



Is nerve-sparing surgery enough to prevent chronic post-thoracotomy pain?

Kristine Pearson-Chauhan, Asokumar Buwanendran

Department of Anesthesiology, Rush University Medical Center, Chicago, Illinois, USA

Correspondence to: Asokumar Buwanendran, MD. Department of Anesthesiology, Rush University Medical Center, 1653 W. Congress Parkway, 759 Jelke, Chicago, Illinois 60612, USA. Email: asokumar@aol.com.

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The economic impact of chronic pain on society is greater than most other health conditions, but these estimates are inadequate when compared with the suffering, potential addiction from chronic opioid use and decreased quality of life experienced by patients (1). Persistent post-operative pain is defined as chronic postsurgical pain when it develops following surgery, was not present prior to the procedure, lasts at least two months in duration and there are no other causes or explanations for the pain (2). Chronic postsurgical pain after thoracotomy can develop in 25–60% of cases (3,4). Acute postoperative pain following thoracotomy is a result of many factors including incisional pain, pain due to damage caused to the musculature and ligaments due to retractors, pleural irritation secondary to chest tubes and most importantly intercostal nerve injury (5). Greater acute post-operative pain has been shown to be one of the predictors for the development of chronic post-surgical pain (6,7).

In this issue of the *Journal*, Jiwnani and colleagues evaluated a nerve-sparing modification for thoracotomy and rib closure using intracostal sutures to prevent entrapment of the intercostal nerve compared with a standard method using pericostal sutures (8). In their study, Jiwnani *et al.* randomized 90 patients undergoing posterolateral thoracotomy for pulmonary resection to standard or modified nerve-sparing thoracotomy. Patients were excluded if they were taking pre-operative analgesics, had a contraindication for any medications in the anesthetic and post-operative pain plan, were unlikely to follow-up, had

chest wall involvement, need for additional incisions or had a history of previous thoracotomy. The primary outcome was worst postoperative pain score in first three postoperative days and secondary outcomes of average pain score and analgesic requirements in the first 3 days. In addition, the incidence of post-thoracotomy pain at six months after surgery was assessed. The posterolateral (standard/control) approach involved incision at the fifth intercostal space, serratus muscle-sparing and pericostal suture closure while the nerve-sparing thoracotomy consisted of protecting and isolating the fifth intercostal muscle and neurovascular bundle and closure with intracostal sutures to avoid nerve compression with closure. A standardized anesthesia and postoperative pain management protocol was used and included intravenous fentanyl and morphine, diclofenac, paracetamol intra-operatively as well as morphine patient-controlled analgesia with scheduled paracetamol and diclofenac postoperatively. The acute pain scores were similar for both groups in the immediate postoperative period. The investigators observed an incidence of chronic postsurgical pain at six-month follow up to be 46% in posterolateral thoracotomy and 41% in the modified nerve-sparing group (study group). No difference in pain intensity, analgesic consumption, or incidence of chronic pain was observed between groups.

Neuropathic pain is one of the most challenging diseases to treat and is present in about half of patients with chronic post-thoracotomy pain (9). Neuropathic pain is

thought to be due to nerve injury and in the case of post-thoracotomy pain, injury to the intercostal nerves. Jiwnani *et al.* employed the technique of intracostal sutures in their modified technique to suture directly through the rib and avoid compression of intercostal nerves during closure. In a prior study, Bayram *et al.* evaluated intracostal closure with sutures through holes drilled in 5th and 6th ribs and partial dissection of 5th intercostal nerve bundle with closure via holes in 6th rib and over upper edge of fifth rib (10). They found lower visual analog scores and observer verbal ranking scale scores for the intracostal approach but did not assess chronic postsurgical pain.

