INTERCOSTAL NEUROLYSIS FOR THE TREATMENT OF POSTSURGICAL THORACIC PAIN: A CASE SERIES

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Abstract

Introduction. We investigated the possible role of intercostal surgical neurolysis in relieving chronic neuropathic pain refractory to other non-surgical treatments in patients with postsurgical thoracic pain.

Methods. We retrospectively collected clinical data on patients referred to the Neurosurgery Unit of Policlinic Hospital of Milan. Ten patients (age range: 20-68 years) suffering from neuropathic pain for at least two months following thoracic surgery underwent intercostal neurolysis.

Results. Compared to pre-neurolysis, pain intensity decreased one month post-neurolysis and remained stable two months post-neurolysis [median score (IQR): 8 (6; 9) pre-neurolysis, 4 (3; 5) one month after and 3 (2; 5) two months after, $p<0.0001$]. Antiepileptic drugs for pain control decreased after neurolysis (10/10 *vs.* 2/10, $p= 0.008$).

Discussion. Surgical intercostal neurolysis may be a promising therapeutic option in patients with chronic neuropathic pain in association with neurological deficits.

Introduction

Persistent pain is one of the most common complications after thoracic surgery. Patients can develop post-thoracotomy pain syndrome (PTPS), a long term disabling condition (1–3).

PTPS is defined as pain that recurs or persists along a thoracotomy incision for at least two months following the surgical procedure, and which cannot be attributed to any other cause or condition (4). PTPS has been variably reported in 5-80% of patients following thoracic surgery, with as many as 30% of patients still experiencing pain 4 to 5 years after surgery (2).

Since post-thoracotomy pain is aggravated by the extent of surgical trauma, minimally invasive surgical approaches have become the procedure of choice for many thoracic surgeons (3). Video-assisted thoracic surgery (VATS) is a minimally invasive procedure that has some advantages over open surgery, including less post-operative pain and earlier recovery (5)**.** However, pain or paraesthesia due to intercostal nerve compression during VATS is often seen (6), and this procedure still carries a potential for PTPS (1). Although patients undergoing VATS have less acute post-operative pain when compared with those undergoing open thoracotomy, results have been mixed regarding chronic pain (2,7).

Although the etiology of PTPS is multifactorial, iatrogenic intercostal nerve injury appears to be the most important pathogenic factor for its development

(8). In addition to incision and trocar insertion, nerve damage related to the insertion of chest tubes and drains has been reported (9).

Neuropathic pain of PTPS may be resistant to medical, psychiatric, physical or more invasive treatments such as nerve blocks, trigger point injections and neuromodulation techniques (3). Trends and new evidence in the management of PTPS have been recently published, but intercostal surgical neurolysis was not mentioned as a possible therapeutic option (10). Approaches such as continuous extrapleural infusion and epidural analgesia may cause severe adverse events (4), whereas surgical neurolysis is a more conservative approach preserving the integrity of the nerve. Surgical nerve neurolysis involves a local intervention with a small incision and has potential clinical benefits in a short period. The aim of our study was to investigate the role of surgical intercostal nerve neurolysis in relieving chronic neuropathic pain refractory to other treatments in patients with postsurgical thoracic pain.

Methods

Study design and participants

We retrospectively collected clinical data on patients referred to the Neurosurgery Unit of Policlinic Hospital of Milan from March 2012 to October 2016. All patients had thoracic neuropathic pain related to the insertion of chest tubes, which persisted for at least two months following surgery

(thoracotomy in two patients, VATS in eight patients) and was refractory to medical and/or local treatment. Patients were excluded if they were under 18 years old, carried a diagnosis of major depressive disorder or neuromuscular disease, or had a cardiac pacemaker. Other etiologies were ruled out. Follow-up visits were established at one month and two months after neurosurgery. The study was approved by the local Ethics Committee and written informed consent was obtained from each patient.

