

## Preventing and Treating Pain after Thoracic Surgery

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THE pain that accompanies thoracic surgery is notable for its intensity and duration. Acutely, moderate to severe levels of pain may not decrease substantially over the course of hospitalization and the first postoperative month.<sup>1</sup> Chronically, pain can last for months to years, and even low levels of pain can decrease function.<sup>1,2</sup> Other than pain syndromes associated with limb amputation, pain after thoracic surgery may be the most recognized pain syndrome associated with a specific surgery. Although used with increasing frequency, thoracoscopic approaches have not had the favorable impact on pain that many had anticipated.<sup>3,4</sup> Given that the adverse effects of thoracic surgery on pulmonary function can be mitigated by effective perioperative analgesia,<sup>5-7</sup> it is not surprising that thoracic surgeons have joined anesthesiologists in becoming strong advocates of analgesic interventions known to limit the pain accompanying thoracic surgery. Here, we review evidence-based strategies for preventing and treating this type of pain.

### Intensity, Duration, and Impact of Pain after Thoracic Surgery

Noxious input associated with thoracic surgery is conveyed to the central nervous system along the intercostal, vagus, and phrenic nerves. Afferent phrenic activity is believed to be the source of the shoulder pain that frequently accompanies thoracic procedures because this is curtailed by phrenic<sup>8</sup> but not suprascapular or epidural blockade.<sup>9</sup> Intercostal nerve dysfunction resulting from incision, retraction, trocar placement, or suture is common<sup>10</sup> and likely plays a significant role in the pain accompanying thoracic surgery. In addition, the need for

constant respiratory effort and enhanced pulmonary toilet produces an intense and relentless barrage of noxious input to the central nervous system.

Initial reports indicated that 50% of patients describe pain 1 yr after thoracotomy, with many continuing to report pain even years later.<sup>2</sup> Fortunately, the prevalence of postthoracotomy pain may be modifiable, with rates as low as 21% one year after surgery when perioperative pain is managed aggressively.<sup>1</sup> Surprisingly, video-assisted thoracic surgery (VATS) is associated with a prevalence of chronic pain comparable to that of open procedures,<sup>3,4</sup> with rates of pain ranging from 22%<sup>3</sup> to 63%,<sup>4</sup> which is probably due to intercostal nerve and muscle damage from trocar insertion. In contrast, residual pain 1 yr after surgery is reported to be 25% after median sternotomy,<sup>11</sup> emphasizing the role that reduced intercostal nerve disruption and improved stability of the closure may play in reducing chronic pain. Several demographic and clinical factors help to identify patients predisposed to development of chronic postsurgical pain. These include anxiety, depression, previous surgery, concurrent pain, lesions of the chest wall, youth, female sex, and increased levels of pain and analgesic use in the perioperative period.<sup>1,12-19</sup>

Lung volumes after thoracic surgery may be reduced by up to 50%, and aggressive analgesic therapy leads to improvements in pulmonary function not observed with standard therapy.<sup>5-7</sup> Supraventricular tachydysrhythmias are commonly observed after thoracic surgery<sup>20</sup> and may be less likely in conjunction with certain thoracic epidural analgesic regimens,<sup>21</sup> although this is more likely due to modification of sympathetic outflow than the associated analgesia. When pain persists, physical activity is reduced,<sup>1</sup> and even low levels of pain have been associated with reduced physical and social activity as well as global perceptions of decreased health.<sup>1,12</sup>

### Perioperative Strategies

The optimal perioperative analgesic strategy (fig. 1) is preemptive and multimodal. Although the definition<sup>22</sup> and efficacy<sup>23</sup> of preemptive analgesia are debated, several studies strongly suggest that preemptive approaches lead to reductions in pain and/or analgesic use after thoracic surgery.<sup>1,7,24-27</sup> However, it is equally clear that intraoperative nociception represents only a small por-