Other studies have evaluated intercostal nerve damage in relation to type of thoracotomy performed. Ochroch *et al.* found no difference in postoperative pain scores between the posterolateral thoracotomy (latissimus muscle divided, and serratus anterior muscle spared) and the muscle-sparing axillary thoracotomy (11). The authors concluded that factors other than the muscle-sparing incision contribute to pain and stressed the importance of aggressive perioperative pain control. Benedetti *et al.* used electrophysiologic techniques to evaluate the evoked responses from abdominal walls and found that patients with absent reflexes experienced more severe postoperative pain (12). This led the authors to conclude that since abdominal reflexes are mediated partially by intercostal nerves that nerve damage may be contributing to postoperative pain. In a subsequent study they evaluated the correlation between nerve damage in posterolateral and muscle-sparing thoracotomy with chronic post-thoracotomy pain (13). In the later study, they found that compared to posterolateral thoracotomy the muscle-sparing approach resulted in less intercostal nerve impairment and less pain at one-month follow-up.

Rib retraction may play a role in the extent of nerve damage. In an animal model for evaluation of persistent post-thoracotomy pain we evaluated allodynia and histopathologic changes in intercostal nerves after rib retraction at 5, 30 and 60 minutes (14). Allodynia developed in 50% of animals with 60-minute retraction but in only 10% of the animals at 30 minutes (14). Extensive axon loss was noted in the intercostal nerves following rib retraction further supporting the basis for short duration of rib retraction and nerve damage. Rogers *et al.* studied thirteen patients undergoing thoracotomy by assessing motor evoked potentials from intercostal muscles before and after entering pleural space, after rib removal, and after intercostal space closure (15). They found that after the rib retractor was removed there was a total conduction block of the impulses

above the incision in all patients and below the incision in all but one patient. In a single patient where there was no use of rib retractor there was no nerve conduction impairment. This shows that nerve injury occurs routinely, seemingly due to rib retraction and in multiple levels above and below the incision. Maguire *et al.* assessed thirty-three patients and assessed intraoperative nerve conduction and found that nerve conduction block usually occurs discretely at site of rib retractor and affects the whole nerve during lengthy periods of retraction (16). They also found that additional patients incurred further nerve damage after closure. The extent of nerve injury was not correlated with chronic pain and they concluded that either intraoperative nerve damage does not reflect nerve-damage that will persist long-term or there is a “more significant cause for chronic pain than intercostal nerve injury” (16).

In Jensen and Kehlet's commentary questioning if pain following thoracotomy is neuropathic, they describe how it is difficult to identify neuropathic pain using existing questionnaires as the criteria used to develop a tool are often also used for validation (17). A specific constellation of sensory symptoms may not have a clear link to underlying pathology. Steegers *et al.* concluded that while up to half of the chronic pain is neuropathic there is a suggestion of a visceral component apart from nerve injury (9). Pain after thoracotomy arises from a combination of nociceptive somatic afferents, nociceptive visceral afferents, neuropathic and referred pain (18). The combination of inputs from surgical incision and rib retraction to injury of bronchi and visceral pleura contribute to nociceptor activation and primary sensitization which can ultimately lead to central sensitization and thus chronic pain after surgery.

Jiwnani *et al.* designed a relevant study considering the role of intracostal closure as well as neurovascular preservation considering studies suggesting the significant role of intercostal nerve injury in the development of chronic pain. Nerve injury occurs at levels immediately above and below as well as the adjacent nerve above and below immediate to retractor so salvaging the neurovascular bundle at the fifth intercostal space may not be enough. Additionally, nerve damage intraoperatively may not correlate with the development of chronic pain. The extent of the surgery is predictive of chronic pain and may be related to a combination of prolonged rib retraction and extent of visceral injury. Chronic pain development is a complex interplay of pre-existing patient factors including but not limited to genetic predisposition, psychosocial and intraoperative factors including surgical approach,

anesthetic technique as well as post-operative pain management. Post-thoracotomy pain is the most common sequelae of thoracotomy as it occurs in over half the patients. It is suggested that the possibility of chronic pain be addressed with patients and set reasonable expectations for healing and recovery.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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