Pre-operative assessment

All subjects underwent neurological examination. Skin sensitivity was examined by comparing the painful thoracic area with contralateral or adjacent non-painful areas for the presence of allodynia (pain as a result of a stimulus which does not normally provoke pain) or hyperalgesia (an increased response to a stimulus which is normally painful), which are often associated with neuropathic pain (11). When pain clearly localized to a single intercostal space, a positive Tinel's sign was considered as being indicative of focal nerve injury. When patients complained of diffuse thoracic pain, both neuropathic and non-neuropathic, intercostal nerve conduction studies (NCS) were used along with Tinel sign to confirm the presence of focal nerve damage as responsible of neuropathic pain. NCS were performed on the thorax bilaterally using surface electrodes. Patients were asked to lie on their

side opposite to that of examination, with their arms rested over the head. The intercostal nerve was stimulated just below the rib at middle or posterior axillary line, depending on the location of the surgical scar, with electrical stimuli of 0.2 ms duration. A compound muscle action potential (CMAP) was recorded from the intercostal muscles of the same space, anterior to the scar, using a distance of 6-9 cm between the stimulation and recording sites. The study was repeated on the other side while maintaining the same points of stimulation and recording. An initial negative deflection of the motor response was required as a criterion of the optimal site of the recording electrode (12)**.** A side-to-side difference ≥ 50% in CMAP amplitude was considered consistent with local nerve injury (13)**.** CMAP latency differences were also evaluated. Patients were also given self-report measures to complete, evaluating pain and neuropathic pain intensities and sleep quality.

Neurosurgical procedure

A reduction of pain score (< 50% from baseline) following intercostal block was required to confirm the presence of nerve injury before proceeding to surgical nerve exploration. When pre-operative assessment was suggestive of focal nerve injury, the neurosurgical procedure was performed on the awake patient, lying on the healthy side. The patient's vital signs were continuously monitored.

For clinical diagnosis, we performed an intercostal block using a short-action local anaesthetic (lidocaine 2%, 3-5 ml, depending on the body weight). The infiltration was performed in the area of presumed focal nerve injury, just below the rib in the region of intercostal bundle (14), at the site of the Tinel's sign.

A skin incision of 3 cm was performed, corresponding to the cutaneous scar from the thoracotomy. After fascial incision, the intercostal nerve was identified using a microscopic. The nerve always was pale upon visual inspection or hard upon palpation. We performed external neurolysis to separate it from scar and neighbouring fibrous tissues. This neurosurgical procedure had a mean duration of 30-40 minutes and was performed by experienced peripheral neurosurgeons.

When the nerve appeared transacted (in one case only), external neurolysis was followed by epineurial repair consisting of nerve end-to-end suture. The nerve was then protected by fatty tissue.

Outcomes

Pain intensity, sleep quality and drugs used for pain control were the outcomes of the study. These were collected before surgery and one and two months after neurosurgical intervention.

Presence and intensity of neuropathic pain were assessed by using the self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) score (15). S-LANSS is a validated, multidimensional 7-item assessment tool designed to identify pain of predominantly neuropathic origin. The tool has a maximum score of 24, with scores over twelve indicating neuropathic pain. The intensity of the pain was measured by the numeric rating scale (NRS) of the S-LANSS tool, a unidimensional measure of pain intensity. The NRS is a segmented numeric scale in which patients select a whole number (0-10) that reflects the intensity of their pain. It is anchored at 0 indicative of “no pain” and 10 indicating pain “as severe as it could be”. Sleep quality was evaluated by a 10-point NRS with 0 indicating “slept well” and 10 indicative of “did not sleep at all”.

Use of nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, antiepileptic drugs and opioids for pain control were collected before neurosurgery and at follow-up visits.

Statistical analysis

Categorical variables are expressed as frequencies and percentages, whereas continuous variables are given as medians and ranges. The Friedman test (16), a non-parametric rank-based analysis of variance, was used to verify statistically significant changes from pre-surgery values.

Changes in analgesic medications after neurosurgery were verified by exact McNemar test. All tests were two-sided and *p*-values of less than 0.05 were considered statistically significant.

