



Opioid-sparing opportunities in the thoracic surgery pathway

Genevieve F. Gilson¹, Sandeep J. Khandhar²

¹General Surgery, Inova Fairfax Medical Campus, Fairfax, VA, USA; ²Thoracic Surgery, Inova Fairfax Medical Campus, Fairfax, VA, USA

Correspondence to: Genevieve F. Gilson. Department of Surgery, Inova Fairfax Medical Campus, Fairfax, VA, USA. Email: ggilson926@gmail.com.

Comment on: Qiu Y, Lu X, Liu Y, *et al.* Efficacy of the intraoperative opioid-sparing anesthesia on quality of patients' recovery in video-assisted thoracoscopic surgery: a randomized trial. *J Thorac Dis* 2022;14:2544-55.

Keywords: Anesthesia; opioid-sparing; thoracic surgery; video-assisted thoracic surgery (VATS)

Submitted Nov 02, 2022. Accepted for publication Jan 24, 2023. Published online Feb 03, 2023.

doi: 10.21037/jtd-22-1556

View this article at: <https://dx.doi.org/10.21037/jtd-22-1556>

Pain control is an important component of postoperative care after all types of surgery and becomes particularly crucial in the management of the thoracic surgery patient. Pain must be properly addressed in these patients to allow for full re-expansion of the lungs, mucus expectoration, and prevent complications such as pneumonia. The introduction of video-assisted thoracic surgery (VATS) as a minimally invasive approach has led to great improvements in postoperative pain, recovery time, and complications compared to open thoracotomy, though it does come with its own challenges. Compression and retraction on the intercostal nerves, edema around the incision sites, and damage to the muscle fibers all contribute to pain experienced after VATS, and some go on to develop chronic neuropathic pain. The rate of chronic postsurgical pain, defined as pain persisting at least 3 months after surgery, occurs in 20% to 47% of patients after VATS, and has been found to be correlated with severe pain on the first day after surgery (1). This further underscores the importance of postoperative pain control. There is a careful balance to strike in designing a pain control regimen with adequate analgesia to allow for frequent ambulation and pulmonary hygiene, while also limiting the harmful side effects of opioid medications such as drowsiness, respiratory compromise, constipation, and dependence.

The use of regional epidural or paravertebral blockade has become a frequent component of multimodal pain control regimens to decrease postoperative opioid consumption. More recently, opioid-sparing anesthesia has gained attention as a strategy to reduce perioperative opioid use as well as the associated complications. It has been

studied as a safe, effective option in other types of surgery such as laparoscopic cholecystectomy, breast cancer surgery, spine surgery, and bariatric surgery (2). It has gained interest in the field of Thoracic surgery but so far has not claimed a heavy presence in the literature.

An *et al.* performed a randomized controlled study comparing opioid-free anesthesia versus opioid-based anesthesia for lung cancer patients undergoing VATS resection with emphasis on intraoperative pain control and depth of sedation, which revealed equally effective analgesia but higher levels of sedation required for the opioid-free group (2). This study described the use of Dexmedetomidine, sevoflurane, and thoracic paravertebral blockade for intra-operative anesthesia, but other studies have described patient-centered anesthesia using various combinations including dexmedetomidine, ketamine, clonidine, and other agents to achieve appropriate levels of analgesia and sedation.

A retrospective cohort study performed by Larue *et al.* compared the amount of postoperative opioid consumption, measured in oral morphine equivalents, in patients who underwent VATS with opioid-sparing anesthesia versus opioid-based anesthesia. Opioid consumption was found to be decreased in the immediate postoperative period and at 30 days after surgery, but no difference was found at 24 or 48 hours (3). The immediate difference in pain was attributed to the relatively long 2.5-hour half-life of Dexmedetomidine. The difference at 30 days was thought to be due to an opioid-sparing effect with overall fewer doses administered and therefore lower propensity to build a tolerance. While the power and design of this study was

not sufficient to make any assertion as to the superiority or non-inferiority of opioid-sparing anesthesia, it provided a framework to guide future investigation.

Qiu *et al.* performed a randomized controlled trial comparing postoperative outcomes in patients undergoing VATS who received routine anesthesia versus opioid-sparing anesthesia. They primarily investigated the quality of recovery in the postoperative period, as measured by the Quality of Recovery-15 scale (QoR-15) at 6 hours after surgery, and additionally compared QoR-15 at 24 and 48 hours after surgery, Overall Benefit of Analgesia Score Satisfaction with pain treatment (OBAS) and acute pain at 2, 24, and 48 hours after surgery. They concluded that opioid-sparing anesthesia did not demonstrate a clinically significant improvement in pain control at 6 hours after surgery, though the improved quality of recovery at 24 hours after surgery was of clinical significance. The opioid-sparing techniques also reduced the adverse effects of opioid anesthesia including postoperative nausea and dizziness, had shorter time to mobilize by 2 hours, and shorter time to first flatus by 5 hours (4).

