



Neuropathic Pain After Thoracotomy: Risk Factors and Incidence

Torakotomi Sonrası Nöropatik Ağrı: Risk Faktörleri ve İnsidansı

Emel Gündüz,¹ Hakan Keskin²

¹Department of Anesthesiology and Reanimation, Akdeniz University, Antalya, Türkiye

Akdeniz Üniversitesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Antalya, Türkiye

²Department of Thoracic Surgery, Akdeniz University, Antalya, Türkiye

Akdeniz Üniversitesi, Göğüs Cerrahisi Anabilim Dalı, Antalya, Türkiye

ABSTRACT

Objectives: Chronic persistent post-operative pain, which persists for about 2 months or longer in 25–75% of patients who underwent thoracotomy operation, adversely affects patients' lives for years. In this study, we aimed to elucidate the etiology and incidence of neuropathic pain in patients undergoing thoracotomy.

Methods: Patients over the age of 18, who applied to the department of thoracic surgery with different diagnoses between 2017 and 2019 and underwent thoracotomy or video-assisted thoracoscopic surgery, and whose operation was performed 3 months before or more were asked to fill the previously prepared "Neuropathic Pain After Thoracotomy Incidence and Pain Evaluation of Risk Factors" form, during their polyclinic controls. In addition to demographic information such as age, gender, height, weight, body mass index, comorbidities, pre-operative hypnotic use, and neuropathic pain scores were also determined according to the LANSS pain scale.

Results: Of the 109 cases in which we evaluated the incidence and risk factors of neuropathic pain after thoracotomy, LANSS pain score was higher in females ($p=0.03$). The LANSS pain score was statistically significantly higher when viewed according to the smoking per pack/year.

Conclusion: If a thoracotomy is to be performed in female patients with heavy smoking, permanent thoracotomy pain should be prescribed, attention should be paid to the severity of the pain, and if necessary, individual analgesic methods should be determined.

Keywords: Incidence, neuropathic pain, risk factors, thoracotomy

ÖZ

Amaç: Torakotomi operasyonu geçiren hastaların %25-75'inde yaklaşık iki ay ve daha uzun süre devam eden kronik persistan postoperatif ağrı; yıllarca hastaların yaşamlarını olumsuz yönde etkilemektedir.

Yöntem: Göğüs cerrahisi kliniğine Nisan 2017-Aralık 2019 tarihleri arasında farklı tanımlarla başvurup torakotomi ya da video yardımlı torakoskopik cerrahi geçiren 18 yaşından büyük; operasyonun üzerinden üç ay veya daha uzun süre geçmiş hastalardan, poliklinik kontrolleri sırasında, daha önceden hazırlanmış olan "Torakotomi Sonrası Nöropatik Ağrı İnsidansı ve Risk Faktörlerinin Değerlendirilmesi" formunun doldurulması istendi. Yaş, cinsiyet, boy, kilo, beden kitle indeksi, ek hastalık, sigara ve alkol kullanımı ayrıca preoperatif hipnotik kullanımı gibi demografik bilgilerin yanında LANSS ağrı skalası üzerinden nöropatik ağrılarının skoru saptandı.

Bulgular: Torakotomi sonrası nöropatik ağrı insidansını ve risk faktörlerini değerlendirdiğimiz 109 olgunun 74'ünde (%67,9) bir ek hastalık mevcuttu. Hipertansiyon 46 olgu (%42,2) ile en sık görülen hastalık iken diyabet 17 olgu (%15,6) ile en çok görülen ikinci hastalıktı. Bu parametre ile LANSS ağrı skorlaması karşılaştırıldığında anlamlıydı. Çalışmamızda 109 olguda LANSS skoru > 12'den 8 olguda (%7,3) kronik persistan postoperatif ağrı gelişti.

Sonuç: Çalışmamızda 109 olgudan sekizinde nöropati geliştiğini bu olguların hepsinin açık torakotomi olduğunu, duyu kaybı geliştiğini bunlardan beşinin algoloji polikliniğine başvurduğunu ve gabapentin başlandığını tespit ettik. Kalıcı torakotomi ağrısı önceden öngörülmesi, ağrının şiddetine özen gösterilmeli, gerekirse bireysel bazda analjezik yöntemler belirlenmelidir.