Results

We selected 10 patients from 33 who underwent surgical neurolysis for PTPS. The remaining 23 patients were rejected because of costal or lung tumours, multiple costal resectiona, diabetic neuropathy or major depressive disorder. Demographics and clinical characteristics of the 10 subjects are given in Table 1. All patients reported nerve hypersensitivity and had a positive Tinel's sign. Clinical evaluation, the S-LANSS score and, when required, intercostal NCS confirmed the diagnosis of neuropathic pain. The majority of patients reported pain-related difficulty in moving the ipsilateral arm and limitations in daily living activities. Neurological examination and electrophysiogical studies were consistent with a focal nerve injury at the site of scar related to the insertion of chest tubes during thoracic surgery in all patients. NCS were performed in 6 patients, and the results are shown in Table 2. The stimulus intensity required for maximal stimulation of the intercostal nerves on the symptomatic side (median: 77.7 mA, range 68.5 - 90 mA) was higher than that needed on the normal side (median: 54.3 mA, range: 49.6 - 72.2 mA, p= 0.031). Neurolysis with scar tissue debridement

was performed in 9 patients, and nerve repair in one patient with a transacted nerve.

Compared to pre-surgery, the pain intensity score considerably decreased one month post-procedure and remained stable two months after the neurosurgical intervention. Similarly, the multidimensional 7-item pain score diminished at one month and remained stable after two months. None of the patients reported a 7-item pain score of more than 12 at one month and two months after neurosurgery. Sleep quality improved at one month and the improvement was maintained at two months post-surgery (Table 3).

The percentage of patients requiring anti-epileptic drugs decreased after neurosurgery (Table 4).

No complications related to the neurolysis procedure, such as hematoma, infections or pneumothorax, were reported.

Discussion

In our small, uncontrolled, non-blinded study, intercostal neurolysis showed promising effects in reducing neuropathic pain and improving sleep quality. The percentage of patients requiring antiepileptic drugs for pain control also decreased after neurosurgery.

All the patients included in our study reported an improvement of pain around the ipsilateral shoulder, a common condition after both thoracotomy and VATS. This kind of pain severely impairs activities of daily living and is only partially attenuated by drugs (17,18).

Several drugs have been used in the treatment of postsurgical thoracic pain, such as NSAIDs, cyclooxygenase-2 (COX-2) inhibitors, acetaminophen, N-methyl D-aspartate (NMDA) receptor antagonists, glucocorticoids, tricyclic antidepressants, anticonvulsants and opioids. Unfortunately, no single drug or drug combination is completely effective in all patients (19,20). Moreover, side effects are common with prolonged use of these drugs (21–23) and tolerance can develop after opioid use (24). Pre-emptive analgesia was also not effective in reducing chronic post-thoracotomy pain (25,26).

Some patients failing conservative medical treatments might require more sophisticated treatments such as nerve blocks, trigger point injections and neuromodulation techniques (4). None of these techniques has been clearly proven to besuperior to the others and they may have a high risk of pneumothorax and postoperative hyperesthesia (27).

Intra-operative electrophysiological assessment of intercostal nerve function during thoracic surgical procedures has been performed by a few authors (8,9). Rogers et al. demonstrated for the first time that intercostal nerves are injured during thoracotomy and that this usually affects multiple nerves during

rib spreading. The authors also suggested that rib retraction could result in direct injury or stretch injury (8). Maguire et al. (9) confirmed the presence of two patterns of nerve injuries: discrete block by direct pressure from the retractor, and conduction failure along the whole nerve length probably due to ischemia of persistently stretched tissues. However, they suggested that the amount of intra-operative intercostal nerve injury was not indicative of long-term nerve damage and that there were other causes of chronic pain. These authors also performed a pre-operative assessment of intercostal nerve function using magnetic nerve stimulation. Although some excellent recordings were obtained, many recordings were not interpretable and this technique was therefore abandoned (9). Reports of electrophysiological studies on intercostal nerves outside of the intra-operative setting are scarce. In 1989, Pradhan and Taly reported a new surface technique for conduction studies of the lower intercostal nerves in normal subjects, recording motor response over the rectus abdominis muscle (28). Electrodes placed over rectus abdominis have also been used by other authors to record motor responses from T7-11 using both electrical and magnetic stimulation (29,30). Another study assessed the presence of superficial abdominal reflexes and somatosensory-evoked responses after electrical stimulation of the surgical scar to measure the degree of intercostal nerve impairment in thoracotomy (31). This study monitored T7,8 supplying the abdominal wall, and not T5,6, but most thoracotomies are performed through the fourth, fifth or sixth

intercostal space, making T4-6 the most likely levels to be damaged. The only muscles reliably innervated by T6 and above are the intercostal muscles themselves (8). Needle examination of muscles innervated by the intercostal nerves is complicated by difficulties with localization and a high reported rate of pneumothorax (8).