This study exhibited several limitations which create a challenge in generalizing the findings. In considering the study design, it would have been helpful to control for the type of VATS procedure performed and therefore match for factors expected to contribute to postoperative pain such as length of procedure, number and size of incisions, extent of resection, and amount of torque placed on the ribs. The use of paravertebral blockade only for patients in the opioid-sparing group likely skewed their postoperative pain scores favorably, particularly in the first several hours after surgery as the regional anesthetic fully metabolized. The use of patient-controlled analgesia pumps postoperatively in both groups further complicated the quantification of pain control, especially if not analyzing the amount of demand doses required. The use of opioid-sparing anesthesia may decrease the total number of oral morphine equivalents given to a patient during the first several hours of their hospitalization, but there has yet to be adequate evidence that it improves patient outcomes to a clinically meaningful extent. In discussing the effects of opioid use in the thoracic surgical patient, it is the postoperative deleterious effects that we focus on such as respiratory drive, ability to ambulate, constipation, and dependence. Minimizing the amount of oral morphine equivalents used intra-operatively is unlikely to be of any benefit relating to those outcomes if all patients are placed on a opioid-based pain control regimen postoperatively regardless. And providing all

patients from both study groups PCAs without tracking the quantity of pain medication received takes away from the ability to prove that minimizing opioids during surgery helps minimize opioid consumption after surgery. Despite these limitations in the study design, this paper still presents an important contribution to the literature by considering all steps along the operative pathway as opportunities to minimize the patient's overall opioid intake.

In our experience with implementing a thoracic enhanced recovery after surgery (T-ERAS) program at a large tertiary center, the minimization of opioid use started not in the operating room, but much before that. A major component in the pathway which our program stresses is the preoperative office visit, where the first opportunity occurs for counseling and expectation setting, as was also mentioned in the discussion section of the Qiu *et al.*'s paper. It is at this time when the surgeon and the patient develop a mutual agreement for the subsequent steps in the pathway including early and frequent ambulation, minimization of pain medications, and the active role the patient must play in their own recovery. Members of the patient's support system are also encouraged to attend the preoperative visit, including spouses, family members, or friends. These are the people who will be at the patient's bedside after surgery and can play active, vital roles in recovery by holding the patient accountable to the agreements made during that first appointment. When the regional block begins to wear off and reinforcement is required after surgery, all parties involved in the patient's care hold a shared understanding of postoperative expectations and can participate in keeping the patient on track. And by informing the patient beforehand that opioids will not be part of their postoperative pain regimen, we find that they are less likely to stray from that pathway and require those additional medications (5).

We hypothesize several physical and psychological mechanisms which may have a role in the management of pain in the perioperative setting.

- (I) Managing expectations appears to be a critical facet of any successful endeavor. Understanding what is going to happen, when it will happen, and why it happens is not only educational for the patient but also empowers them to be active participants in the recovery process.
- (II) We routinely remind our patients that surgery and recovery is not "what we do to you", but "what we accomplish together". There is a short period of time where most everything is controlled by the

surgical team—the few hours of the operation—however the effort that is put into preparation and most everything that happens afterwards is in the hands of the patient. And we find the efforts of both parties become better aligned once we reach the mutual understanding that pain is an expected part of surgery.

- (III) The numerous analog and pictorial pain scales have done us a disservice in the perioperative period by creating the false association between happiness and being pain-free. We agree that if given the choice, pain-free surgery would be ideal however this is not a realistic expectation. Surgery elicits pain, and surgery in the chest elicits pain that is particularly challenging to treat, even with opioids. Perhaps a primary driver for this phenomenon is the division and then repetitive manipulation of the intercostal muscles. We know from other injuries that immobilizing an injured muscle greatly mitigates the pain such as when a broken arm or leg is placed in a cast. In the thorax however, immobilization of the chest would require the cessation of breathing and therefore pain is inevitable.
- (IV) Pain control is indeed a mainstay of postoperative care of the Thoracic Surgery patient, but not simply for the benefit of patient satisfaction. Rather it is emphasized because of the impact it has on ambulation, incentive spirometry, and mucus expectoration-factors that are also negatively impacted by opioid pain medications. The quantity of opioids necessary becomes a difficult balance between effectiveness of pain relief and degree of respiratory depression, all the while recognizing that other side effects such as bowel motility, constipation, lability of blood pressure, lightheadedness, dizziness, and cognitive decline all serve to reduce the patient's control of the recovery process and increase the risk of salient complications that actually can result in mortality, unlike pain. The available modalities for pain control pre and postoperatively all have significant limitations in effectiveness and side effect profile.

Opioids in the operating room have also become a routine part of anesthetic management but their necessity has been questioned as evidenced by the paper by Qiu *et al.* in this edition of the Journal and others. Based on the understanding above of the detriment of exogenous opiates postoperatively, perhaps the introduction of opiates

during surgery serves more to create a reliance on the administration of exogenous opiates later than it does to truly reduce pain. The human body evolutionarily has developed pain pathways for survival benefit and has the capacity to secrete endogenous opiates for similar benefit. Perhaps the administration of opiates during anesthesia slows the body's own mechanisms for endogenous opiate production and effectiveness. And perhaps the mechanisms at play are far too variable from patient to patient for one to make any generalization at this time.

It is conceivable that excluding opioid-based anesthesia would effectively decrease the total amount of opioid-based medication administered in the perioperative period, but the study design of further investigations must be altered to make any assertion regarding that relationship. We have seen a fall in the respiratory complications after thoracic surgery with minimally invasive techniques and must continue to seek opportunities at each step of the perioperative period to optimize patient outcomes and truly garner the benefit of a minimally invasive approach.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Thoracic Disease*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-22-1556/coif>). SJK reports that over the past 3 years, he serves as a consultant, advisory board member, and speaker and PI for Medtronic. Travel support was also provided by Medtronic. He serves as an advisory board member and speaker for Astra Zeneca, and advisory board member and speaker for Bristol Myers Squibb. Travel support was also provided by Bristol Myers Squibb and Intuitive Surgical. None of these relationships are pertinent to the work submitted but included in the interest of full disclosure. The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

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Cite this article as: Gilson GF, Khandhar SJ. Opioid-sparing opportunities in the thoracic surgery pathway. *J Thorac Dis* 2023;15(2):256-259. doi: 10.21037/jtd-22-1556