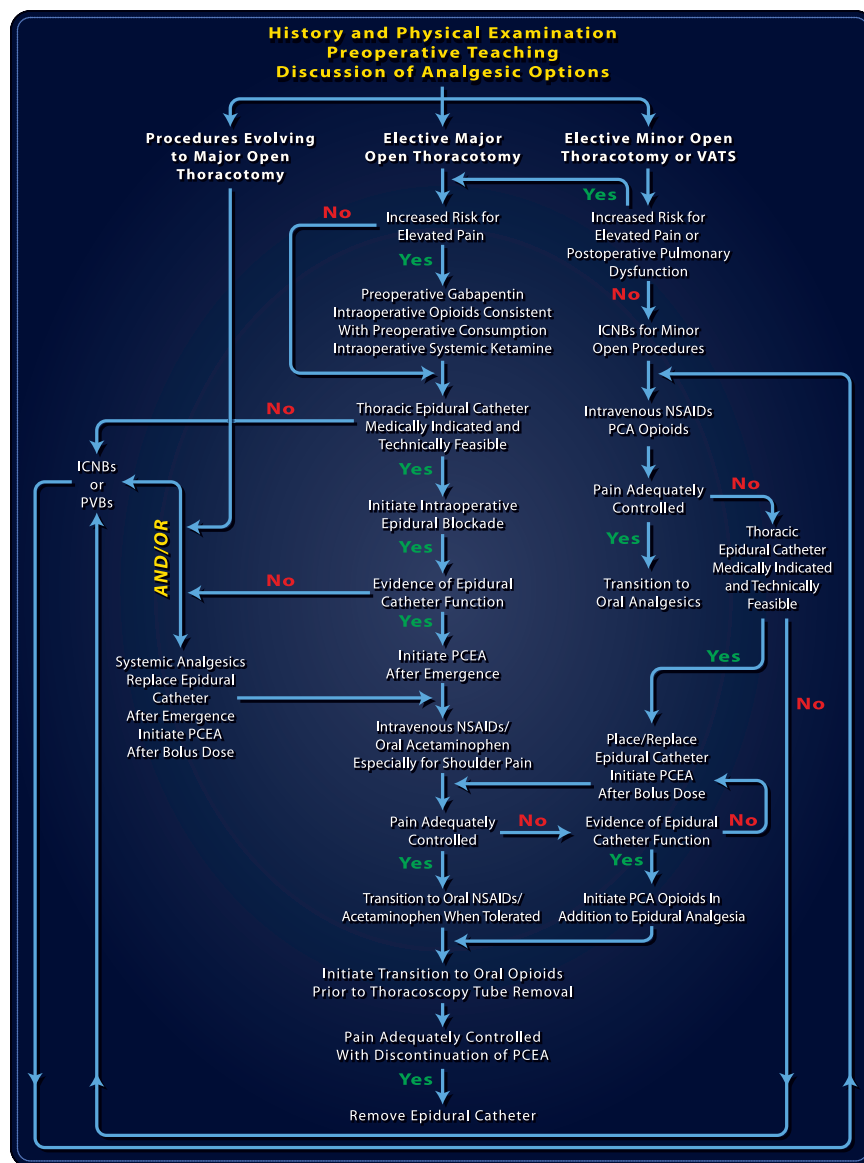
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Fig. 1. Flow diagram for management of acute perioperative pain associated with thoracic surgery. Preoperative evaluation and teaching permits risk assessment for increased pain, appropriateness of potential interventions, and the opportunity to ally anxiety. Thoracic epidural analgesia is the mainstay of recommended therapy, with alternative interventions for situations where thoracic epidural analgesia is not suitable. Special attention should be paid to patients at risk for increased perioperative pain or pulmonary dysfunction where more aggressive interventions and additional adjuncts may be valuable. When epidural catheters fail intraoperatively, intercostal nerve blocks (ICNBs) or paravertebral blocks may supplant epidural analgesia or serve as a bridge to the immediate postoperative period when an epidural catheter can be safely replaced. Ideally, the analgesic plan considers the entire perioperative period. See text for additional details. NSAID = nonsteroidal antiinflammatory drug; PCA = patient-controlled analgesia; PCEA = patient-controlled epidural analgesia; PVB = paravertebral block; VATS = video-assisted thoracic surgery.