Anahtar sözcükler: İnsidans, nöropatik ağrı, risk faktörleri, torakotomi

Please cite this article as: "Gündüz E, Keskin H. Neuropathic Pain After Thoracotomy: Risk Factors and Incidence. GKDA Derg. 2022;28(4):312-317".

Address for correspondence: Emel Gündüz, MD. Akdeniz Üniversitesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Antalya, Türkiye

Phone: +90 544 434 17 19 **E-mail:** dregunduz@hotmail.com

Submitted: September 26, 2022 **Accepted:** October 28, 2022 **Available Online:** November 22, 2022

©Copyright 2022 by The Cardiovascular Thoracic Anaesthesia and Intensive Care - Available online at www.gkdaybd.org

OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



Introduction

Chronic persistent post-operative pain (CPSP) is a serious health problem that affects daily life and quality of life in patients who develop. It lasts for about 2 months or more after thoracic surgery and is observed in 25–75%.^[1,2] Every surgical procedure involves an incision and accompanying nerve damage. Post-operative pain in thoracotomy can turn into a complex form of pain with a neuropathic component, with damage to the intercostal nerves. The importance of acute postoperative neuropathic pain is that most of it turns into chronic neuropathic pain. In a meta-analysis including many prospective studies of the incidence of CPSP, it has been reported that it is approximately 57% at the 3rd month and 47% at the 6th month after thoracotomy.^[3]

Chronic thoracotomy pain syndrome is a burning, stabbing, electric shock-like neuropathic pain that develops due to many physiological events, including surgical trauma, persists despite analgesic use and treatment, includes symptoms ranging from hypoesthesia to hyperalgesia; however, its pathogenesis is not fully elucidated. It is known that this pain is closely related to acute post-operative pain and begins after trauma in the somatosensory system and becomes chronic as a result of poorly planned or inadequate postoperative treatment.^[4]

It has been shown in many studies that risk factors such as age, gender, pre-existing pain, type, technique and duration of surgery, genetic predisposition, the psychosocial status of the cases, and intraoperative nerve damage contribute to its development.^[5,6] Although it has been reported that they contribute to neuropathic pain after thoracic surgery in studies examining both patient and surgery-related risk factors, there is no consensus in the literature on this issue.^[7]

In this study, we aimed to elucidate the etiology and incidence of neuropathic pain in patients undergoing thoracotomy.

Methods

Patients over the age of 18 applied to the department of thoracic surgery with different diagnoses between April 2017 and December 2019 and underwent thoracotomy or video-assisted thoracoscopic surgery (VATS), whose operation was performed 3 months before or more were included in the study. Emergency cases, patients with the previous thoracic surgery, who had pre-operative neuropathic pain, and underwent median sternotomy were excluded from the study. The study protocol was approved by Clinical Research Ethics Committee (approval number KAEK-396). A written informed consent form was obtained from each patient. Patients were asked to fill the previously prepared "Neuropathic Pain After Thoracotomy Incidence and Pain Evaluation of Risk Factors" form during their polyclinic

controls. In addition to demographic information such as age, gender, height, weight, body mass index, comorbidities, smoking and alcohol use, and pre-operative hypnotic use, neuropathic pain scores were also determined according to the LANSS pain scale.^[8] The data of the patients who met the inclusion criteria for the study were obtained using our hospital's data system and by interviewing the patients verbally. Information such as the reason for the operation, the surgical procedure, and its type, whether there was an intraoperative rib fracture, the duration of the operation and extubation, the need for additional post-operative analgesics, the number of days spent in the intensive care unit, chest tube and hospital stay were recorded. The size of the incision was measured with an elastic meter during outpatient control. All patients were placed in the lateral decubitus position after general anesthesia. Tramadol hydrochloride 100 mg 3×1 intravenously and Diclofenac sodium 100 mg 1×1 intramuscularly were routinely administered to all patients without questioning their pain levels after extubation. The post-operative additional analgesic requirement was recorded as analgesic agents applied according to the patients' pain levels as a result of pain questioning with visual pain scoring (VAS) performed at 4-h intervals after extubation. As analgesic agents; if the pain level was 5 and above according to the VAS, Paracetamol 500 mg 1×1 intravenously was administered first, and if the pain did not decrease when the pain level was questioned, Diclofenac sodium 100 mg 1×1 intramuscularly and finally Pethidine HCl was administered at a dose of 30 mg.

