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Incidence, Risk Factors, and Impact on Quality of Life of Patients with Chronic Post-Thoracotomy Pain: A Large-Sample Prospective Cohort Study

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ABSTRACT

Objective: The objective of this large-sample prospective cohort study was to investigate the incidence, risk factors, and impact on quality of life of patients with chronic post-thoracotomy pain (CPTP). CPTP, defined as pain lasting at least three months after surgery, poses a significant challenge for postoperative patients and negatively affects their recovery and overall quality of life.

Methods: The study was conducted in a tertiary hospital in Henan, China, from March 2022 to March 2023. A total of 2118 patients undergoing selective thoracic surgery were recruited and followed up for 12 months post-surgery. Patients were assessed for CPTP using the Numerical Rating Scale (NRS) at rest and during movement within two days post-surgery, and through telephone follow-ups at 3, 6, and 12 months. Quality of life was evaluated using the 8-item Short-Form Health Survey (SF-8) scale. Univariate and multivariate logistic regression analyses were performed to identify risk factors for CPTP.

Results: Of the 2118 patients, 1917 (90.5%) completed the 12-month follow-up, with an overall CPTP incidence of 28.5%. The major risk factors for CPTP included female gender (HR = 4.824, 95% CI: 1.825–12.734, P = 0.001), high preoperative anxiety (HR = 3.047, 95% CI: 1.224–7.585, P = 0.017), high preoperative depression (HR = 3.895, 95% CI: 1.493–10.162, P = 0.005), preoperative pain at the surgical site (HR = 1.266, 95% CI: 1.045–1.535, P = 0.016), no diabetes (HR = 1.299, 95% CI: 1.142–1.478, P < 0.001), thoracotomy surgery (HR = 4.720, 95% CI: 2.232–9.983, P < 0.001), non-receipt of combined patient-controlled intravenous analgesia (PCIA) and thoracic paravertebral block (TPVB) (HR = 5.389, 95% CI: 1.492-19.468, P = 0.010), and high maximum NRS scores at rest and during activity on the 14th postoperative day. CPTP patients showed significantly lower scores in various SF-8 domains, including physiological function, role, body pain, vitality, social function, mental health, and general health (all P < 0.001), indicating a profound impact on their quality of life.

Conclusion: CPTP affects a substantial proportion of patients after thoracic surgery, with multiple risk factors identified. The negative impact on patients' quality of life underscores the need for comprehensive interventions to prevent and manage CPTP, including preoperative psychological assessment and interventions, optimized surgical techniques, and multimodal postoperative pain management strategies.

Abbreviations: ASA: American Society of Anesthesiologists; BMI: Body Mass Index; CPTP: Chronic Post-Thoracotomy Pain; IASP: International Association for the Study of Pain; NRS: Numerical Rating Scale; PCIA: Patient Controlled Intravenous Analgesia; SF-8: 8-item Short-Form Health Survey; TPVB: Thoracic Paravertebral Block; F = Female; M = Male

Introduction

Chronic post-thoracotomy pain (CPTP) poses a significant and enduring challenge for postoperative patients. It not only persists for an extended period but can also severely hinder the patient's recovery process and diminish their overall quality of life. Notably, CPTP has a relatively high incidence rate and constitutes a major concern in the postoperative management of thoracotomy patients. According to the definition provided by the International Association for the Study of Pain (IASP), CPTP refers to pain that lasts for at least three months after surgery [1]. In thoracic procedures, particularly after thoracotomy, its incidence ranges from 25% to 57%, significantly higher than in other types of surgeries. Despite advancements in thoracotomy techniques as a crucial method for treating various thoracic diseases, CPTP remains prevalent. This chronic pain often exhibits neurogenic features such as a burning sensation and sensory disturbances, causing considerable distress to patients. Additionally, it affects patients' psychological states, leading to anxiety and depression, further reducing their quality of life. Multiple risk factors contribute to the development of CPTP [2].

Firstly, the patient's general condition, including age and sex, may influence the incidence of chronic pain, with female patients being more susceptible. Secondly, operational conditions play a vital role; factors such as intraoperative nerve injury and prolonged operation time can increase the risk of CPTP. Furthermore, CPTP may be associated with anesthesia methods, postoperative care, and other factors. It not only causes physical pain and activity limitations, affecting patients' daily lives and work, but also profoundly impacts their psychological and social functioning. Chronic pain can also lead to psychological issues such as anxiety and depression, further diminishing patients' quality of life. Long-term chronic pain may increase medical expenses for patients and impose a financial burden on families and society. While some studies have investigated the incidence of CPTP, its risk factors, and impacts on patients' quality of life, most have small sample sizes and employ various methods, leading to inconsistent results.

