risk factors that contribute to the exacerbation and persistence of peri-operative pain in patients undergoing hernia repair is imperative¹⁶. Previous research has demonstrated that these patients often exhibit altered pain threshold, as well as heightened pain intensity when compared to healthy volunteers¹⁷. Moreover, this patient population frequently manifests signs of pain sensitization¹⁸. Maladaptive cognitive responses to pain and hernia often result in long-term psychological stress, including anxiety, depression, and fear of enduring pain or losing functionality¹⁹. Patients who are inadequately informed about the surgical procedure, peri-operative analgesia, and strategies for coping with stress and pain may engage in catastrophic thinking, exacerbating acute pain and prolonging its course^{20,21}. Therefore, the genesis and perpetuation of peri-operative pain are multifactorial, influenced not merely by physical determinants such as surgical trauma and comorbid conditions, but also significantly modulated by the psychological capacity to cope with such pain^{22,23}. Consequently, the refinement of perioperative multimodal analgesia should encompass a more comprehensive, psychosomatic multimodal approach²⁴. Pain neuroscience education (PNE) has emerged as a viable cognitive therapeutic intervention for pain management. It typically involves elucidating the etiological underpinnings and remedial strategies of pain sensitization, promoting patient engagement in rehabilitative exercise and cognitive modifications. PNE is also aimed at bolstering patients' psychological resilience and cognitive fortitude against pain, recommendations for adapting peri-operative lifestyle behaviors such as sleep patterns and physical exercise. It also encouraged active patient involvement in the analgesic regimen and provides a platform for real-time feedback, bolstered patients' psychological resilience and cognitive fortitude against pain^{25,26}. These components collectively contribute to enhanced pain control, improved quality of life, and augmented physical functionality²⁷, yet, its use in peri-operative setting are still rare and its effect is undefined²⁸.

In this randomized controlled study, to minimize post-operative complications, augment patient comfort, and expedite physical recuperation, we have meticulously crafted a peri-operative pain neuroscience education (PNE) protocol specific to laparoscopic inguinal hernia repair, which aimed to help patients coping with surgically-induced pain associated with this procedure. We synergistically pair this customized PNE protocol with traditional perioperative multimodal analgesia in patients undergoing laparoscopic inguinal hernia repair. Our study aims to contrast the intensity, characteristics, and duration of peri-operative pain in this cohort against a control group receiving conventional analgesia alone. This investigation thus aspires to pioneer a novel psychological approach in analgesic management for patients undergoing laparoscopic inguinal hernia repair.

Methods

Procedure

Upon rigorous review by the Institutional Review Board of the First Affiliated Hospital of Chongqing Medical University, this study received formal approval (IRB Number: 2022-068) and subsequent registration at Chinese Clinical Trial Registry (ChiCTR2200058634) on 12 April, 2022. It was conducted in a university-affiliated tertiary medical institution, this prospective, randomized controlled investigation strictly adhered to the ethical stipulations delineated by the Declaration of Helsinki as well as the requirements set forth by the Institutional Review Board. Prior to commencing the study, informed consent was meticulously procured from all eligible participants. Subjects undergoing elective laparoscopic inguinal hernia repair were enrolled during the period extending from May 1, 2022 to December 31, 2022 after completion of trial registration. The reporting of this trial was in strict compliance with the Consolidated Standards of Reporting Trials (CONSORT) statement²⁹. The protocol of the trial was uploaded as attached files.

Subsequent to acquiring informed consent, candidates were recruited from the Department of General Surgery. Inclusion criteria encompassed the following prerequisites: provision of informed consent prior to study initiation, laparoscopic inguinal hernia repair as the elected procedure, age range of 18 to 80 years, body mass index (BMI) ranging from 18 to 30, and American Society of Anesthesiology (ASA) grading between I and III. Exclusion criteria included ASA grading exceeding III; New York Heart Association (NYHA) grading surpassing III; perioperative mental disorders; compromised cognitive function as assessed by the Mini-Cog test (with criteria < 2); pregnancy; pre-operative history of gastrointestinal surgery; conversion from laparoscopic to open surgical modality; re-operation necessitated by hemorrhage or infection; participants who, despite prior informed consent, opted out of the follow-up; intraoperative cardiac arrest; and subjects unable to be extubated in the post-anesthesia care unit.

Sample size calculation

Preliminary data indicated an approximate 35% incidence rate of acute moderate-to-severe postoperative pain upon motion following laparoscopic inguinal hernia repair, this outcome was defined as the visual analogue score (VAS) for pain ≥ 4 while the participants were engaged in ambulatory activity or other forms of motility 12 h post-operatively before rescue analgesia. Anticipating a 15% reduction in incidence upon implementing peri-operative pain neuroscience education in conjunction with traditional multimodal analgesia, the minimum requisite sample size for each group to achieve statistical significance was calculated to be 90 subjects. This calculation factored in a projected 10% attrition rate over the course of the follow-up period. The study was designed to achieve a statistical power of 90% at a Type I error rate of 0.05.

Allocation, randomization, and blinding

A total cohort of 184 patients was algorithmically assigned in a balanced 1:1 ratio to either the optimized Analgesia cohort or the conventional multimodal analgesia cohort. Randomization was conducted using computer-generated random numbers encapsulated within opaque blocks, accommodating eight patients for each block, to ensure an equitable distribution amongst all eligible participants, the computer. The 184 subjects

were divided into 23 blocks. For each divided block, a simple randomization method can be used to obtain the grouping result: first the statistician give the subject number (1–8) in each block, and then randomly take 8 random numbers from a certain position in the random number table to each subject in each block, and sequence each random number according to its size. Subjects with random numbers in the range of 1–4 in each group were assigned to PNE group, and subjects with random numbers in the range of 5–8 were assigned to conventional analgesia group. Each patient was assigned a unique randomized identification code, formatted as “PNE-##” (where ## ranged from 01 to 184). This data was securely housed in an encrypted digital repository, with exclusive accessibility granted solely to the overseeing statistician.