In our experience, intercostal nerve stimulation proximal to the scar was useful to confirm the clinical diagnosis of focal nerve injury, and it influenced the decision for neurolysis for patients with more diffuse thoracic pain.

The study has several limitations including the limited number of patients, short follow-up, lack of a control group and blinding. The latter two are unavoidable in a retrospective case series such as this one. Moreover, the inclusion criteria of the study resulted in the enrollment of a highly selected population limiting the generalizability of our results. However, our promising results pave the way for further investigation of the role of surgical neurolysis in the treatment of PTPS through larger prospective studies with longer follow-up.

There is a lack of intercostal nerve conduction data on normal subjects. One of the problems we encountered was the different extent of the surgical scar in the transverse plane of the intercostal space among patients. This led to the performance of nerve stimulation in the middle axillary line in some patients, where we found it easier to perform, and at the posterior axillary line

in others. Despite the variation of distance from the stimulating to the recording electrode among the patients, the same distance was maintained on both sides in each subject to compare CMAP results. Furthermore, nerve stimulation at the middle or posterior axillary lines was well tolerated by all patients. We did not stimulate lateral to the paraspinal muscles, as reported by Pradhan and Taly (28), since stimulus duration (0.5 ms) in that study was higher than in our study (0.2 ms). When lower stimulus intensity is required, nerve stimulation is associated with less discomfort (32).

In conclusion, surgical exploration with neurolysis and eventually nerve reconstruction could be promising therapeutic options in patients with chronic neuropathic pain. It requires only a minimal incision under local anaesthesia, and in our patients rapidly reduced symptoms and the need for pharmacological therapy. These results, if confirmed, have the potential to improve quality of life, reduce the number of working days lost due to postsurgical pain and decease health care costs. Randomized clinical trials, comparing standard medical treatment with intercostal neurolysis are needed to confirm its effectiveness. We also recommend further studies to better define the role of intercostal NCS in diagnostic planning and in estimating prognosis in patients with PTPS.

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List of Abbreviations:

CMAP: compound muscle action potential

COX-2: cyclooxygenase-2 inhibitors

NCS: Nerve Conduction Studies

NMDA: N-methyl D-aspartate

NRS: Numeric Rating Scale

NSAIDs: Nonsteroidal Anti-inflammatory Drugs

PTPS: Postthoracotomy Pain Syndrome

S-LANSS: Self-completed Leeds Assessment of Neuropathic Symptoms and Signs

VATS: Video-assisted Thoracic Surgery

References

1. Shanthanna H, Aboutouk D, Poon E, Cheng J, Finley C, Paul J, et al. A retrospective study of open thoracotomies versus thoracoscopic surgeries for persistent postthoracotomy pain. J Clin Anesth. 2016;35:215–20.
2. Karmakar M, Ho A. Postthoracotomy pain syndrome. Thorac Surg Clin. 2004;14(3):345–52.
3. Koehler R, Keenan R. Management of postthoracotomy pain: acute and chronic. Thorac Surg Clin. 2006;16(3):287–97.
4. Hazelrigg S, Cetindag I, Fullerton J. Acute and chronic pain syndromes after thoracic surgery. Surg Clin North Am. 2002;82:849–65.
5. Waller D, Forty J, Morritt G. Video-assisted thoracoscopic surgery versus thoracotomy for spontaneous pneumothorax. Ann Thorac Surg. 1994;58:372–7.
6. Yang Y, Dong J, Huang Y. Single-incision versus conventional three-port video-assisted surgery in the treatment of pneumothorax: a systematic review and meta-analysis. Interact Cardiovasc Thorac Surg. 2016;23(5):722–8.

