

Chronic pain following thoracotomy for lung surgeries: It's risk factors, prevalence, and impact on quality of life - A retrospective study

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ABSTRACT

Background and Aims: Chronic post thoracotomy pain (CPTP) is a nagging complication and can affect quality of life (QOL). Studies conducted across globe have found a wide variability in the risk factors predisposing to chronic pain following thoracotomy. As no study on CPTP is available from India, we aim to detect the prevalence of CPTP, assess the predisposing factors implicated in its causation and study the impact of CPTP on QOL. **Methods:** After obtaining clearance from Institutional ethics committee, medical records of patients who underwent open posterolateral thoracotomy between January 2012 and December 2015 were reviewed. Data on perioperative variables, address, and contact number were collected from the patient records. All patients were mailed the Telugu translation of medical outcome study short form -36(MOS-SF-36) QOL questionnaire and were contacted telephonically to enquire about presence of CPTP and QOL. A univariate analysis was done to assess factors associated with CPTP and a multivariate logistic regression analysis was done subsequently to identify independent risk factors of CPTP. QOL indices were compared between those patients who suffered from CPTP and those who did not. **Results:** The prevalence of pain in our study was 40.86% (85/208). The factors implicated in the causation of CPTP were diabetes mellitus, preoperative pain, rib resection, and duration of chest tube drainage with odds ratio of 9.8, 2.6, 6.7, and 1.03, respectively. The health-related QOL showed poor scores in all domains in patients suffering from CPTP. **Conclusion:** The prevalence of CPTP was high. It significantly impacts health-related QOL.

Key words: Chronic pain, quality of life, thoracotomy

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INTRODUCTION

International society for the study of pain defines chronic pain as pain that persists after 3 months.^[1] Chronic pain following thoracotomy is one of the most nagging complications. The prevalence of chronic post thoracotomy pain (CPTP) varies between 25 and 68%^[2-9] Many studies conducted across the globe have identified various factors implicated in the development of CPTP. There is wide variability in the reported factors predisposing to post thoracotomy pain. Geographic factors may play an important role in perception of pain leading to difference in prevalence. As per our knowledge no study on CPTP is available

from India. Thus, the aim of the study was to detect the prevalence of chronic pain following thoracotomy in a tertiary referral center from India, assess the predisposing factors implicated in its causation, and study the impact of CPTP on quality of life (QOL).

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METHODS

This retrospective study was carried out in a tertiary referral center, on all adult patients who were discharged home after undergoing open lung surgery through posterolateral thoracotomy between the period of January 2012 and December 2015. Patients belonging to American society of anesthesiologists (ASA) grades IV or V, patients undergoing emergency surgery or surgery following trauma to chest wall, patients having malignancy infiltrating into chest wall, previous thoracotomy, or patients who developed major adverse cardiovascular or cerebrovascular events (MACCE) or musculoskeletal condition affecting day-to-day activity after surgery (either in hospital or after discharge) were excluded from the study. Patients having incomplete records were also excluded from study.

This study was approved by institute ethics committee. Written consent was considered unnecessary in this very low risk study and thus verbal informed consent was approved by the ethics committee. The case records and anaesthesia charts of all patients deemed suitable for the study as per above-mentioned inclusion and exclusion criteria were retrieved from the electronic database of cardiothoracic surgery department and anaesthesia department, respectively.

Data on age, sex, weight, ASA physical status, smoking, comorbidities (hypertension, diabetes mellitus), presence of preoperative moderate to severe pain over the ipsilateral thorax, malignancy, preoperative chemotherapy/radiotherapy, use of thoracic epidural analgesia (TEA), duration of surgery, duration of anaesthesia, rib resection, type of surgery, number of chest drains, duration of chest tube drainage, and postoperative surgical site infection was collected. The cell phone numbers and the address of the patients were also noted.