Methodologically, the study adopted a single-blind design, in which evaluators remained impartial and uninformed regarding patient group assignments, perioperative analgesic regimens, surgical procedure, perioperative analgesia, while the anesthesiologists and patients were aware of whether they received pain neuroscience education or not. It is crucial to note that the faculty responsible for outcome assessments remained blind to the group allocations and specific interventions, thereby maintaining the study’s methodological rigor. For patients who were discharged, remote follow-up was conducted via online platforms or telephonic communication to secure ongoing outcome measurements.

Conventional analgesia group

The conventional multimodal postoperative pain management comprised preoperative ultrasound-guided ilioinguinal/iliohypogastric nerve blockade (utilizing ipsilateral or bilateral administration of 20 mL of 0.33% ropivacaine) and intraoperative administration of sufentanil (0.3–0.6 µg/kg) and remifentanil (7–8 µg/kg/h). As all patients are asked to be discharged within 24 h after surgery, these patients were monitored and treated in the ambulatory ward. In the post-anesthesia care unit (PACU), all patients received the loading medication for analgesia as tramadol hydrochloride at 0.4 mg/kg. After extubation, patients who were fully awake and feeling pain for the first time were assessed for pain while lying supine in bed, those with numerical rating scale larger than 4, intravenous parecoxib at a dose of 40 mg (with an 80 mg daily maximum) or flurbiprofen at a dose of 50 mg (with a 100 mg daily maximum) was administered before the transfer from PACU to ambulatory ward. In the ambulatory ward, patients complained moderate-to-severe pain 12 h post-operatively were given opioid rescue agents—either fentanyl at doses ranging from 25 to 50 µg or morphine ranging from 2.5 to 5 mg. At the time of discharge, oral analgesics—either celecoxib or compound tramadol hydrochloride tablets—were prescribed for prevention of rebound pain after discharge. A transitional pain service team, composed of anesthesiologists, nurses, and surgeons, conducted routine patient visits at 4–6 h intervals until the time of the patients’ discharge, on-line or telephone contact were conducted for the obtaining of pain scores and related parameters.

PNE group

In addition to conventional multimodal analgesic regimen delineated previously, patients allocated to the pain neuroscience education (PNE) group received an enriched educational intervention focusing on the pathogenesis and cognitive coping of surgical pain. Upon admission for surgical intervention, these individuals were afforded an in-depth consultation detailing the PNE paradigm, which was bifurcated into preoperative educational encounters (two sessions) and postoperative feedback sessions (two instances).

The inaugural preoperative consultation encapsulated salient aspects such as the pathophysiological underpinnings of surgical pain, the contributors to heightened pain sensitization, behavioral modification recommendations, and cognitive coping strategies for patients. The second preoperative briefing demystified the surgical procedure, elucidated the mechanisms of multimodal analgesia, expounded upon contingency plans for rescue analgesia, and discussed strategies for optimizing sleep, while also laying the groundwork for postoperative feedback concerning pain management. Pedagogical materials, including patient brochures and powerpoint presentations, were employed to facilitate both online and offline education. Each session was meticulously designed to span a duration of 1 h.

Subsequent to the surgical intervention, postoperative feedback sessions were conducted at both 24 and 48-h intervals. These interactions accentuated key tenets such as the imperative of adhering to the prescribed analgesic regimen, discourse on issues and satisfaction levels related to pain control, alternative therapeutic approaches, assessment and optimization of sleep quality, incentivizing ambulatory behavior and physical exercise, as well as addressing any patient queries pertaining to analgesia. Each postoperative session was structured to occupy a 1-h duration of time. The first session was conducted at the time of discharge, which the second one was implemented online in a face-to-face manner.

Formatted metaphors employed as educational tools within the perioperative PNE framework are comprehensively outlined in Fig. 1 and Appendix 1. The PNE protocol was executed by a cadre of two seasoned anesthesiologists who were scrupulously uninvolved in patient recruitment, allocation, or the assessment of outcomes. Except for the difference in peri-operative analgesia, all patients in both groups received identical peri-operative protocol of analgesia and surgery (Appendix 2).

Measures

Baseline measures included age, gender, body mass index (BMI), years of formal education, smoking history, American Society of Anesthesiologists (ASA) grading, pre-operative serum albumin concentrations, laterality of the surgical site (bilateral or ipsilateral), and the specific variant of laparoscopic procedure being performed. Cardiopulmonary reserve functionality was meticulously assessed according to the New York Heart Association (NYHA) classification system. On the pre-operative day, the psychological well-being of eligible patients was quantified employing the validated Hospital Anxiety and Depression Scale (HADS)³⁰. Both the surgical and anesthetic durations were also recorded.

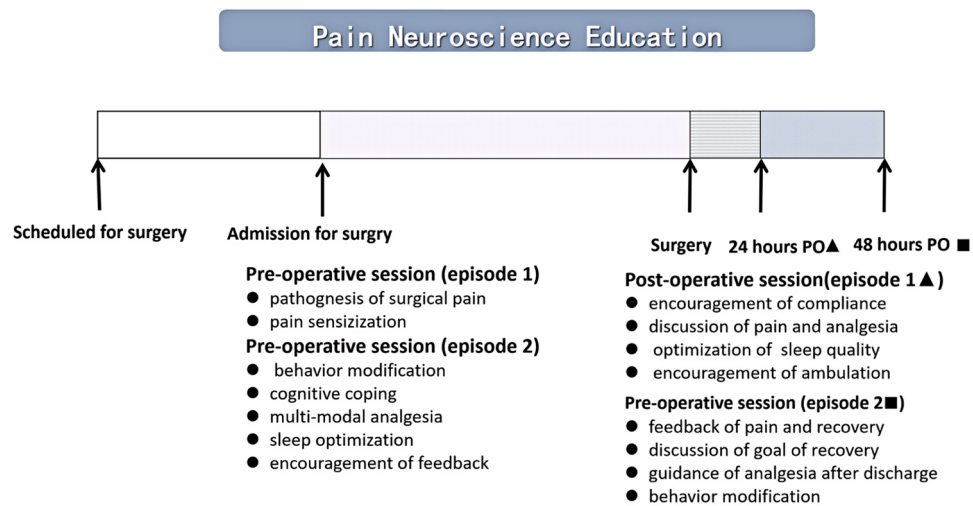


Fig. 1. Work flow of pain neuroscience education for patients receiving laparoscopic inguinal hernia repair.