Therefore, the present study aims to systematically and comprehensively explore relevant issues of CPTP through a large-sample prospective cohort design. This will help us gain a deeper understanding of CPTP mechanism, risk factors, and impacts on patients' quality of life, providing more scientific and accurate references and foundations for clinical treatment and nursing.

Materials and Methods

General Information

This study, a prospective cohort research, is carried out strictly following the principle of Declaration of Helsinki, and has received the approval by the medical ethics committee of this hospital before starting [Ethical Approval No.: (2021) Lunshen No. (10-04)] and registered in Chinese Clinical Trial Registry (Registration No.: ChiCTR2200057438). It has acquired the approval by the medical ethics committee of this hospital and the informed consent form has been signed by the patient and the authorizer. The patients receiving selective thoracic surgery in Henan Provincial Chest Hospital & Affiliated Chest Hospital of Zhengzhou University during the period from March 2022 to March 2023 were recruited.

Inclusion criteria were as follows:

a) Patients receiving thoracic surgery who met the surgical indications;

b) Man and women;

c) Patients with the age of 18 to 65 years;

d) Patients with Class I to III by the American Society of Anesthesiologists (ASA);

e) Patients who were voluntary to receive relevant treatments and sign the informed consent form; and

f) Patients who can understand Numerical Rating Scale (NRS).

Exclusion criteria were as follows:

a) Patients receiving the emergency operation;

b) Patients who did not receive the surgery during the hospitalization;

c) Patients who had pulmonary infection or acute pulmonary infection uncontrolled pre-operatively or acute attack of chronic obstructive pulmonary disease;

d) Patients who did not regain consciousness postoperatively, those who were discharged without the doctor's order, or those who died in the perioperative period;

e) Patients with the definite diagnosis of serious coagulation disorders;

f) Patients with postoperative cerebral, hepatic and renal insufficiency;

g) Patients with serious infectious diseases;

h) Patients with incomplete clinical data; or

i) Patients who took drugs or had long-term use of psychotropic medicines, steroid or hormone drugs.

Patients' General Data

Patient's general information was recorded, with the main contents as follows:

1) Age: patient's specific age was recorded;

2) Gender: patient's gender was record;

3) Body mass index (BMI): the BMI value based on the patient's height and weight was calculated;

4) Years of education: the number of years of education corresponding to the highest academic qualification completed by the patient was recorded;

5) Marital status: patient's marital status, such as married, unmarried, divorced, widowed, etc. were recorded.

6) Living situation: patient's living conditions, such as living alone, living with family, or residing in a nursing home, etc. were described.

7) Occupation:patient's primary occupation or type of work was recorded;

8) Preoperative pain at the surgical site: patient's preoperative pain at the surgical site, including pain intensity and duration were assessed and recorded; and

9) Concurrent diseases: patients' current other diseases or health conditions were recorded.

Postoperative Medical Record Information

Surgical duration: Record the start and end time of the surgical procedure. Surgical name: Accurately record the specific name of the surgery the patient underwent. Anesthesia method: Detailedly document the anesthesia technique used during the surgical procedure.

Evaluation of Postoperative Pain and Analgesia

The postoperative analgesic methods were patient controlled intravenous analgesia (PCIA), thoracic paravertebral block (TPVB) or their combination, and the analgesia lasted until 2 d after surgery, and the maximal NRS score at rest and during movement within 2 d after surgery was recorded.

Assessment of CPSP

The occurrence of CPTP was tracked and documented through telephone follow-up interviews conducted at 3, 6, and 12 months post-surgery. The diagnosis of CPTP was performed by referring to the literature [1]: incisional pain occurs postoperatively and lasts for at least three months, which was not induced by the other factors (malignant transformation, incisional infection, other reasons before surgery). The patients were divided into CPTP and non-CPTP group based on the presence and absence of CPTP.