tion of the noxious activity encountered during the entire perioperative period that could ultimately sensitize the central nervous system, exacerbating acute pain and initiating chronic pain. A multimodal approach takes into account the multiple pathways by which nociceptive input is conveyed to the central nervous system, the number of pharmacologically distinct mechanisms of modulating this input, the need for effective analgesia throughout the perioperative period and after discharge, and the importance of minimizing side effects, particularly respiratory depression. Although many aspects of analgesic management focus on specific analgesic interventions by the anesthesiologist and surgeon, other features of the surgical management may also impact on the intensity and duration of pain experienced by the patient.

#### Analgesic Strategies

**Thoracic Epidural Analgesia.** Thoracic epidural analgesia is currently the standard for analgesia for thoracic

surgery and, in the absence of contraindications, all patients undergoing major open thoracic surgical procedures should have a thoracic epidural catheter placed preoperatively.<sup>28,29</sup> Epidural catheter placement may also be useful in smaller open procedures and VATS in patients at high risk of severe perioperative pain, pulmonary dysfunction, or both. Ideally, for posterolateral and transverse sternothoracotomy, the tip of the catheter should reside at the dermatome along which the incision will be made. In the case of median sternotomy and muscle-sparing incisions, placement at the T6 interspace is effective. Although the *intraoperative* use of epidural analgesia may not confer substantial long-term benefits,<sup>1</sup> intraoperative use may still be desirable as an adjunct to general anesthesia, to ensure epidural catheter function and to facilitate a comfortable transition to the immediate postoperative period.

Typical intraoperative management of a thoracic epi-

dural catheter incorporates initial and maintenance doses with a combination of a local anesthetic and a relatively lipophilic opioid. Maintenance doses can be administered as boluses or continuous infusions. Some degree of hypotension is to be expected given the potential for sympathectomy. Judicious fluid and pressor administration avoids the large fluid shifts that could adversely affect physiology, particularly in patients who present with limited cardiac or pulmonary reserve.

Postoperatively, patient-controlled epidural analgesia should be initiated and continued until after thoracotomy tube removal. Typically, for thoracic epidural catheters, the epidural infusate combines a low concentration of a long-acting local anesthetic (e.g., 0.5–1 mg/ml bupivacaine or 1–2 mg/ml ropivacaine) and a relatively lipophilic opioid (e.g., 5 µg/ml fentanyl<sup>30</sup> or 10–25 µg/ml hydromorphone). Several well-designed studies have demonstrated improved analgesia when 2 µg/ml epinephrine was added to the infusate.<sup>31,32</sup> A large number of drugs, including ketamine<sup>33</sup> (with some reservations),<sup>34</sup> clonidine,<sup>35</sup> and neostigmine,<sup>36</sup> have been advocated as components of epidural analgesia but have not gained widespread acceptance. Typical patient-controlled epidural analgesia regimens after thoracotomy with an epidural catheter at the optimal dermatome would combine a continuous infusion of 4–6 ml/h with demand boluses of 2–4 ml every 10 min. Dysfunctional catheters should be replaced as quickly as possible.