7. Tsubokawa N, Harada H, Takenaka C, Misumi K, Yamashita Y. Comparison of Postoperative Pain after Different Thoracic Surgery Approaches as Measured by Electrical Stimulation. Thorac Cardiovasc Surg. 2015;63(6):519–25.

8. Rogers M, Henderson L, Mahajan R, Duffy J. Preliminary findings in the neurophysiological assessment of intercostal nerve injury during thoracotomy. Eur J Cardiothorac Surg. 2002;21(2):298–301.

9. Maguire MF, Latter JA, Mahajan R, Beggs FD, Duffy JP. A study exploring the role of intercostal nerve damage in chronic pain after thoracic surgery. Eur J Cardio-thoracic Surg. 2006;29(6):873–9.

10. Rodriguez-Aldrete D, Candiotti K, Janakiraman R, Rodriguez-Blanco Y. Trends and New Evidence in the Management of Acute and Chronic Post-Thoracotomy Pain-An Overview of the Literature from 2005 to 2015. J Cardiothorac Vasc Anesth. 2016;30(3):762–72.

11. Bridges D, Thompson S, Rice A. Mechanisms of neuropathic pain. Br J Anaesth. 2001;87(1):12–26.

12. Han T, Chung S, Kwon Y. Optimal electrode placement in facial nerve conduction study. Electromyogr Clin Neurophysiol 1998. Electromyogr Clin Neurophysiol. 1998;38(5):279–84.

13. Weiss L. Injuries to peripheral nerves. In: Easy EMG A guide to

performing nerve conduction studies and electromyography 2nd Edition. Silver JK. Elsevier; 2016. p. 69–74.

14. Rendina E, Ciccone A. The intercostal space. Thorac Surg Clin. 2007;17(4):491–501.

15. Bennett M, Smith B, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. J Pain. 2005;6(3):149–58.

16. Friedman M. The Use of Ranks to Avoid the Assumption of Normality Implicit in the Analysis of Variance. J Am Stat Assoc. 1937;32:675–701.

17. Gerner P. Postthoracotomy pain management problems. Anesth Clin. 2008;26(2):355–67.

18. Bunchungmongkol N, Pipanmekaporn T, Paiboonworachat S, Saeteng S, Tantraworasin A. Incidence and risk factors associated with ipsilateral shoulder pain after thoracic surgery. J Cardiothorac Vasc Anesth. 2014;28(4):979–82.

19. Slinger P. Principles and Practice of Anesthesia for Thoracic Surgery. Springer Science; 2011. 674-707 p.

20. Moulin D, Boulanger A, Clark A, Clarke H, Dao T, Finley G, et al. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. Pain Res Manag.

2014;19(6):328–35.

21. Bottiger B, Esper S, Stafford-Smith M. Pain management strategies for thoracotomy and thoracic pain syndromes. Semin Cardiothorac Vasc Anesth. 2014;18(1):45–56.

22. Mathews T, Churchhouse A, Housden T, Dunning J. Does adding ketamine to morphine patient-controlled analgesia safely improve post-thoracotomy pain? Interact Cardiovasc Thorac Surg. 2012;14(2):194–9.

23. Niesters M, Martini C, Dahan A. Ketamine for chronic pain: risks and benefits. Br J Clin Pharmacol. 2014;77(2):357–367.

24. Guignard B, Bossard A, Coste C, Sessler D, Lebrault C, Alfonsi P, et al. Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requirement. Anesthesiology. 2000;93(2):409–17.

25. Brulotte V, Ruel M, Lafontaine E, Chouinard P, Girard F. Impact of pregabalin on the occurrence of postthoracotomy pain syndrome: a randomized trial. Reg Anesth Pain Med. 2015;40(3):262–9.

26. Bong C, Samuel M, Ng J, Ip-Yam C. Effects of preemptive epidural analgesia on post-thoracotomy pain. J Cardiothorac Vasc Anesth. 2005;19(6):786–93.