Before the initiation of study, the medical outcome study short form -36(MOS-SF-36) QOL questionnaire was translated to local language (Telugu), which is the vernacular language of this region. Standard procedure was followed for preparing translated version which is as follows. Four competent professionally experienced bilingual (native Telugu speaking, but proficient in English) translators were involved in the translation process. Two translators independently translated the English version of questionnaire to Telugu with culturally equivalent adaptations.^[10] Emphasis was given to conceptual rather than literal equivalence. The

forward translations were reviewed by the investigators and translators together and a final consensus on the questionnaire was reached. This questionnaire was subjected to backward translation to English by the other two translators. The backward translation was reviewed again by investigators and translators for conceptual equivalence with the original version. In case of discrepancies, required modification in the language was done to suit the general public.

All patients were sent a letter by post, which contained information regarding the study and also the Telugu translation of MOS-SF-36 QOL questionnaire. This was done to enable them decide on their wish to participate in the study and to prepare for answering the QOL questionnaire. One month after dispatch of the letter, telephonic interviews were started.

Two trained interviewers telephonically contacted the patients on phone numbers retrieved from the case records. After obtaining the verbal informed consent, the patients were asked about the presence or absence of pain at the thoracotomy site. The nature and severity of pain was also noted along with day of surgery to telephonic interview time interval (in months). Patients also answered to the health-related QOL MOS-SF-36 questionnaire. Patients who refused to participate in the study or failed to comprehend the questionnaire due to poor literary skills at the time of telephonic interview were excluded. Letter was resent to patients who had not received the earlier letter and interviewed fifteen days later. Patients whose cell phone number were not reachable or patients who did not attend call even after three attempts were excluded from the study. Patients who had expired or had MACCE after hospital discharge were also excluded from study.

Standard anaesthesia technique as per institution protocol was used in all patients. Thoracic epidural catheter was inserted in all patients except for contraindication or patient refusal. A balanced anaesthesia technique including O₂/air/sevoflurane/fentanyl infusion was used in all patients. Muscle relaxation was maintained with atracurium infusion. Postoperative pain was measured by visual analog scale (VAS) every 4th hourly and analgesia was managed by epidural infusion of bupivacaine 0.125% continuously during the intensive care unit stay. Injection Paracetamol 1 gm was administered 6th hourly in all patients and Tramadol 100 mg was given as rescue analgesic as and when necessary (VAS >4).

Chest tube was removed when there was no air leak or when pleural drain was <100 mL for 24 h. Two experienced surgical teams were involved in the surgical procedures. Standard posterolateral thoracotomy with or without rib resection was used in all patients.

Data were analyzed using SPSS version 20 (2011, IBM, Armonk, NY, United States of America). Continuous variables were expressed as mean ± standard deviation (S.D). Categorical variables were expressed as numbers and percentages. Continuous variables were analyzed using Students' *t* test and chi square test was used to analyze categorical variables. A *P* value of less than 0.05 was considered significant. Variables with significant *P* value were further subjected to multiple forward step-wise logistic regression analysis to identify the independent risk factor.

RESULTS

As shown in flow diagram of Figure 1, data from 208 patients were analyzed after pre- and post-telephonic exclusion. Their baseline characteristics are summarized in Table 1.

The point prevalence of CPTP at the time of telephonic interview was 40.86% (85/208 patients). Forty-five patients (52.9%) complained of mild pain, while moderate and severe pain was experienced by

28.23% (24) and 18.82% (16) patients, respectively. Majority of patients, 36 (42.3%) complained of a numb type of pain. The other varieties of pain reported were, dull aching 15 (17.6%), throbbing 12 (14.1%), itchy 6 (7.05%), shooting 5 (5.8%). Rest 11 patients could not describe the nature of their pain.

The study showed that the prevalence of pain was high (58.3%) in patients interviewed within 12 months' time frame after surgery. The prevalence decreased and remained nearly constant between 13–24 and 25–36 months. Thereafter, it further decreased to a value of 26% at >48 months.