Postoperatively, intravenous nonsteroidal antiinflammatory drugs are useful for treating shoulder pain refractory to epidural analgesia and, given their safety and effectiveness as analgesic adjuncts, patients using patient-controlled epidural analgesia should continuously receive oral or intravenous nonsteroidal antiinflammatory drugs during hospitalization and upon discharge.<sup>37,38</sup> Although the limited effect on platelets of drugs that specifically inhibit cyclooxygenase 2 may be important, the potential of these drugs in the setting of thoracic surgery awaits resolution of their cardiovascular safety.<sup>39</sup> Regular administration of acetaminophen may also be useful for treating shoulder pain<sup>40</sup> and can be used in addition to nonsteroidal antiinflammatory drugs. Patient-controlled analgesia with opioids can be used to supplement working epidural infusions, particularly in opioid-tolerant patients. For simplicity, a fixed epidural infusion is complemented by a patient-controlled intravenous infusion of opioids, where the safest initial approach is to permit patient-controlled analgesia demand doses only. For analgesic continuity when making the transition to oral opioid analgesics, the first oral dose should be administered at the time patient-controlled epidural analgesia is discontinued. For patients where pain management may be difficult, the epidural catheter

can remain in place to permit rescue analgesia until a satisfactory oral analgesic regimen is established.

**Alternatives to Thoracic Epidural Analgesia.** There are times when for technical, medical, or other reasons thoracic epidural catheter placement is unsuccessful, undesirable, or not possible. There may also be times when surgery, thoroscopic or other, evolves to an open thoracic procedure or when it is learned intraoperatively that an epidural catheter is dysfunctional. The prompt identification of these situations and institution of alternatives is essential for preventing severe postoperative pain. Although it may facilitate pain management, several case reports demonstrate the profound risks of placing or replacing an epidural catheter while a patient is under general anesthesia.<sup>41</sup> Although a degree of safety has been demonstrated for *lumbar* epidural catheter placement during general anesthesia,<sup>42</sup> it has been argued<sup>43</sup> that such data may not be reassuring when considering rare but catastrophic events. In addition to addressing problems with thoracic epidural catheter placement, alternatives to epidural catheter placement may also be suitable for VATS and smaller thoracic procedures when many practitioners would otherwise not place an epidural catheter.

Alternatives to midthoracic epidural analgesia include lower thoracic and lumbar epidural catheter placement, intercostal nerve blocks (ICNBs), paravertebral blocks, intrapleural catheters, local anesthetic infiltration, and systemic analgesia with one or more agents. Epidural catheters placed several dermatomes from the surgical site require larger volumes of analgesic. Even lumbar placement can be efficacious, particularly when used with hydrophilic opioids such as morphine.<sup>44,45</sup> ICNBs can be performed percutaneously or under direct vision, using single injections or placement of an intercostal catheter, or with cryotherapy. ICNBs are generally administered as single injections at least two dermatomes above and below the incision. Intercostal catheters can be placed, they but tend to be associated with less reliable spread of local anesthetic as well as rapid local anesthetic absorption and may be less effective than epidural analgesia.<sup>46–48</sup> Although cryotherapy of the intercostal nerves under direct vision avoids many of these issues, it is not as effective as epidural analgesia with respect to both quality of acute pain relief and preservation of lung function,<sup>49</sup> and it may also lead to increases in chronic pain.<sup>7</sup> Paravertebral blocks can be performed as single injections or *via* a paravertebral catheter. Paravertebral catheters can be placed percutaneously or intraoperatively under direct vision and are more suitable than epidural catheters when coagulopathy is of concern. Intraoperative paravertebral catheter placement precludes to an extent its use in a preemptive fashion. However, as indicated earlier, experience with epidural catheters suggests that this may not be very detrimental,



particularly if analgesia for the remainder of the perioperative period is effective. In at least some studies of acute pain, paravertebral blocks may be as effective as thoracic epidural analgesia with respect to pain control and preservation of pulmonary function after thoracotomy.<sup>50</sup> Intrapleural catheter placement can be performed percutaneously or under direct vision at the time of surgery. Intrapleural catheters are notable for the absorption of local anesthetic and less effective pain control when compared with epidural analgesia.<sup>51</sup> Local anesthetic infiltration added little to a combination of epidural analgesia and ICNBs.<sup>52</sup>