Assessment of Patients' Quality of Life

The 8-item Short-Form Health Survey scale (SF-8) was used for evaluation of quality of life by referring to the literature [3], which involved physiological function and role, body analgesia, energy and social function, as well as emotional role, mental health and general health. If there is no response to three telephone follow-up visits within one week, or the follow-up visit was refused, loss to follow-up was considered.

Loss to Follow-up Handling

If a patient does not respond after being contacted three times by phone within one consecutive week during each follow-up, or if the patient explicitly refuses to participate in the follow-up, the patient is considered lost to follow-up.

Statistical Methods

SPSS 18.0 was adopted for analysis. The measurement data normally distributed were expressed as mean ± standard deviation, and group t-test was used for inter-group comparison; those with skewed distribution were expressed as the median (inter-quartile range) [M (Q)] and rank sum test was employed for inter-group comparison; the enumeration data were compared by $\chi 2$ test. For the statistically significant factors on inter-group comparison, logistic regression analysis was performed, and $P < 0.05$ was considered statistically significant.

Results

Risk Factors for CPSP in the Two Groups of Patients

All 2118 patients completed the survey during the hospitalization period, and wherein, the 12-month postoperative follow-up was not completed in 201 (loss rate to follow up: 9.5%) while was completed in 1917 (success rate of follow up: 90.5%). The total incidence of CPTP was 28.5%, with the distribution proportion of disease course being 26.7% for the range of 3 months to 6 months, 16.8% for the range of 6 months to 12 months, and 42.5% for the range of ≥ 12 months. There were statistical differences in the ratio of female, pre-operative anxiety and depression score, pre-operative use of analgesic, pre-operative pain at the operative site, diabetes, hypertension, thoracotomy and PCIA combined with TPVB with the maximal NRS score 2 and 14 d after surgery between CPTP and non-CPTP group ($P < 0.05$), and no statistical difference was noted in the other indicators ($P > 0.05$), as shown in Table 1.

Multiple Logistic Aggression Analysis on Risk Factors of CPTP

The multivariate logistic regression analysis of risk factors for CPTP revealed that female patients had a significantly higher risk of developing CPTP compared to male patients (HR = 4.824, 95% CI: 1.825–12.734, P = 0.001). Patients with high preoperative anxiety scores had an increased risk of CPTP (HR = 3.047, 95% CI: 1.224–7.585, P = 0.017). Patients with high preoperative depression scores had a significantly increased risk of CPTP (HR = 3.895, 95% CI: 1.493–10.162, P = 0.005). Patients who experienced pain at the surgical site before the operation had a significantly increased risk of developing CPTP (HR = 1.266, 95% CI: 1.045–1.535, P = 0.016). Compared to

patients with diabetes, those without diabetes had a higher risk of CPTP (HR = 1.299, 95% CI: 1.142–1.478, P < 0.001). Patients who underwent thoracotomy had a significantly increased risk of CPTP (HR = 4.720, 95% CI: 2.232–9.983, P < 0.001). Patients who did not receive a combination of PCIA and TPVB had a significantly increased risk of CPTP (HR = 5.389, 95% CI: 1.492–19.468, P = 0.010). Patients with high maximum NRS scores at rest on the 14th postoperative day had an increased risk of CPTP (HR = 2.492, 95% CI: 1.313-4.729, P = 0.005). Patients with high maximum NRS scores during activity on the 14th postoperative day had a significantly increased risk of CPTP (HR = 3.117, 95% CI: 1.655–5.871, P < 0.001), as shown in Table 1.

Comparison of Living Quality Score Between the Two Groups

Patients in the CPTP group had significantly lower scores in physiological function [(8.5±2.0) vs (9.2±1.3), t = 9.028, P < 0.001], physiological role [(8.6±1.9) vs (9.4±1.3), t = 10.570, P < 0.001], body pain [(8.1±1.7) vs (9.1±1.6), t = 12.130, P < 0.001], vitality [(7.8±1.8) vs (8.2±1.5), t = 4.968, P < 0.001], social function [(9.3±1.3) vs (9.5±1.2), t = 3.215, P = 0.001], mental health [(9.3±1.3) vs (9.6±1.0), t = 5.420, P < 0.001], and general health [(6.1±1.7) vs (7.0±1.6), t = 10.920, P<0.001] compared to the Non-CPTP group. Emotional role scores were similar between the two groups [(9.3±1.4) vs (9.2±1.3), t = 1.478, P = 0.137], as shown in Tables 1-3.