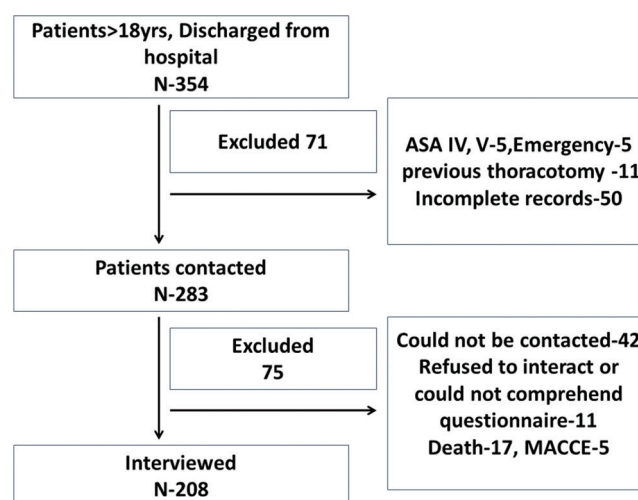


Figure 1: Flow chart of patient recruitment. ASA- American society of Anaesthesiologists, MACCE- Major adverse cerebral and cardiovascular events

Table 1: Comparison of variables in patients with and without CPTP

Variables	CPTP (n=85)	No CPTP (n=123)	P
Age	40.2 (12.8)	38.3 (14.6)	0.31
Sex (M/F)	59/26	79/44	0.27
Weight	53.45 (12.1)	53.6 (15.7)	0.92
ASA physical status I/II/III	47/32/6	89/26/8	0.06
DM	29	8	0.00
Smoking	12	20	0.70
Hypertension	14	14	0.19
Preop pain on ipsilateral thorax (Percentage)	26 (30.5%)	21 (17.07%)	0.01
Malignancy	9	18	0.26
Chemotherapy/radiotherapy	1	2	0.63
TEA	76	105	0.26
DOS	258.9 (63.4)	253 (66.3)	0.52
DOA	290.2 (72.5)	288.2 (69.7)	0.84
Rib resection	64	26	0.00
Number of drains			
1	13	31	0.05
2	72	92	
Duration of drainage (hours)	79 (49.7)	40.6 (20.2)	0.001
Postoperative surgical site infection	7	1	0.009

Data expressed as (n) or Mean (Standard Deviation), CPTP – Chronic post thoracotomy pain, M – Male, F – Female, ASA – American society of anaesthesiologists, DM – Diabetes Mellitus, TEA – Thoracic epidural analgesia, DOS – Duration of surgery, DOA – Duration of anaesthesia

Table 1 shows the factors significantly associated with the causation of chronic pain. On univariate analysis, diabetes mellitus, preoperative moderate to severe pain on ipsilateral thorax, rib resection, duration of chest tube drainage, and postoperative surgical site infection were found to be significant factors. However, multivariate regression identified diabetes mellitus, preoperative moderate to severe pain on ipsilateral thorax, rib resection, and duration of chest tube drainage as independent predictors of CPTP [Table 2]. SF-36 questionnaire was used to assess the effects of chronic pain on QOL. All the components of QOL questionnaire were found to have significantly lower values in patients with CPTP as compared to those, who did not have CPTP [Figure 2].

DISCUSSION

Our study found the prevalence of chronic pain following thoracotomy to be high (40.86%). The prevalence of CPTP varies across studies between 25% and 68%.^[2-9] The significant risk factors implicated in the genesis of chronic pain in our study were diabetes mellitus, preoperative moderate to severe pain over ipsilateral thorax, rib resection, and duration of chest tube drainage. The QOL in

patients having CPTP was poorer compared to those not having it.

Some degree of tissue and nerve injury is inevitable following thoracotomy but all patients do not develop CPTP. In an attempt to answer this discrepancy, many researchers have looked in to the risk factors associated with development of chronic pain. There may be great variation in the risk factors in Indian context, due to differences in geographic, cultural, ethnicity, and socioeconomic status. A recent study by Saxena *et al.* found higher prevalence of chronic pain in Indian patients as compared to Pan Asian region.^[11] Antony and Merghani concluded that lower socioeconomic and educational background was associated with a lower complaint of chronic pain in patients receiving home-based nursing care.^[12] As there are no previous research on CPTP in Indian subcontinent, considering the above-mentioned factors we aimed to study the same.