Results

Of the 109 cases, in which we evaluated the incidence and risk factors of neuropathic pain after thoracotomy, 41 (37.6%) were female, and 68 (62.4%) were male. The LANSS pain score was higher in females ($p=0.03$). The mean age of the cases was 54 ± 13.97 years, and no significant difference was detected.

Comorbidity was present in 74 (67.9%) of the patients. While hypertension was the most common disease with 46 cases (42.2%), diabetes was the second most common disease with 17 cases (15.6%). When the comorbidities were examined, there was no significant difference in LANSS pain scoring between those with and without comorbidities ($p=0.36$).

In the pre-operative drug history, six cases were taking hypnotic drugs ($p=0.88$); there was also no significant difference in smoking and alcohol use ($p=0.72$, $p=0.15$). However, the mean value of the smoking duration and frequency per pack/year was 33.1 ± 14.1 packs/year. When this parameter was compared with LANSS pain scoring, it was significant ($p=0.05$).

The surgical types of the cases were as follows: 103 cases (94.5%) underwent thoracotomy and 6 cases (5.5%) un-

Table 1. Demographic characteristics of the subjects

Participants	All patients (n=109)		LANSS>12 (n=8)		p
	n	%	n	%	
Gender					
Male	68	62.4	4	50	0.03
Female	41	37.6	4	50	
Age (years)		54±13.97		47.5±10.6	0.77
Hypertension	46	42.2	4	50	0.35
Diabetes	17	15.6	2	25	0.54
Smoking history (pack/year)		33.1±14.1		21.8±19.7	0.05
Pre-operative use of hypnotic medication	6	5.5	1	12.5	0.88
Surgery					
Thoracotomy	103	94.5	8	-	0.52
VATS	6	5.5	-	-	
Operation type					
Pneumonectomy	7	6.4	2	25	0.32
Lobectomy	31	28.4	2	25	0.75
Segmentectomy	6	5.5	1	12.5	0.27
Wedge resection	39	35.7	-	-	0.59
Decortication	14	12.8	1	12.5	0.07
Pleural/chest Wall tumor resection	12	11	2	25	0.68
Costal fracture	47	43.1	5	62.5	0.74
Surgery incision size (cm)		12.51±4.93		14±5.45	0.51

LANSS: Leeds Assessment of Neuropathic Symptoms and Sign; VATS: Video-assisted thoracoscopic surgery.

derwent VATS. As the reason for the operation, the most common reason was bronchial cancer with 32 (29.4%) cases, pleural effusion with two cases, and mediastinal mass with two cases. The type of surgery ($p=0.52$) and reason were insignificant.

Although intraoperative rib fracture was seen in 47 (43.1%) cases, it was insignificant ($p=0.74$).

As the type of surgical procedure, wedge resection was performed in 39 cases (35.8%), lobectomy in 31 cases (28.4%), and decortication in 14 cases (12.8%). Although it was very close to the significance value in decortication patients ($p=0.07$), it was insignificant when compared with the surgical technique applied with the LANSS pain score.

While the mean incision size was 12.51 ± 4.93 cm, it was found to be 13.09 ± 4.36 cm in thoracotomies. When this parameter was compared with thoracotomy and VATS, the data of all cases were according to LANSS pain score ($p=0.51$); it was $p=0.39$ in VATS, $p=0.67$ in thoracotomy, and the data were found to be insignificant (Table 1).

When the analgesic needs of 109 cases were evaluated, additional analgesia (500 mg Paracetamol $p=0.80$) was required in 89 cases, and diclofenac sodium 100 mg was administered ($p=0.44$) when paracetamol was not sufficient in 67 of these cases. However, Pethidine HCl 30 was admin-

istered as second additional analgesia in only 8 of the cases treated with Diclofenac sodium 100 mg. Statistical analysis of eight cases administered 30 mg of pethidine HCl was found to be significant ($p=0.03$) (Fig. 1).

The LANSS pain score of the cases who received additional analgesics was 6.1 ± 4.58 in paracetamol, 6.45 ± 4.92 in Diclofenac sodium, and 6.75 ± 3.05 in Pethidine HCl. We found that neuropathic pain developed in eight patients with a LANSS pain score above 12.