Table 1: Screening of suspected risk factors of CPTP.

Items	CPTP group (N. =546)	Non-CPTP group (N. =1371)	t /Z/χ2 value	P value
Age (years)	44±12	43±13	1.553	0.121
Sex			96.11	<0.001
M	205 (37.5%)	853 (62.2%)		
F	341 (62.5%)	518 (37.8%)		
Marital status			0.446	0.979
Unmarried	118 (21.6%)	281 (20.5%)		
Married	275 (50.4%)	703 (51.3%)		
Divorced	62 (11.4%)	150 (10.9%)		
Widowed	49 (9.0%)	128 (9.3%)		
Remarried	42 (7.7%)	109 (8.0%)		
Inhabiting information			1.117	0.291
Living with the child (or parent)	93 (17.0%)	262 (19.1%)		
Living with the spouse	453 (83.0%)	1109 (80.9%)		
Occupation type			1.189	0.977
Civil servant	32 (5.9%)	84 (6.1%)		
Institution staff	48 (8.8%)	125 (9.1%)		
Employee	54 (9.9%)	148 (10.8%)		
Service staff	58 (10.6%)	138 (10.1%)		
Self-employed person	19 (3.5%)	51 (3.7%)		
Farmer	289 (52.9%)	698 (50.9%)		
Freelancer	46 (8.4%)	127 (9.3%)		
BMI (kg/m^2)	22.3±3.0	22.1±2.9	1.349	0.177
ASA classification			1.401	0.496
Class I	200 (36.6%)	541 (39.5%)		
Class II	265 (48.5%)	642 (46.8%)		
Class III	81 (14.8%)	188 (13.7%)		
Hypertension	103 (18.9%)	263 (19.2%)	0.026	0.873
Diabetes	35 (6.4%)	268 (19.5%)	50.645	<0.001
Coronary heart disease	28 (5.1%)	85 (6.2%)	0.808	0.369

Smoking	138 (25.3%)	379 (27.6%)	1.113	0.291
Drinking	126 (23.1%)	298 (21.7%)	0.408	0.523
Education years (years)	9.6±3.5	9.3±3.5	1.694	0.091
Pre-operative use of analgesic	108 (19.8%)	212 (15.5%)	5.233	0.022
Pre-operative pain at the operative site	156 (28.6%)	224 (16.3%)	36.767	<0.001
Preoperative chemotherapy	117 (21.4%)	260 (19.0%)	1.501	0.221
Preoperative radiotherapy	49 (9.0%)	121 (8.8%)	0.011	0.918
Preoperative anxiety score (score)	21.0±4.1	18.2±3.4	15.31	<0.001
Preoperative depression score (score)	27.9±4.7	24.4±4.0	16.42	<0.001
Operation type			24.587	<0.001
Thoracotomy	317 (58.1%)	624 (45.5%)		
Thoracoscopic surgery	229 (41.9%)	747 (54.5%)		
Operation time (min)	115 (130)	125 (135)	-1.955	0.051
Postoperative analgesia type			13.118	0.001
Patient controlled intravenous analgesia (PCIA)	213 (39.0%)	417 (30.4%)		

Table 2: Multiple Logistic aggression analysis on risk factors of CPTP.

Factors	B	SE	Wald $\chi 2$	P value	OR	95% CI
Female	1.547	0.495	10.097	0.001	4.824	1.825–12.734
Preoperative anxiety score	1.114	0.465	5.736	0.017	3.047	1.224–7.585
Preoperative depression score	1.36	0.489	7.719	0.005	3.895	1.493–10.162
Pre-operative pain at the operative site	0.236	0.098	5.813	0.016	1.266	1.045–1.535
No concurrent diabetes	0.262	0.066	15.86	<0.001	1.299	1.142–1.478
Thoracotomy	1.552	0.382	16.484	<0.001	4.72	2.232–9.983
No combination of PCIA and TPVB	1.684	0.655	6.607	0.01	5.389	1.492–19.468
Maximal NRS score at rest 14 d after surgery	0.913	0.327	7.799	0.005	2.492	1.313–4.729
Maximal NRS score during movement 14 d after surgery	1.137	0.323	12.393	<0.001	3.117	1.655–5.871

Table 3: Comparison of living quality score between the two groups.