A younger age (<60 years) was found to have a causal relation with chronic pain in many studies.^[7,9,13] Further, a study by Mongarden concluded that patients with chronic pain were about 10 years younger than those not having it.^[6] This association could possibly be due to the fact that younger patients have a stronger inflammatory and immune reaction and increased neuroplastic response. However, we failed to elicit any influence of age on CPTP probably because of an overall younger study population.

Females have consistently revealed a greater sensitivity to pain both in experimental and clinical models.^[14,15] Gender-specific differences in pain sensitivity has also been found in many studies on chronic post thoracotomy pain.^[7,16,17] However in a recent meta-analysis in cancer patients, pain was not found to be significantly different in males and females.^[18] Our study also could not elicit any contribution of gender in the genesis of pain.

Our study revealed that diabetic patients had a 9.8 odd of developing chronic pain as compared to nondiabetics. Painful polyneuropathy is a well-known entity in

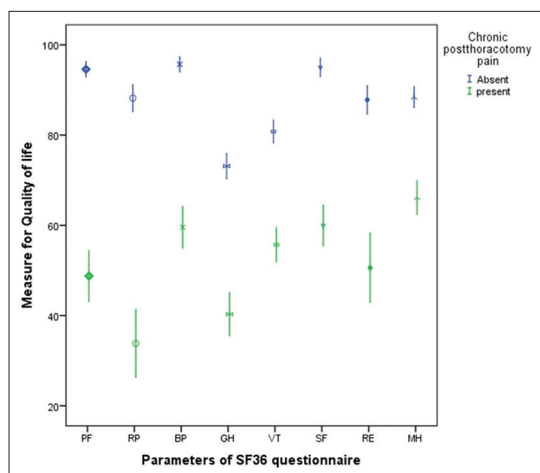


Figure 2: Comparison of SF-36 domain scores in patients having and not having CPTP. PF- physical function, RP (role physical)- role limitations due to physical problems, BP-body pain, GH-general health, VT-vitality, SF-social function, RE (role emotional)- role limitations due to emotional problems, MH- mental health

Table 2: Results of logistic regression showing risk factors for development of chronic post thoracotomy pain

Variables	B	SE	Wald	Odds ratio	Confidence interval	P
DM	2.28	0.56	16.43	9.8	3.2-29.6	<0.001
Preoperative pain over ipsilateral thorax	0.96	0.45	4.59	2.6	1.08-6.38	0.03
Rib resection	1.9	0.38	25.003	6.7	3.18-14.22	<0.001
Duration of chest tube drainage	0.029	0.007	17.48	1.03	1.01-1.04	<0.001

B – Coefficient for constant (intercept), SE – Standard error, DM – Diabetes Mellitus

patients with diabetes. Its mechanism is complex and is due to interplay of various inflammatory, microvascular, and immune mechanisms.^[19,20] However, literature on the association of diabetes mellitus and development of chronic pain is sparse. We hypothesize that pre-existing neuropathy in diabetic patients may be accentuated due to surgical stress resulting in chronic pain. Wang *et al.* also reported an odds ratio of 6.6 for developing chronic pain in patients with diabetes.^[9]

TEA was used in 181 patients for intraoperative and postoperative analgesia, while in the rest, analgesia was maintained with intravenous analgesics. The results of this study did not show a relationship between TEA and CPTP. Similar results were noted by earlier investigators.^[21,22] The smaller sample of patients without TEA could have limited the establishment of statistical relation between TEA and CPTP. We could not test the relationship between acute postoperative pain and CPTP as the pain management protocols in the intensive care unit ensured a VAS <4 in all patients using other analgesic regimens even in the absence of TEA.