The primary measure was moderate-to-severe pre-operative pain 12 h post-operatively before rescue analgesia (MTSP). The intensity of post-operative pain was measured while the participants were in motion through the utilization of the Visual Analogue Scale (VAS).

The secondary measures were as follows:

1. The quantification analysis of intensity of post-operative pain and a 0–10 mm calibration scale was also employed for the visual analogue scale in pain assessment. The timepoints for assessing post-operative pain were 12, 24, 48, 72, 96 h and 1 month post-operatively as the worst grading of pain on that day. The incidence of moderate-to-severe pain 24 h post-operatively (VAS ≥ 4 regardless of rescue analgesia) was also recorded.
2. The characteristics of pain were systematically explored through the Douleur Neuropathique Questionnaire (DN-4) and the Pain Catastrophizing Scale (PCS)^{31,32}, thus probing the neuropathic and catastrophizing components, respectively. Complementary to this, the central sensitization Inventory (CSI) and pressure pain threshold evaluations were implemented to assess pain sensitization mechanisms^{33,34}. Pressure pain threshold was ascertained via a handheld pressure algometer (Wagner Instruments, Greenwich, CT, USA) featuring a 1 cm² round rubber tip that made contact with the patient's skin³⁴. The timepoints for calibration of pain thresholds were 24 h pre-operatively, 6, 12 and 24 h post-operatively. An anatomical line situated 2 cm above and parallel to the inguinal ligament was elected for pre-operative measurements, with the more painful site chosen for bilateral repairs. Following a preliminary demonstration, the investigator applied pressure at a consistent rate of approximately 1 kg/s until the patient reported a VAS score equal to or greater than 4. The displayed pressure on the algometer was subsequently documented as the patient's pressure pain threshold. To mitigate any risk of injury or discomfort, the maximum exerted force was confined to 15 kg. The mean value was calculated based on three distinctive anatomical points along the chosen line (medial, middle, and lateral points) (Appendix 3)³⁴. Pain Catastrophizing Scale (PCS) and central sensitization Inventory were rigorously assessed at time points of 12 h, at the time of hospital discharge (24 h post-operatively), 72 h and 1 month post-operatively. Douleur Neuropathique Questionnaire (DN-4) was assessed 24 h pre-operatively and post-operatively. On line interview with the assistance of video was used for the calibration of the characteristics of post-operative pain after participants' discharge.
3. Perioperative quality of life, which was assessed using the EuroQol Five Dimensions Questionnaire (EQ-5D-5L), encompassing domains such as mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. To mitigate any translational biases, the validated Chinese version of the questionnaire was employed³⁵. Each dimension was rated on a Likert scale ranging from 0 to 4, which respectively indicated 'no problem' to 'extremely severe problem.' Quality of life was assessed the day before surgery, 24 and 72 h, as well as upon 96 h post-operatively, and at 1 and 3 months subsequent to the surgical procedure.
4. Analgesic satisfaction score, it served as a subjective evaluation metric at the time of hospital discharge, constituting an amalgamation of parameters including informed consent, medication strategy, technical execution, and overall patient experience. This was gauged utilizing a 0–10 point Likert scale, wherein a score of zero epitomized complete dissatisfaction and a score of ten indicated unequivocal satisfaction.
5. Chronic Post-Surgical Pain (CPSP), the diagnostic criteria for Chronic Post-Surgical Pain (CPSP) were rigorously adhered to, as delineated by the International Association for the Study of Pain (IASP)³⁶.
6. Post-operative rescue analgesia, which included the frequencies of analgesic rescue events (both non-opioid and opioid episodes), dosages of post-operative analgesic rescue medications, specifically the dosage of opioids utilized for peri-operative routine and rescue interventions, were recorded and subsequently transmuted into intravenous equianalgesic ratios vis-a-vis morphine³⁷.

Statistical analysis

Data were subjected to rigorous statistical analysis utilizing the Statistical Package for the Social Sciences (SPSS) version 23.0, provided by SPSS Inc., Chicago, IL, USA. An initial descriptive examination was executed for all variables under consideration. For continuous variables exhibiting a normal distribution, metrics were conveyed as mean values accompanied by the standard deviation (SD). Alternatively, non-normally distributed continuous variables were articulated through their median values, encapsulated within an interquartile range (IQR). Enumeration data were delineated by presenting both the aggregate sample size and the corresponding percentage distributions. Subsequent inferential statistical techniques were judiciously selected based on the inherent characteristics of the data. For continuous variables, a myriad of parametric and non-parametric tests were employed, including but not limited to the Independent t-test, Wilcoxon Rank-Sum test, Kruskal-Wallis test, and Repeated Measures Analysis of Variance (ANOVA), each contingent on the underlying data distribution. Categorical data were scrutinized through Chi-square tests, supplanted by Fisher's Exact tests in instances where the event count was less than five. To ascertain determinants potentially influencing the occurrence of moderate-to-severe pain till 24 h post-operatively, univariable analyses were initially performed. Subsequent to this, variables that exhibited a significance level where $p < 0.20$ were included in a multivariate logistic regression model to identify independent risk factors correlated with the primary outcome. Effect size for primary outcomes were expressed as Odds Ratios (OR) or standard mean difference with their respective 95% Confidence Intervals (95% CI). Adhering to the principle of Intention-To-Treat (ITT) analysis, all data were treated consistently, thereby enhancing the internal validity of the study. A two-tailed significance level was employed across all statistical evaluations, wherein a p value of less than 0.05 was considered indicative of a statistically significant discrepancy or association.

Results

Baseline demographics and clinical characteristics

Upon obtaining informed consent, a total of 234 patients were screened for study eligibility. Of these, 50 were subsequently excluded due to non-compliance with the inclusion criteria or voluntary withdrawal from the study. The final cohort comprised 184 patients, who were stratified into two treatment arms: the optimized analgesia group (group PNE, $n=93$) and the conventional multi-modal analgesia group (group CA, $n=91$). A diminution in participant numbers was observed at the 3-month follow-up, with 10 patients from the PNE group and eight from the CA group being unavailable for the per-protocol analysis of chronic post-surgical pain (CPSP). Adherence to the CONSORT guidelines was rigorously maintained throughout the reporting of this study's workflow (Fig. 2). Comprehensive baseline characteristics of the qualified participants are systematically tabulated in Table 1. No adverse events occurred during the conduction of the trial and follow-up related to interventions of the trial.