**Systemic Analgesics and Adjuncts.** Systemic analgesics are the main alternative to more invasive techniques, can be adjuncts to these techniques, and become the mainstay of analgesic therapy when invasive approaches are discontinued. Opioids, ideally administered initially *via* intravenous patient-controlled analgesia and upon discharge orally, are the main component of systemic analgesic therapy for thoracic procedures. Although respiratory depression is a potential side effect with systemic opioids, it should be appreciated that some patients may hypoventilate because of inadequate analgesia, in which case ventilation may actually improve after systemic opioid administration. As with more invasive approaches, nonsteroidal antiinflammatory drugs continue to be an important adjunct to opioid analgesia,<sup>53,54</sup> along with acetaminophen.<sup>40</sup> Tramadol administered by continuous intravenous infusion may be as effective as thoracic epidural morphine.<sup>55</sup> Given their efficacy in other types of surgery, the *N*-methyl-D-aspartate receptor antagonists ketamine and dextromethorphan, which both enhance *epidural* analgesia,<sup>56-58</sup> and the anticonvulsant gabapentin<sup>59-61</sup> may eventually play prominent roles in providing analgesia for thoracic procedures. Their ability to decrease subsequent pain and analgesic consumption in other procedures and animal models of thoracotomy pain argue for their use, particularly in individuals at high risk of development of substantial perioperative pain or in those individuals in whom more invasive analgesic regimens are not possible.

**Complications.** Initial concern that thoracic epidural catheter insertion would lead to more frequent complications has not been borne out. In fact, upper thoracic epidural catheter placement may be associated with fewer serious complications than lower thoracic or lumbar epidural placement.<sup>62,63</sup> The reason for this probably resides in the increased distance from nerve roots involved in lower extremity, bowel, and bladder function. The potentially catastrophic complications of epidural or intraspinal hematoma are best prevented by realization that motor blockade should not occur with dilute local anesthetic solutions, and postoperative motor weakness should trigger immediate imaging studies and neurosurgical consultation. Clearly, concerns about coagulopathy can limit epidural catheter placement.

The concern about pneumothorax with performance of ICNBs is obviated in the case of thoracic surgery because a chest tube is generally placed. However, the total dose of local anesthetic should be carefully calculated, because ICNBs are notable for high systemic blood levels from rapid absorption of local anesthetic. The issues related to paravertebral blocks are similar to those of ICNBs and also include hypotension from sympathectomy in some patients because of the proximity of the paravertebral space to the neuraxis.

### *Surgical Strategies*

Although many factors related to patient selection and the need for a particular surgical procedure are unalterable, there remain a number of modifiable technical aspects of the surgery purported to affect postoperative pain. These include the surgical approach (open thoracotomy *vs.* VATS), the type of incision for open procedures (posterolateral *vs.* muscle sparing *vs.* sternotomy *vs.* transverse sternothoracotomy ["clamshell"]), whether or not ribs are resected, the extent of intercostal nerve preservation, and the method of rib approximation at the conclusion of the procedure. As delineated above, the minimally invasive approach offered by VATS seems to have limited impact on the development of long-term postthoracotomy pain,<sup>3,4</sup> which is probably due to intercostal nerve and chest wall muscle trauma from trocar insertion. However, there is some evidence that VATS is associated with reductions in acute postsurgical pain, which is likely related to the smaller length of the incision and less rib retraction.<sup>64</sup> Although the surgical objective may dictate the operative approach, it is useful to note that the incidence of long-term pain after sternotomy<sup>11</sup> is reported to be less than after thoracotomy. This may be the result of less intercostal nerve and chest wall muscle trauma coupled with a surgical closure that produces a more stable chest wall. Although there are currently no data on pain after transverse sternothoracotomy, the possibility of intercostal nerve trauma and chest wall instability seems to be at least as great as for thoracotomy. Despite their distinct cosmetic advantages, muscle-sparing incisions seem to have minimal impact on postoperative pain development when compared with posterolateral incisions.<sup>65-67</sup> This is somewhat inconsistent with data indicating reduced intercostal nerve dysfunction after muscle sparing incisions when compared with posterolateral incisions.<sup>10</sup> Rib resection could reduce intercostal nerve trauma by avoiding trauma created by rib retraction or trocar insertion, and retrospective data from open thoracotomy<sup>7</sup> and VATS<sup>68</sup> support this contention. However, it is conceivable that periosteal scarring from rib resection might become a source of pain. Although preservation of the intercostal nerves seems to be a worthy surgical goal, accomplishing this is encumbered by frequent anatomical variation in the course of the nerves<sup>69</sup> and their lack of bony