The mean operation time was 2.35 ± 1.03 h, and the extubation time was 2.94 ± 0.85 h. The intensive care unit stay was 3.21 ± 1.52 days. Chest tube length of stay was detected to be 5.81 ± 3.96 days, and hospital stay was 8.42 ± 4.79 days. When the LANSS pain scores of all time parameters examined in our cases were evaluated one by one, p values (0.49, 0.29, 0.88, 0.37, and 0.81) were found to be insignificant, respectively.

Discussion

In our study, CSPA developed in eight patients (7.3%) among those with a LANSS score >12 among 109 patients. Consistent with recent studies showing a low rate of CSPA. The LANSS pain score was found to be statistically significantly higher in heavy smokers and female patients.

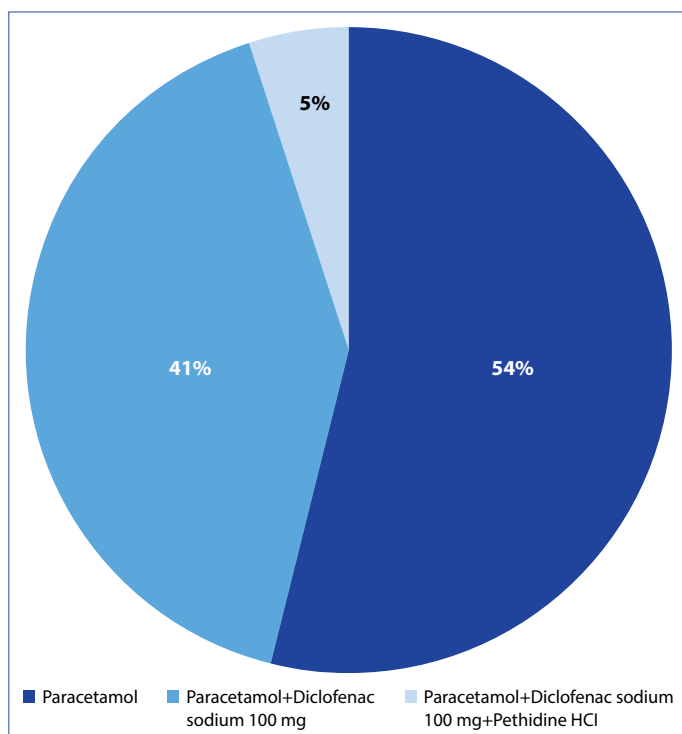


Figure 1. Post-operative analgesia needs of patients.

HCl: Hydrochloride.

The incidence of chronic pain after thoracotomy is quite high in the previous studies in the literature.^[9,10] In a meta-analysis conducted by Bayman et al.^[5] in 2014, 1439 patients have been followed up for 3 months in 17 studies, and in 15 different studies including 1354 cases, they have found CSPPS to be 54% and 47%, respectively, after 6 months postoperatively.

Although this rate has been reported as 11–80% depending on the selected patient and type of surgery, the incision applied, the technique, and the type of pre-operative-intra-operative-post-operative treatment; in their recent studies, Fiorelli et al.^[4] have reported that they observed CSPPS at a low rate of 35%, Arends et al.^[11] at 28.6%, and Yoon et al.^[12] at 14.3% in 3200 cases.

Despite many studies, CSPPS still has not been standardized, and there is no protocol. In general, those who accept the defined duration of post-operative chronic pain as 3 months or more or as 2 months or more like Macrae, different anesthesia techniques, different pain treatments, and the number of cases change the possible results.^[13] CSPPS developed in eight patients (7.3%) among those with a LANSS score >12 among 109 patients. Consistent with recent studies showing a low rate of CSPPS. It has also been stated in studies that the incidence of CSPPS decreases in a time-dependent manner.^[4,14]

Pre-operative risk factors including female gender being over 60 years old smoking history and comorbidities, especially diabetes mellitus and hypertension, are known to contribute

to CSPPS.^[10,15] Results were similar in our study. However, we found significance in patients with a large number of packs per day rather than years of smoking. It has been reported that sexual hormone receptors may be effective as the reason why CSPPS is observed more in the female gender.^[5]

If we look at the surgical-related risk factors of CSPPS, the incidence of neuropathic pain is seen in VATS cases, although it is less common than open thoracotomy. When the patient's results after thoracic surgery are evaluated together with the ERAS protocol, the application of intercostal muscle and nerve-separating muscle-sparing techniques in thoracotomy^[6,16] is accepted as moderate evidence strong recommendation. During thoracotomy closure, the inferior intercostal nerve should be separated while the ribs are approached.