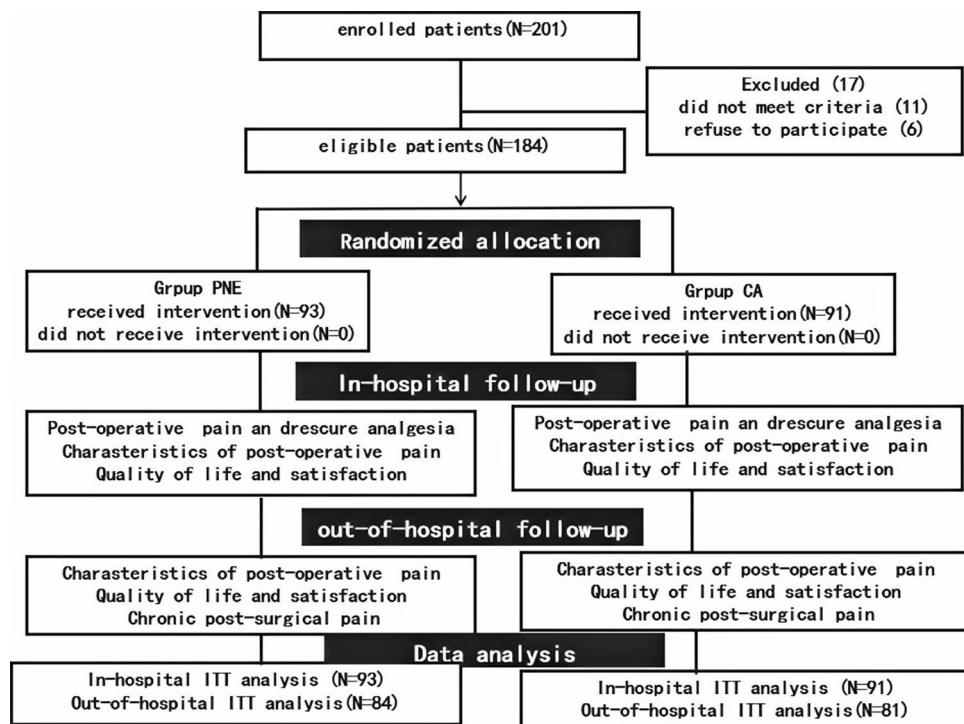


Fig. 2. The workflow of study following CONSORT statement.

Pre-operative characteristics	Group PNE (N = 93)	Group CA (N = 91)	p value
Age (years)—Mean \pm SD	55.2 \pm 16.4	56.8 \pm 18.0	0.221
Male sex—no. (%)	63 (60)	59 (59)	0.345
Body mass index (kg/m ²)—Mean \pm SD	22.1 \pm 4.5	22.7 \pm 5.3	0.113
NYHA grade II–III—no. (%) ^a	78 (83.9)	81 (89)	0.318
Current smokers—no. (%)	34 (36.6)	36 (39.6)	0.110
Pre-operative hemoglobin (g/L)—Mean \pm SD	116 \pm 29	118 \pm 32	0.120
Pre-operative albumin (g/L)—Mean \pm SD	34.5 \pm 7.8	35.2 \pm 8.0	0.410
Education year—Mean \pm SD	13.1 \pm 5.2	13.7 \pm 6.4	0.113
Anxiety subscore of HADS—(Mean \pm SD) ^a	13 \pm 5.9	12 \pm 5.7	0.283
Depression subscore of HADS—(Mean \pm SD)	14 \pm 6.2	13 \pm 5.6	0.164
ASA grading ^b			
Grade I—no. (%)	6 (6.5)	7 (7.7)	
Grade II—no. (%)	53 (57.0)	48 (52.7)	
Grade III—no. (%)	34 (36.5)	36 (39.6)	0.430
Chronic pain at surgical site—no. (%) ^c	67 (72.0)	63 (69.2)	0.195
Pre-operative pain intensity at surgical site			
VAS score at rest—Mean \pm SD	2.1 \pm 1.0	2.3 \pm 0.9	0.209
VAS score in motion—Mean \pm SD	5.6 \pm 1.7	5.7 \pm 1.9	0.301
Pre-operative moderate-to-severe pain—no. (%) ^d	38 (40.9)	39 (42.3)	0.110
Intra-operative characteristics			
Time of anesthesia (min)—Mean \pm SD	89.7 \pm 16.4	92.2 \pm 19.0	0.219
Time of surgery (min)—Mean \pm SD	76.5 \pm 15.8	78.4 \pm 16.2	0.301
Types of surgery			
Transabdominal preperitoneal hernioplasty (TAPP)—no. (%)	67 (72.0)	64 (70.3)	0.145
Totally extraperitoneal hernioplasty (TEP)—no. (%)	26 (28.0)	27 (29.7)	0.119
Other procedure—no. (%) ^e	3 (3.3)	6 (6.6)	0.566
Site of procedure			
Bilateral—no. (%)	35 (37.6)	30 (33.0)	
Ipsilateral—no. (%)	58 (62.4)	61 (67)	0.507

Table 1. Baseline characteristics of eligible patients. Student t test was used for the comparison of means \pm SD. Chi square test or Kruskal–Wallis test was used for the comparison of number. Wilcoxon rank-sum test was used for the comparison of median (Interquartile Range). ^aNYHA was for New York Heart Association, HADS was for Hospital Anxiety and Depression Scale. ^bASA grading was advocated by American Society of Anesthesiologists. ^cChronic pain at surgical site was defined if the patients complained pain at surgical site for more than 3 months. ^dPre-operative moderate-to-severe pain was defined as visual analogue scale for pain in motion \geq 4. ^eOther types of surgery included intra-abdominal patch implantation (IPOM), robot-assisted procedure etc.