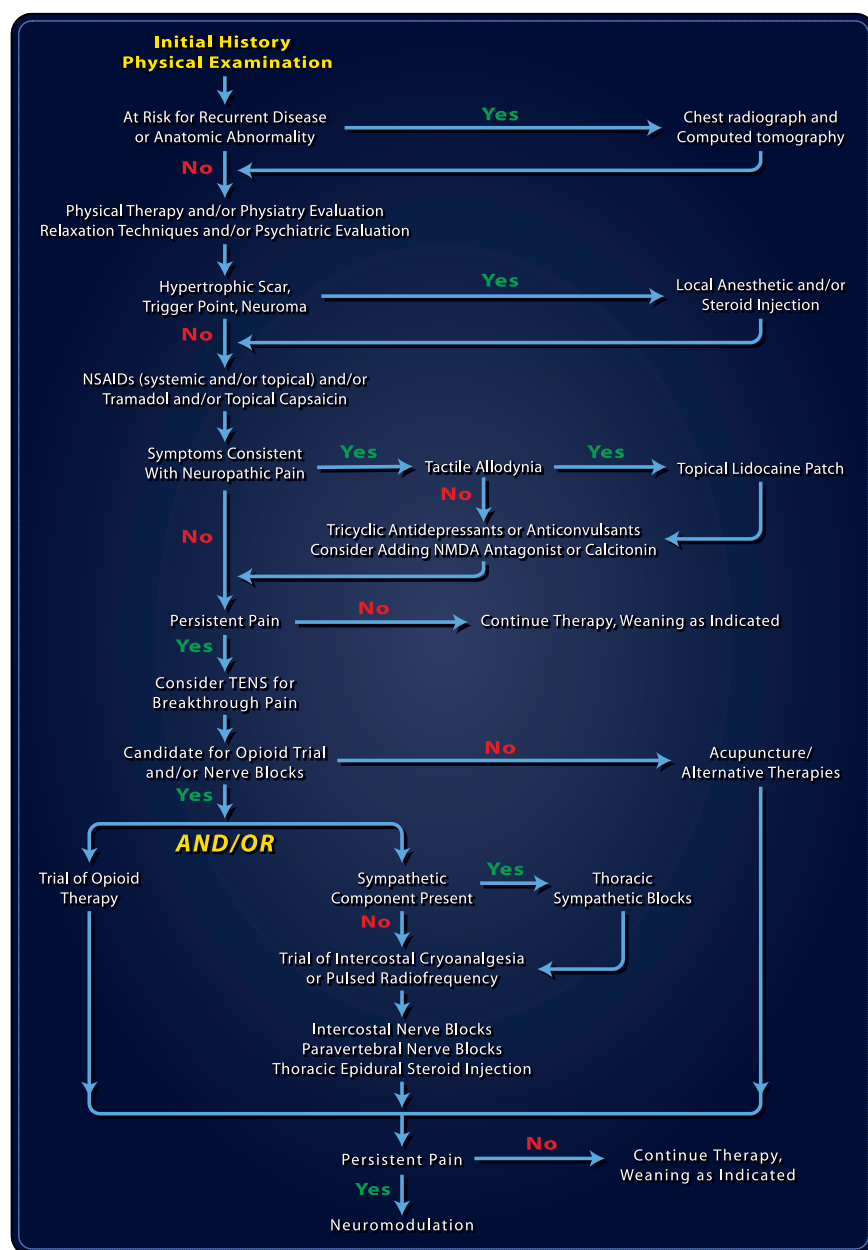
protection along the entire length of the rib.<sup>70</sup> Finally, techniques that approximate the ribs so as to minimize suture impingement of the intercostal nerves<sup>71</sup> or improve rib fixation<sup>72</sup> have been demonstrated to reduce pain after surgery.