Items	CPTP group (N. =546)	Non-CPTP group (N. =1371)	t value	P value
Physiological function sore (score)	8.5±2.0	9.2±1.3	9.028	<0.001
Physiological role (score)	8.6±1.9	9.4±1.3	10.57	<0.001
Body analgesia score (score)	8.1±1.7	9.1±1.6	12.13	<0.001
Energy score (score)	7.8±1.8	8.2±1.5	4.968	<0.001
Social function score (score)	9.3±1.3	9.5±1.2	3.215	0.001
Emotional role score (score)	9.3±1.4	9.2±1.3	1.478	0.137
Mental health score (score)	9.3±1.3	9.6±1.0	5.42	<0.001
General health score (score)	6.1±1.7	7.0±1.6	10.92	<0.001

Discussion

Defined by the IASP, CPTP encapsulates the enduring ache that persists for at least three months post-operation. Research both domestically and internationally has extensively tracked this phenomenon at 3, 6, and 12 months post-surgery, or even longer. Adhering to this practice, we conducted follow-ups at these crucial milestones to delve into the prevalence, risk factors, and the profound impact of CPTP on patients' quality of life through a meticulous, large-scale prospective cohort design. Our findings are compelling: CPTP affects an alarming 28.5% of patients, with a prolonged duration that extends to over 40% of cases even a year after surgery. This underscores CPTP as a pivotal clinical concern that necessitates heightened attention from both healthcare professionals and patients alike. Unraveling the tapestry of risk factors of CPTP, we discovered several pivotal threads. Notably, female patients emerged as more susceptible, potentially tied to sex-specific physiological and psychological nuances such as heightened pain sensitivity and intensified social-psychological stressors during the post-operative recovery phase.

Moreover, patients harboring high preoperative anxiety and depression scores bore an increased risk, emphasizing the imperative of preoperative psychological adjustment and the proactive administration of psychological interventions to mitigate the onset of CPTP [4]. Furthermore, the presence of preoperative pain at the surgical site significantly escalated CPTP risk, likely stemming from nervous tissue damage that complicates postoperative pain alleviation [5]. Intriguingly, non-diabetic patients stood at a higher risk, a phenomenon that may be rooted in diabetic patients' metabolic traits, particularly diabetic peripheral neuropathy, which can impair pain perception. Of particular note, thoracotomy stands as an independent risk factor for CPTP. Its greater surgical trauma and complexity, in comparison to thoracoscopic surgery, predispose patients to postoperative nerve injury and inflammatory responses, thereby escalating CPTP risk [6]. Hence, surgical method selection must meticulously consider the patient's specific condition and surgical risks, favoring minimally invasive approaches with expedited recovery whenever feasible.

Postoperative pain management also emerged as a pivotal aspect. Patients forgoing the combination of PCIA and TPVB experienced a heightened CPTP incidence, highlighting the crucial role of postoperative pain management in CPTP prevention. By embracing multimodal analgesia and individualized pain management strategies, we can effectively mitigate postoperative pain and potentially reduce the prevalence of CPTP [7]. Utilizing the SF-8, we comprehensively assessed patients' postoperative quality of life, encompassing physiological function and role, bodily pain, vitality, social function, emotional role, mental health, and general health [8]. Notably, CPTP patients scored lower in all domains except emotional role, underscoring multifaceted impact of CPTP, extending beyond physical pain to profound psychological and social repercussions. Thus, postoperative management must prioritize not just surgical outcomes and complication prevention but also pain management, ensuring timely interventions to alleviate CPTP and enhance patients' overall well-being.

In conclusion, CPTP represents a pervasive and formidable challenge that significantly undermines patients' quality of life. Our study sheds new light on the prevalence, risk factors of CPTP, and underscores the significance of psychological interventions and postoperative pain management. As we forge ahead, further research must delve into the pathogenesis and treatment strategies of CPTP, striving to better prevent and manage this common complication. It is imperative that we emphasize the prevention and treatment of CPTP, harnessing preoperative assessments, psychological interventions, surgical method optimization, and pain management to diminish the incidence of CPTP and elevate patients' quality of life.

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Conflicts of Interest

The authors declare that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' Contributions

Juan Shu and Yanjiao Zhang have given substantial contributions to the conception or the design of the manuscript, Wei Zhong, Yanjiao Zhang and Gaoyuan Xi to acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript, Junhui Zhou revised it critically. All authors read and approved the final version of the manuscript.

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