Acute post-operative pain intensity metrics

Twelve hours subsequent to surgical intervention, the incidence of moderate-to-severe pain in motion (MTSP) was manifestly lower in the PNE group at 22.8%, compared to 39.7% in the CA group ($p = 0.004$) (OR 0.395 95% confidence interval [0.207–0.753]). Further, the PNE group exhibited a statistically significant reduction in post-operative pain intensity in motion (4.4 ± 2.9 vs. 5.5 ± 3.1 ; $p = 0.034$) (SMD 0.36 95% confidence interval [0.056–0.717, $p = 0.042$]). This trend persisted at the 24, 48, and 72-h post-operative timepoints. However, no significant disparities were identified in pain intensity at the time of discharge or at 1-month follow-up (Fig. 3).

Characterization of peri-operative pain phenotypes

The pre-operative prevalence of neuropathic pain, as determined by the Douleur Neuropathique 4 questionnaire (DN-4 \geq 4), did not differ significantly between the PNE and CA groups (11.8% vs. 10.8%; $p = 0.858$). Additionally, pre-operative pressure pain thresholds were equivocal across both cohorts. Post-operatively, the PNE group exhibited a more precipitous decline in the incidence of neuropathic pain at the 12 and time of discharge (4.3% vs. 13.2% and 4.3% vs. 9.9%; $p = 0.032$ and 0.139, respectively). Moreover, the PNE group revealed a significant elevation in pain pressure threshold when juxtaposed with the CA group (Fig. 4). A congruent pattern was observed with respect to the pain catastrophizing Scale and the central sensitization inventory (Figs. 5 and 6). No statistical difference was found for DN-4 \geq 4 24 h post-operatively (8.4% vs. 9.2%; $p = 0.310$).

Quality of recovery, patient satisfaction, and chronic post-surgical pain

Initial assessment via the EQ-5D-5L questionnaire revealed no significant disparities in sub-scores between the two experimental cohorts on the day of surgical admission. At the 24-h post-operative juncture, divergent

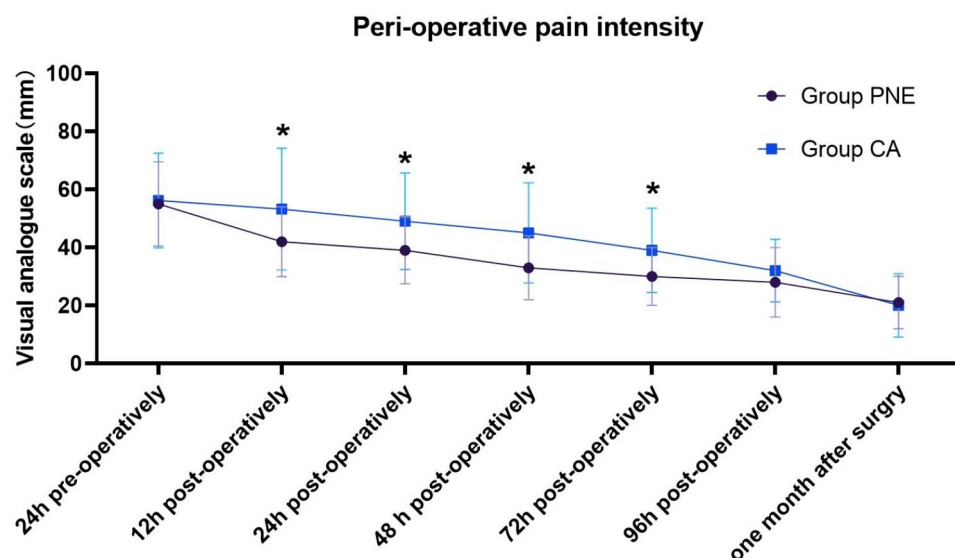


Fig. 3. Peri-operative pain intensity(in motion). *Significant statistical difference was found between the two groups, $p < 0.05$.

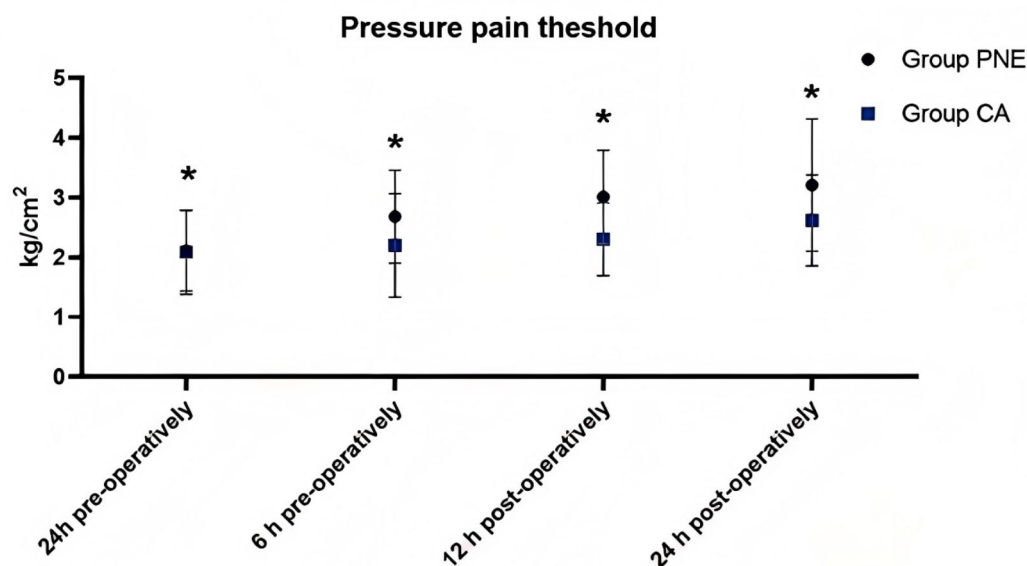


Fig. 4. Peri-operative pressure pain threshold. *Significant statistical difference was found between the two groups, $p < 0.05$.

patterns were observed in the realms of pain/discomfort and anxiety/depression between the two groups (1[1–1] vs. 2[2–2], $p = 0.022$; 1[1–1] vs. 2[2–3], $p < 0.001$). This trend persisted at the 72-h post-operative assessment. However, upon discharge and at the 1-month follow-up, the groups converged to a state of statistical parity in all EQ-5D-5L sub-score dimensions (Table 2). Three months post-operatively, the data showed no statistically meaningful difference in the incidence of chronic post-surgical pain (3.2% in the PNE group vs. 3.0% in the CA group, $p > 0.05$). Additionally, at the time of discharge, the PNE cohort exhibited a markedly enhanced analgesic satisfaction score (9.1 ± 1.5 vs. 6.7 ± 2.1 , $p = 0.013$).