Intercostal nerve damage due to the compression of the perioperative retractor and the immune response to the incision cause both peripheral and central sensitivity in the sensory system and contribute to the formation of neuropathic pain stages.^[2,10,17,18] Intraoperative rib fractures, passing through the intercostal nerve while suturing, VATS and trocar site may also cause postoperative neuropathic pain.

We did not apply intercostal block, which contributes to postoperative pain management applied by the surgeon in thoracic interventions.^[14,19] We thought to determine how effective analgesic agents can be in postoperative neuropathic pain. In addition, we did not prefer the use of opioids for postoperative analgesia since CSPPS is one of the risk factors, and it reduces the active participation of the patients in respiration due to its central effect.

The reason for the limitation of our study may be our thought that the low number of VATS causes the LANSS score to be insignificant. The reasons for the operation were different in the cases in which we detected neuropathic pain. In summary, less invasive technique, reduction of surgical nociceptive stimuli, reduction of tube drainage, early withdrawal and use of closed systems, nerve blocks and multimodal effective analgesic treatment, even preemptive analgesia, the addition of adjuvants such as ketamine (nociceptive suppression and modulation) can reduce sensitization and chronicity of the acute pain with synergistic action.

In analgesic treatment, 30.3% nonopioids, 25.2% opioids, and 10.9% anticonvulsants, and 1.7% antidepressants have been used.^[14] Additional analgesic paracetamol 500 mg was required in 89 cases (81.6%); we found that diclofenac sodium 100 mg was added in 75.2% of these cases. Pethidine HCl 30 mg was administered in 8 of 67 cases who received diclofenac sodium 100 mg. The results were significant in these cases. The mean operation, extubation, intensive care unit stay, and chest tube length of stay times were found to be insignificant according to the LANSS score. In most cases,

analgesic medication fails because it is administered at low doses and with non-specific agents for neuropathic pain.^[6]

Limitations

Our study has some limitations. The small number was the major limitation. Due to the small sample size, subgroup analyses could not be performed. To determine risk factors for CSPS, it is essential to design a prospective multicenter study in accordance with protocols with specific primary and secondary endpoints.

In our study, we found that eight out of 109 patients developed neuropathy, all of these patients had an thoracotomy, and five patients with sensory loss applied to the algology outpatient clinic and were started on gabapentin. Permanent thoracotomy pain should be foreseen, attention should be paid to the severity of pain, and analgesic methods should be determined on an individual basis if necessary.

Today, the concepts of post-operative chronic pain and acute neuropathic pain are included in the definition of postoperative pain. It is not possible to evaluate post-operative pain only as nociceptive pain. It is defined as a condition that includes nociceptive and neuropathic components and is likely to become chronic.

Disclosures

Ethics Committee Approval: The study was approved by The Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (Date: 09/06/2021, No: KAEK-396).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – E.G.; Design – E.G.; Supervision – H.K.; Fundings – H.K.; Materials – E.G.; Data collection &/or processing – H.K.; Analysis and/or interpretation – H.K.; Literature search – E.G.; Writing – E.G.; Critical review – E.G., H.K.

Etik Kurul Onayı: Çalışma Akdeniz Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylandı (Tarih: 09/06/2021, Numara: KAEK-396).

Hasta Onamı: Hastalardan yazılı onam alınmıştır.

Hakem değerlendirmesi: Dışarıdan hakemli.

Çıkar Çatışması: Çıkar çatışması bulunmamaktadır.

Finansal Destek: Yazarlar bu çalışmanın herhangi bir finansal destek almadığını beyan etmişlerdir.

Yazarlık Katkıları: Fikir – E.G.; Tasarım – E.G.; Denetmeler – H.K.; Kaynaklar – H.K.; Malzemeler – E.G.; Veri Toplanması ve/veya İşlenmesi – H.K.; Analiz ve/veya Yorum – H.K.; Literatür Taraması – E.G.; Yazıyı Yazan – E.G.; Eleştirel İnceleme – E.G., H.K.