27. Yeung J, Gates S, Naidu B, Wilson M, Gao S. Paravertebral block

versus thoracic epidural for patients undergoing thoracotomy. Cochrane Database Syst Rev. 2016;21:2:CD009121.

28. Pradhan S, Taly A. Intercostal nerve conduction study in man. J Neurol Neurosurg Psychiatry. 1989;52(6):763–6.

29. Carls G, Ziemann U, Kunkel M, Reimers CD. Electrical and magnetic stimulation of the intercostal nerves: a comparative study. Electromyogr Clin Neurophysiol. 1997;37(8):509–12.

30. Chokroverty S, Deutsch A, Guha C, Gonzalez A, Kwan P, Burger R, et al. Thoracic spinal nerve and root conduction: a magnetic stimulation study. Muscle Nerve. 1995;18(9):987–91.

31. Benedetti F, Vighetti S, Ricco C, Amanzio M, Bergamasco L, Casadio C, et al. Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. J Thorac Cardiovasc Surg. 1998;115(4):841–7.

32. Cappellari A. Electrophysiological Study of the Frontal Branch of the Facial Nerve in Normal Subjects. J Clin Neurophysiol. 2018;35:130–2.

Table 1. Demographics and clinical characteristics of the study population before neurosurgery

Demographic or Characteristic	Number of Patients (unless otherwise indicated)
Sex (Females/Males)	8/2
Age (years)	
Median (range)	43 (20; 68)
Type of previous thoracic surgery	
Bullectomy	8
Apicoectomy	2
Thoracotomy/VATS	2/8
Time since thoracic surgical intervention (months)	
Median (range)	11 (5: 12)
Localization of neuropathic pain	
Anterior	8
Both sides	2
Damaged nerve	
T5	4
T6	5
T8	1
Difficulty moving arm	
Present	8
Absent	2
Limitations in daily living activities	
Present	9
Absent	1
7-item S-LANSS score over 12 points	10

Abbreviations: S-LANSS - Self-completed Leeds Assessment of Neuropathic Symptoms and Signs

Table 2. Compound muscle action potential (CMAP) of the intercostal nerves

Patient (Thoracic nerve)	Right side		Left side	
	Amp (mV)	OL (ms)	Amp (mV)	OL (ms)
1 (T6)	2.0	2.2	0.3	2.7
2 (T6)	1.8	2.8	0.8	3.3
3 (T5)	0.4	6.1	1.3	3.0
4 (T5)	1.0	8.5	2.2	3.0
5 (T6)	1.0	5.7	2.1	2.9
6 (T6)	NR	NR	2.4	2.9

CMAP, compound muscle action potential; NCS, nerve conduction studies; Amp, Amplitude from baseline to negative peak; OL, onset latency; T, thoracic nerve; NR, no response.

Abnormal values of CMAP amplitude are underlined.

Table 3. Pain and sleep quality scores before neurosurgical intervention and 1 month and 2 months after neurosurgery

	Pre-surgery	1 month after surgery	2 months after surgery	*p*-value §
Pain intensity score	8 (6; 9)	4 (3; 5)	3 (2; 5)	<0.0001
Multidimensional 7-item S-LANSS score	18 (13; 19)	9 (6; 11)	7 (6; 9)	<0.0001
Sleep quality score	5 (4; 9)	3 (2; 4)	3 (2; 3)	<0.0001

Data are expressed as median and range

Abbreviations: S-LANSS - Self-completed Leeds Assessment of Neuropathic Symptoms and Signs

§ The Friedman test was used to compare the study outcomes over the scheduled visits

Table 4. Analgesic medications pre- and post- neurosurgery

	Pre-surgery	Post-surgery	*p*-value§ Pre- vs. Post-surgery
NSAIDs, No. (%)	10 (100%)	7 (70%)	0.25
Antidepressant drugs, No. (%)	4 (40%)	1 (10%)	0.25
Antiepileptic drugs, No. (%)	10 (100%)	2 (20%)	0.008
Opioids, No. (%)	2 (20%)	0	0.50

Abbreviations: NSAIDs – Nonsteroidal anti-inflammatory drugs

§Exact McNemar test