Opioid consumption and incidence of rescue analgesia

The frequency of analgesic rescue episodes was notably fewer in the PNE group, with 24 instances, compared to 45 in the CA group (25.8% vs. 49.4%; $p = 0.001$). In terms of intra-operative opioid consumption, calculated as intravenous morphine equianalgesic ratios, no statistically significant difference was observed between the PNE

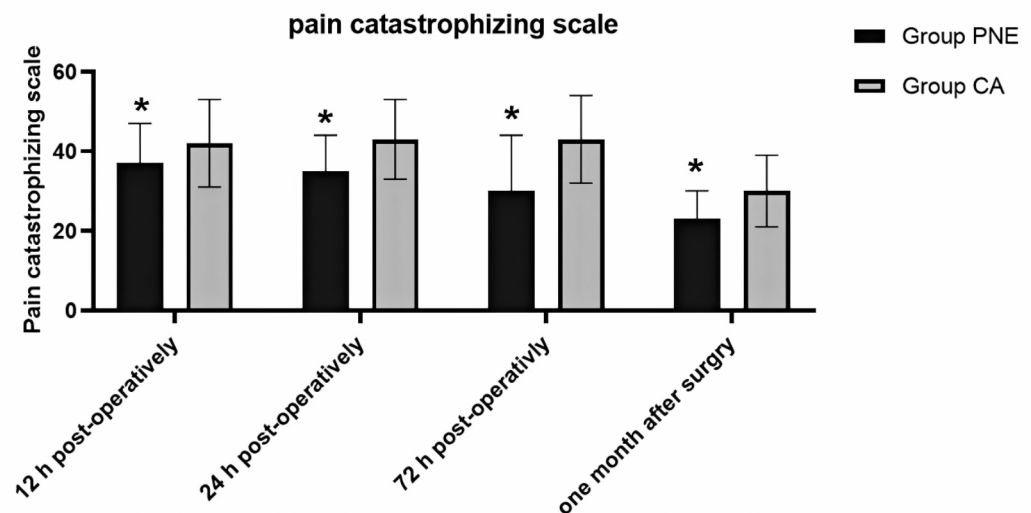


Fig. 5. Post-operative pain catastrophizing scale. *Significant statistical difference was found between the two groups, $p < 0.05$.

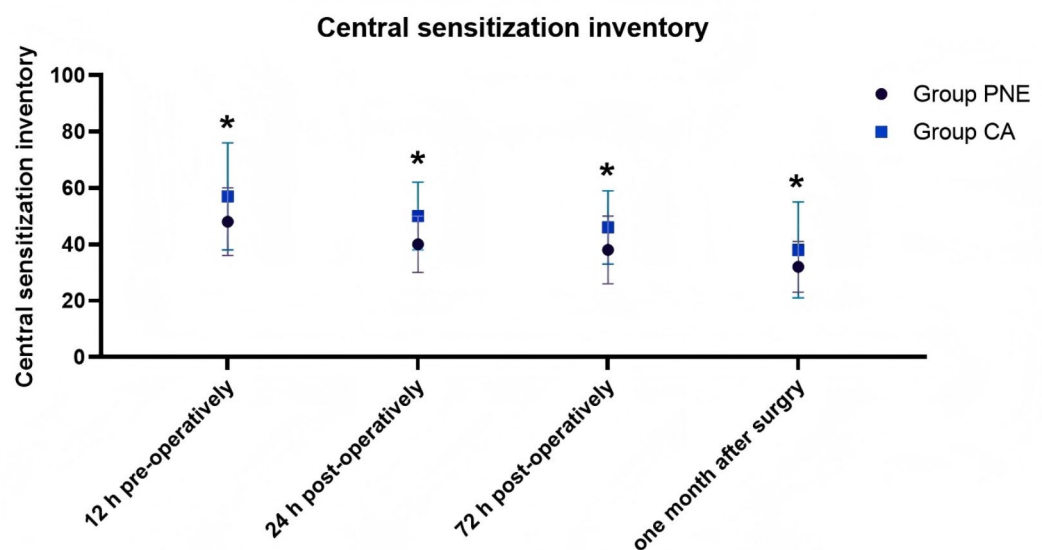


Fig. 6. Post-operative central sensitization inventory. *Significant statistical difference was found between the two groups, $p < 0.05$.

group (4.8 ± 1.4) and the CA group (5.3 ± 2.1 ; $p = 0.205$). In the post-operative period, however, the PNE group necessitated significantly reduced opioid dosages for rescue analgesia (0.30 ± 0.15 vs. 0.50 ± 0.21 ; $p = 0.024$).

Determinants of acute post-operative pain intensity

To elucidate the contributory factors influencing acute moderate-to-severe post-operative pain in motion till 24-h post-operatively, an initial univariate regression analysis was executed. Subsequently, variables demonstrating noteworthy influence ($p < 0.20$) were incorporated into a multivariate regression model to further investigate the same primary outcome (Table 3). The derived model indicated that preoperative moderate-to-severe pain at the surgical site, in conjunction with preoperative anxiety (as quantified by a Hospital Anxiety and Depression Scale [HADS] subscore ≥ 8) or depression (HADS depression subscore ≥ 8), were discernible risk determinants for augmented post-operative pain intensity (Table 4).