There is a well-documented relationship between preoperative pain and development of chronic pain in hernia, amputation, and hysterectomy patients; however, little information is available on CPTP in post thoracotomy patients.^[23-25] A study by Hetmann *et al.* could not elicit association between chronic preoperative pain in extra thoracic regions and postoperative pain. However in another study by Kampe *et al.*, 33.5% patients with preoperative pain in thoracic region developed CPTP.^[26,27] Our study is in agreement with the later. Many of the studies on CPTP excluded patients who had preoperative pain or were on preoperative analgesics.^[17,28] This could be the reason for inadequacy of literature to establish a relation between preoperative pain and CPTP. It is perceived that prolonged activation of pain centers (as in patients with chronic preoperative pain and inadequate pain control) may lead to central sensitization causing chronic pain syndromes. Painful stimuli cause changes in the peripheral and central nervous systems, which increase the impact of painful stimuli and can also cause nonpainful stimuli to be experienced as painful.^[17,29,30]

Neurologic injury during the time of surgery is the likely source of development of long-term CPTP. The nerve injury may occur from use of rib retractors, rib

resection, or use of improper suturing techniques.^[28,31] Studies have proven that modification in surgical techniques to preserve intercostal nerve decreased the incidence of CPTP.^[32-34] Rib resection is often carried out during thoracotomy to improve exposure, prevent rib fracture, and injury to posterior costovertebral elements.^[35] Although Maguire *et al.* concluded that rib resection was associated with higher amount of intercostal nerve injury,^[28] the literature on association of rib resection and CPTP is controversial. Opinion varies as to whether rib resection causes trauma to intercostal nerves or prevents trauma from rib spreading. In a retrospective study of 1000 patients, Richardson *et al.* concluded that that incidence of CPTP was lower in patients who had rib resection than who did not.^[36] However in another study by Hansen, the development of CPTP was higher (14.8%) in patients who had a rib resected than those who did not (3.1%).^[37]

Earlier studies have found positive correlation between number of chest drains and chronicity of pain; however, our study could not demonstrate any such association.^[6] Longer duration of chest tube drainage was a significant factor for development of chronic pain in our study which is consistent with the result of previous studies.^[3,7,38,39] Peng *et al.* showed that chest tube drainage >4 days increased the prevalence of chronic pain in post thoracotomy patients.^[7] Moreover a study by Miyazaki *et al.* clearly showed evidence of damage to intercostal nerve on chest tube insertion.^[40] Using the current concept of threshold testing, their study showed that chest tube placement was harmful to both myelinated (A α and A β) and unmyelinated C fibers.

QOL in patients with CPTP has always been a concern. Many studies have attempted to evaluate QOL earlier, some with subjective questions and others with a structured questionnaire. English SF36 questionnaire is available online, free of cost by Research and development (RAND). It was translated to Telugu using standard protocol as described earlier and was used for our study [Appendix 1 is available online]. Necessary changes were done to achieve cultural equivalence as suggested by Sinha *et al.*^[10] It looks at eight aspects of QOL, physical function (PF), role limitations due to physical problems (role physical, RP), body pain (BP), general health (GH), vitality (VT), social function (SF), role limitations due to emotional problems (role emotional, RE), and mental health (MH). Scores in each category ranges from 0 to 100, 0 being

worst QOL and 100 being best. Our study revealed that CPTP led to lower scores in all domain of SF36 questionnaire. Peng *et al.* used the Chinese version of the SF-36 questionnaire and concluded that PF and BP components were most affected in patients with CPTP.^[7] Only PF and vitality components were found to be decreased in another study by Kinney *et al.*^[4] However, this study followed up the patients only for 3 months and it is possible that emotional and mental changes might have developed later and thus were missed in the observation.

A limitation of this study that it is a single center retrospective study. The shortcomings of telephonic interview and self-reporting of pain by patients must be kept in mind. We did not study the effect of psychosocial factors like anxiety, depression, malignant disease, social network, and social status on CPTP which may have had significant impact on development of chronic pain and QOL. Details of postdischarge analgesic medication intake were also not sought. Further prospective studies are required to study the effect of minimizing risk factors on prevalence of CPTP.

CONCLUSION

CPTP is a common complication in patients undergoing thoracotomy. All domains of medical outcome study short form-36 QOL questionnaire were significantly affected by it.

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Conflicts of interest

There are no conflicts of interest.

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