References

1. Pluijms WA, Steegers MA, Verhagen AF, Scheffer GJ, Wilder-Smith OH. Chronic post-thoracotomy pain: A retrospective study. *Acta Anaesthesiol Scand* 2006;50:804–8.
2. Rogers ML, Duffy JP. Surgical aspects of chronic post-thoracotomy pain. *Eur J Cardiothorac Surg* 2000;18:711–6.
3. Bayman EO, Parekh KR, Keech J, Selte A, Brennan TJ. A prospective study of chronic pain after thoracic surgery. *Anesthesiology* 2017;126:938–51.
4. Fiorelli S, Cioffi L, Menna C, Ibrahim M, De Blasi RA, Rendina EA, et al. Chronic pain after lung resection: Risk factors, neuropathic pain, and quality of life. *J Pain Symptom Manage* 2020;60:326–35.
5. Bayman EO, Brennan TJ. Incidence and severity of chronic pain at 3 and 6 months after thoracotomy: Meta-analysis. *J Pain* 2014;15:887–97.
6. Homma T, Doki Y, Yamamoto Y, Ojima T, Shimada Y, Kitamura N, et al. Risk factors of neuropathic pain after thoracic surgery. *J Thorac Dis* 2018;10:2898–907.
7. Kampe S, Wendland M, Welter S, Aigner C, Hachenberg T, Ebmeyer U, et al. Independent predictors for higher postoperative pain intensity during recovery after open thoracic surgery: A retrospective analysis in 621 patients. *Pain Med* 2018;19:1667–73.
8. Siu E, Quick JS, Xu X, Correll DJ. Evaluation of the determinants of satisfaction with postoperative pain control after thoracoscopic surgery: A single-center, survey-based study. *Anesth Analg* 2019;128:555–62.
9. Hopkins KG, Hoffman LA, Dabbs Ade V, Ferson PF, King L, Dudjak LA, et al. Postthoracotomy pain syndrome following surgery for lung cancer: Symptoms and impact on quality of life. *J Adv Pract Oncol* 2015;6:121–32.
10. Springer JS, Karlsson P, Madsen CS, Johnsen B, Finnerup NB, Jensen TS, et al. Functional and structural assessment of patients with and without persistent pain after thoracotomy. *Eur J Pain* 2017;21:238–49.
11. Arends S, Böhmer AB, Poels M, Schieren M, Koryllos A, Wappler F, et al. Post-thoracotomy pain syndrome: Seldom severe, often neuropathic, treated unspecific, and insufficient. *Pain Rep* 2020;5:e810.
12. Yoon S, Hong WP, Joo H, Kim H, Park S, Bahk JH, et al. Long-term incidence of chronic postsurgical pain after thoracic surgery for lung cancer: A 10-year single-center retrospective study. *Reg Anesth Pain Med* 2020;45:331–6.
13. Macrae WA. Chronic pain after surgery. *Br J Anaesth* 2001;87:88–98.
14. Wu CF, Hsieh MJ, Liu HP, Gonzalez-Rivas D, Liu YH, Wu YC, et al. Management of post-operative pain by placement of an intraoperative intercostal catheter after single port video-assisted thoracoscopic surgery: A propensity-score matched study. *J Thorac Dis* 2016;8:1087–93.
15. Song JG, Shin JW, Lee EH, Choi DK, Bang JY, Chin JH, et al. Incidence of post-thoracotomy pain: A comparison between total

- intravenous anaesthesia and inhalation anaesthesia. *Eur J Cardiothorac Surg* 2012;41:1078–82.
16. Medbery RL, Fernandez FG, Khullar OV. ERAS and patient reported outcomes in thoracic surgery: A review of current data. *J Thorac Dis* 2019;11(Suppl 7):S976–86.
 17. Gottschalk A, Cohen SP, Yang S, Ochroch EA. Preventing and treating pain after thoracic surgery. *Anesthesiology* 2006;104:594–600.
 18. Ochroch EA, Gottschalk A, Augostides J, Carson KA, Kent L, Malayaman N, et al. Long-term pain and activity during recovery from major thoracotomy using thoracic epidural analgesia. *Anesthesiology* 2002;97:1234–44.
 19. Hsieh MJ, Wang KC, Liu HP, Gonzalez-Rivas D, Wu CY, Liu YH, et al. Management of acute postoperative pain with continuous intercostal nerve block after single port video-assisted thoracoscopic anatomic resection. *J Thorac Dis* 2016;8:3563–71.