Discussion

This study represents a randomized controlled investigation aimed at integrating peri-operative pain neuroscience education (PNE) into the analgesic management framework for patients undergoing laparoscopic inguinal hernia

Quality of recovery—median (interquartile range)*	Group PNE (N=93)	Group CA (N=91)	p value*
24 h post-operatively			
#Mobility	2 (2–3)	2 (2–3)	0.108
Self-care	2 (2–3)	2 (2–3)	0.211
Usual activity	2 (2–2)	2 (2–3)	0.056
#Pain/discomfort	1 (1–2)	2 (2–2)	0.022
#Anxiety/depression	1 (1–1)	2 (2–3)	<0.001
72 h post-operatively			
Mobility	1 (1–2)	1 (1–2)	0.210
Self-care	2 (1–2)	2 (1–2)	0.176
Usual activity	2 (1–2)	2 (1–2)	0.270
#Pain/discomfort	1 (1–2)	2 (2–2)	0.021
#Anxiety/depression	1 (1–1)	2 (2–2)	<0.001
96 h post-operatively			
Mobility	0 (0–1)	0 (0–1)	0.301
Self-care	1 (1–1)	1 (1–1)	0.201
Usual activity	1 (1–1)	1 (1–1)	0.256
#Pain/discomfort	1 (1–1)	1 (1–2)	0.027
#Anxiety/depression	1 (1–1)	1 (1–2)	0.034
One month after surgery			
Mobility	0 (0–1)	1 (1–1)	0.501
Self-care	0 (0–1)	0 (1–1)	0.311
Usual activity	0 (0–1)	0 (0–1)	0.461
#Pain/discomfort	0 (0–1)	1 (1–2)	0.019
#Anxiety/depression	0 (0–1)	1 (1–2)	0.010
Three months after surgery			
Mobility	0 (0)	0 (0)	0.421
Self-care	0 (0)	0 (0)	0.404
Usual activity	0 (0–0)	0 (0)	0.381
Pain/discomfort	0 (0–0)	0 (0–0)	0.120
Anxiety/depression	0 (0–1)	0 (0–1)	0.090

Table 2. Quality of recovery measured with EuroQol five dimensions questionnaire (EQ-5D-5L). *Wilcoxon rank-sum test was used for the comparison of median (Interquartile Range). #Statistical difference was considered if p value < 0.05.

repair. Notably, our research elucidates that the incorporation of this non-pharmacologic intervention into a conventional peri-operative analgesic regimen, which could effectively mitigate both the intensity of acute post-operative pain and the requirement for rescue analgesia. This lends credence to the hypothesis that PNE offers an augmented analgesic effect in the post-operative phase. Additionally, the study's findings suggest that PNE significantly attenuates phenomena such as sensitization, catastrophizing, and the emergence of neuropathic components in post-operative pain, particularly during the immediate recovery phase following laparoscopic hernia repair. Furthermore, our analysis—employing the EQ-5D-5L questionnaire—corroborates the salutary impact of PNE on post-operative recovery in terms of quality of life, specifically in the dimensions of pain and psychological well-being (anxiety and depression). Given the rising prevalence of inguinal hernia patients who are notably predisposed to peri-operative pain and discomfort, this psychologically-oriented analgesic approach holds considerable promise for broader clinical implementation³⁸.

Patients afflicted with inguinal hernias frequently report chronic pain localized at the hernial sac site, exacerbated by activities such as exertion, standing, or coughing. Such discomfort poses a tangible impediment to daily functioning and overall quality of life³⁹. Laparoscopic tension-free mesh repair stands as a favored surgical option due to its lower propensity to induce chronic pain and its capacity to elevate patient satisfaction levels. Nevertheless, patients undergoing this procedure often continue to experience pain, which may persist and compromise daily activities^{40,41}.

Contemporary analgesic strategies, encompassing techniques like nerve block and judicious employment of opioid or non-opioid agents, have indeed demonstrated enhanced analgesic efficacy. However, the persistence or anticipation of post-operative pain often results in patient-led demands for elevated dosages of opioids or alternative analgesic agents, consequently elevating the risk of dependency and associated complications⁴². This scenario underscores the importance of non-pharmacologic analgesic interventions.

Among an array of such techniques—including cognitive therapy, virtual reality training or transcutaneous electrical stimulation—peri-operative PNE distinguishes itself by its capacity to recalibrate patients' cognitive and emotional responses to pain. This is especially pertinent for surgical patients who present with pre-existing

Influencing factors	12 h post-operatively			24 h post-operatively		
	Moderate-to-severe pain (n = 58)	Non-moderate-to-severe pain (n = 126)	p value	Moderate-to-severe pain (n = 43)	Non-moderate-to-severe pain (n = 141)	p value
Age ≥ 65 years			< 0.001			0.089
Yes	13	65		14	64	
No	45	61		29	77	
Body mass index (kg/m ²)—Mean \pm SD	22.3 \pm 4.0	22.6 \pm 3.9	0.273	23.0 \pm 5.7	22.6 \pm 4.8	0.210
Pre-operative moderate-to-severe pain at surgical site—n (%) ^a			< 0.001			< 0.001
Yes	40 (69.0)	37 (29.4)		27 (62.8)	50 (35.5)	
No	18 (31.0)	89 (70.6)		16 (37.2)	91 (64.5)	
Chronic pain at surgical site ^b —n (%)			0.140			0.663
Yes	41 (70.7)	88 (69.4)		29 (67.4)	100 (70.9)	
No	17 (29.3)	38 (30.6)		14 (22.6)	41 (29.1)	
Current smoker—n (%)			< 0.001			< 0.001
Yes	43 (74.1)	38 (30.2)		29 (67.4)	52 (36.9)	
No	15 (25.9)	88 (69.8)		14 (32.6)	89 (63.1)	
ASA grading ≥ 3			0.107			0.905
Yes	27 (46.6)	43 (34.1)		19 (44.2)	57 (40.4)	
No	31 (53.4)	83 (65.9)		24 (55.8)	84 (59.6)	
Pre-operative anxiety—Anxiety subscore of HADS ≥ 8			< 0.001			< 0.001
Yes	45 (77.6)	24 (19.0)		37 (86.0)	40 (28.4)	
No	13 (22.4)	102 (81.0)		6 (14.0)	101 (71.6)	
Pre-operative depression—Anxiety subscore of depression ≥ 8			< 0.001			< 0.001
Yes	44 (75.9)	26 (20.6)		30 (69.8)	28 (19.6)	
No	14 (24.1)	100 (79.4)		13 (30.2)	113 (80.4)	
Higher education level (year ≥ 9 years)			0.002			0.031
Yes	20 (34.5)	76 (60.3)		16 (37.2)	79 (56.0)	
No	38 (65.5)	50 (39.7)		27 (62.8)	62 (44.0)	
Bilateral surgery			< 0.001			< 0.001
Yes	40 (69.0)	25 (19.8)		29 (67.4)	36 (25.5)	
No	18 (31.0)	101 (80.2)		14 (32.6)	105 (74.5)	
Transabdominal preperitoneal hernioplasty (TAPP)			0.002			0.165
Yes	34 (58.6)	97 (77.0)		27 (62.8)	104 (73.8)	
No	28 (41.4)	29 (23.0)		16 (37.2)	37 (26.2)	
Duration of surgery (min)—Mean \pm SD	90.4 \pm 18.4	89.4 \pm 20.1	0.321	91.8 \pm 18.6	89.10 \pm 16.9	0.229