## Strategies for Treating Long-term Pain

Although effective analgesic therapy seems to reduce the intensity and prevalence of chronic pain after thoracic surgery,<sup>1,7,26,27</sup> some patients, whether undergoing VATS or open procedures, still have development of chronic pain after thoracic surgery. Chronic postthoracotomy pain has been defined somewhat arbitrarily as “pain that recurs or persists along a thoracotomy scar at

least two months following the surgical procedure.”<sup>73</sup> Despite this definition, it is important to identify as early as possible patients with higher than expected pain levels so that appropriate therapy can be initiated, because analgesic therapy that is initiated earlier may be more effective.<sup>74,75</sup> As indicated above, a number of demographic and clinical factors help to identify patients predisposed to development of chronic postsurgical pain.

Long-term pain after thoracic surgery can be localized or radicular in nature and burning or aching in quality. The pain may have a pleuritic component and be exacerbated by movement of the ipsilateral shoulder.<sup>73</sup> The development of complex regional pain syndrome in the ipsilateral upper extremity can also occur.<sup>76</sup> As with



**Fig. 2.** Flow diagram for management of chronic pain following thoracic surgery. As part of the initial evaluation, medical or surgical problems that could initiate or exacerbate pain must be identified. Although most pain syndromes after thoracic surgery are neuropathic, it is important to identify myofascial pain which is treatable with specific interventions. Multiple topical and systemic medications are available for treating the various types of pain. In suitable patients, a trial of opioids can be instituted in parallel, before, or after a series of nerve blocks. Not all therapeutic options are appropriate for all patients, and care must be individualized. See text for additional details. NMDA = *N*-methyl-*D*-aspartate; NSAID = nonsteroidal antiinflammatory drug; TENS = transcutaneous electrical nerve stimulation.

the evaluation of any pain syndrome, it is essential to consider whether the pain is an indicator of some other process. This is of particular concern when evaluating patients with previous pleural or chest wall lesions, although bony instability, broken wires, retained foreign bodies, and lung herniation can also serve as pain generators. Although most cases of postthoracotomy pain are believed to be neuropathic in origin, myofascial pain can be a contributing and treatable source of discomfort.<sup>77</sup> The approach to pain after thoracic surgery is guided by the intensity of the pain as well as any associated disability. After a comprehensive evaluation, an individualized treatment plan should be crafted from one or more pharmacologic, interventional, and behavioral options (fig. 2).<sup>77-87</sup> Because there are still relatively few outcome studies on the treatment of chronic pain after thoracic surgery, most aspects of the approach advocated in figure 2 are imputed from studies and experience with other types of chronic pain. Referral to a pain specialist may be necessary for pain that is refractory.

## Conclusions

The acute and chronic pain that accompanies thoracic surgery is significant but often underappreciated, with an established level of physiologic and functional impact, and unknown social and economic costs. It is likely that an aggressive perioperative analgesic regimen, apart from its more immediate benefits with respect to comfort and pulmonary function, will lead to reductions in longer-term pain.<sup>1,7,26,27</sup> When it manifests itself, such long-term pain should be pursued early and aggressively using an analgesic strategy tailored to the specific features of that pain.

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