Table 3. Influencing factors of acute post-operative pain. Significant statistical difference was found between two groups, $p < 0.05$. ^aVisual analogue scale was used for evaluation of preoperative moderate-to-severe pain (VAS ≥ 4 in motion). ^bpre-operative chronic pain at surgical site was defined as chronic pain at surgical site of more than 3 months.

chronic pain conditions, often complicated by mental health comorbidities such as anxiety and depression, or fears concerning procedural failure and inability to return to normal life^{25,43}. Surgical patients enduring chronic pain, akin to the population targeted in this study, often exhibit predispositions toward catastrophizing, central sensitization of pain, and heightened nociceptive transmission stemming from surgical trauma^{44,45}. By acculturating patients to the surgical procedure, delineate the natural evolution of peri-operative pain, and illuminate the mechanisms of multi-modal analgesia, PNE serves as a procedure-specific cognitive therapeutic strategy for surgical pain. This tailored educational approach also facilitates the real-time feedback loop for post-operative pain and its management^{46–48}. It also Offered specialized counsel on surgical procedures and analgesia, which enabled patients to recontextualize their coping mechanisms and pain perceptions⁴⁹. Therefore, this novel psychologically-oriented analgesic approach has additional pain-reducing effect for this type of patients.

Several avenues exist to enhance the efficacy of PNE for pain management in surgical settings. Initial patient education could potentially be optimized by commencing at the point of the first hernia-related referral, and employing digital modalities such as online or telephonic consultations. The integration of additional non-pharmacological interventions may further potentiate the effectiveness of PNE. A multidisciplinary approach involving anesthesiologists, nursing staff, and surgeons, who collectively acknowledge the centrality of pain management and cognition-behavior education, could contribute to a more comprehensive care paradigm.

Influencing factors		Moderate-to-severe pain 12 h post-operatively		Moderate-to-severe pain 24 h post-operatively	
		OR (95% CI)	p value	OR (95% CI)	p value
Age ≥ 65 years	Yes	1	0.267		
	No	0.821 (0.713–1.389)			
Preoperative moderate-to-severe pain at surgical site*	No	1	< 0.001	1	< 0.001
	Yes	1.679 (1.438–2.109)		1.410 (1.212–1.935)	
Chronic pain at surgical site			0.216		0.372
	No	1		1	
Current smoker	Yes	1.117 (0.801–1.219)		1.016 (0.694–2.498)	
	No	1	0.380	1	0.419
Pre-operative anxiety—anxiety subscore of HADS ≥ 8*	Yes	1.964 (0.896–1.978)		0.801 (0.654–1.963)	
	No	1	< 0.001	1	0.012
Pre-operative depression—depression subscore of depression ≥ 8*	Yes	2.108 (1.795–2.874)		1.504 (1.180–2.106)	
	No	1	< 0.001	1	0.006
Bilateral surgery	Yes	2.2 (1.659–3.018)		1.899 (1.632–2.543)	
	No	1	0.078	1	0.195
Transabdominal preperitoneal hernioplasty (TAPP)	Yes	1.690 (0.811–3.930)		1.794 (0.790–2.189)	
	No	1	0.160	1	0.490
ASA grading ≥ 3	Yes	1.793 (0.862–2.319)		1.201 (0.763–1.855)	
	No	1	0.465	1	0.651
	Yes	0.690 (0.543–1.378)		0.773 (0.508–1.687)	
	No				

Table 4. Multivariate logistic regression analysis of risk factors of acute moderate-to-severe pain within 24 h post-operatively. *The prominent influencing factors for acute moderate-to-severe pain within 24 h post-operatively during multivariate logistic regression analysis ($p < 0.05$).

Limitations

1. Its single-center nature, devoid of multi-institutional collaboration, necessitates validation across a more heterogeneous patient cohort to ascertain the broader applicability of these findings.
2. The exclusion of patients with mild-to-severe cognitive impairments, although they might still benefit from the program, underscores the need for heightened scrutiny regarding pain and analgesia in this subset.
3. In an attempt to broaden the applicability of this regimen, the study did not stringently exclude patients with pain localized to sites other than the inguinal region; this introduces the complexity of managing pre-operative chronic pain of varied etiologies, thereby necessitating a more nuanced approach to PNE.
4. The relatively brief follow-up duration (3 months) precludes a comprehensive assessment of long-term psychological sequelae related to inguinal pain. Finally, as this investigation served as a pilot study focusing on pain, patient-reported quality of life, and psychological well-being, future research ought to consider the inclusion of stress-related biomarkers, particularly those linked to pain-induced psychological stress.

Conclusion

The incorporation of pain neuroscience education into a peri-operative multi-modal analgesia augments both the analgesic efficacy and quality of post-operative recovery vis-a-vis traditional analgesia for patients subjected to laparoscopic inguinal hernia repair. This innovative analgesic paradigm also demonstrates efficacy in attenuating sensitization and catastrophizing of acute surgical pain during the post-operative recovery phase, thereby meriting ongoing exploration and refinement in clinical settings.

Data availability

Datasets are available through the corresponding author upon reasonable request.

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Author contributions

Lihua Peng and Xiaonan Liu Contributed equally as Corresponding authors. Lihua Peng and Wenjian Wang designed the study, Wenjian Wang, Xiaonan Liu and Dong Zhang carried out the trial intervention. Lihua Peng collected the data. Lihua Peng and Xiaonan Liu analyzed the results. Lihua Peng and Dong Zhang drafted the article. All authors reviewed the final article and approved it for submission.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

Ethics approval was received from the Institutional Review Board of The First Affiliated Hospital of Chongqing Medical University (IRB number: 2022-068).

Additional information

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