Editorial

The challenge of measuring post-operative pain reduction with opioid-sparing anesthetic techniques in video-assisted thoracoscopic surgery

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With the transition to minimally invasive approaches in thoracic surgery, patients are experiencing less post-operative pain (1,2). However, even with these techniques, post-operative pain after thoracic surgery is not negligible (1,2). Additional techniques to limit post-operative pain while minimizing opioid use are critical in order to promote early mobility and deep breathing which in turn can reduce pulmonary infections, decrease hospital length of stay, and lead to cost-savings (3-5). Few randomized, controlled trials exist, however, that assess the benefit of opioid-sparing techniques in terms of post-operative pain control.

Qiu *et al.* have recently performed such a randomized, controlled clinical trial comparing a regional nerve blockade-based opioid-sparing anesthetic technique to a standard opioid-based anesthesia regimen (6). Their study finds several benefits of their opioid-sparing technique over the standard technique. The study makes an important contribution by demonstrating an effective way to reduce intra-operative opioid use for video-assisted thoracoscopic surgery (VATS) patients. However, it also demonstrates several challenges when assessing and comparing pain control techniques among these patients.

First, selection of patient population poses a challenge. Qiu *et al.* include a heterogeneous assortment of VATS lung resections ranging from minor wedge resections to more extensive lobectomies. The post-operative pain after lobectomy is not necessarily comparable to that of a wedge resection due to the additional port sites, lengthier procedure, and more extensive dissection involved in a lobectomy. While similar numbers of wedge resections, segmentectomies, and lobectomies were used in the study by Qiu *et al.*, it may be more effective to include s single type of resection in order to more reliably interpret the results. Alternatively, for studies of heterogeneous patient populations like those of Qiu *et al.*, it would be helpful to see the results stratified by type of surgery, though this may pose a challenge in terms of sample size.

Second, the anesthetic and pain control regimens used must be both conducive to comparison among groups while also relatable to readers who likely use different regimens. Qiu *et al.* effectively detail their specific perioperative anesthetic and analgesic techniques which involves complete omission of long-acting opioid medication in the opioid-sparing group. However, they assigned patient-controlled analgesia pumps which included a continuous rate of sufentanil that was continued until post-operative day two. Use of such post-operative pain regimens may partially mask outcome differences of the variable of interest. Fortunately, in the case of Qiu *et al.*, the total opioid use was similar between the two groups suggesting the other differences were likely not due to differences in post-operative opioid consumption. However, it would be interesting to see if post-operative opioid-consumption could actually be reduced in the opioid-sparing anesthesia group.

Third, while peripheral nerve targeted analgesia in the form of intercostal or paravertebral nerve blockades are strongly recommended as a component of enhanced

recovery after thoracic surgery pathways, the ideal type of nerve blockade agent is not entirely clear (7). Also, the onset and duration of action of the agent of choice must be considered when assessing post-operative pain outcomes. For example, Qiu *et al.* use ropivacaine paravertebral blockade co-administered with dexamethasone as a central component of their opioid-sparing anesthesia technique. There is evidence that co-administration of dexamethasone prolongs the duration of efficacy of ropivacaine in nerve blockade, however, the duration of analgesia for this combination likely does not last beyond 24 hours (8). This is noteworthy given that Qiu *et al.* assess outcomes at several post-operative time points including 48 hours, which is likely beyond the duration of analgesia of the medication used. Our preference is to use a combination of standard bupivacaine and liposomal bupivacaine, which takes advantage of the faster onset standard formulation as well as the slower onset but longer acting liposomal formulation which can provide pain relief up to 96 hours (7,9,10).

Finally, perhaps the most challenging aspect of assessing and comparing efficacy of pain-control regimens is in the choice of a pain control metric. Options include but are not limited to patient reported pain scores, patient satisfaction surveys, composite recovery quality scores, total opioid usage, time to mobilization, and hospital length of stay.

Patient satisfaction surveys and other reported outcomes such as 0–10 numerical rating scales come with inherent subjectivity. While composite scores such as Quality of Recovery-15 (QoR-15) or Overall Benefit of Analgesic Score (OBAS) have been validated for perioperative recovery and pain control in some studies, they suffer from the same subjectivity (11,12). Additionally, such composite scores can mask the individual factors that are actually driving the score which, on their own, may not necessarily be considered the most relevant to pain control. To the credit of Qiu *et al.*, despite using the QoR-15 score at 6 hours as their primary outcome, they include a breakdown of the individual factors driving this score. Interestingly, the individual components of the score that they found to be different were the degree to which the patient felt rested, the patient's ability to look after personal toilet/hygiene, and the degree to which the patient felt comfortable/in control. While these may be indicators of improved pain control, they are perhaps not as direct measures of pain as other components of the score such as moderate pain, severe pain, or ability to breathe easily. Another important point when using numerical pain scores or QoR-15 scores, is that preoperative measurements should ideally be recorded because baseline scores and expected post-operative scores are associated with actual post-operative scores (13,14). Without a preoperative baseline assessment, report of such post-operative scores involves risk of confounding by unrecorded differences in baseline scores.

Total opioid usage can be an effective metric of pain control, however, it is not necessarily effective in isolation. For example, comparison of pain control regimens may result in equivalent opioid consumption among patients in two groups, however, other metrics such as pain scores, time to mobilization, and hospital length of stay may all be improved in one group suggesting that the same amount of opioid allowed for improved pain control over the comparison group.

Time to ambulation and hospital length of stay are especially interesting metrics of pain control, but they are downstream outcomes that are affected by several factors that include, but are not limited to, peri-operative analgesia.

While a perfect single metric for measuring post-operative pain does not exist, a combination of outcomes should be measured and reported to provide a holistic understanding of effects on post-operative pain. Care must be taken, however, using composite scores because the actual drivers of differences in such scores may be masked.

Overall, when attempting to identify better methods of perioperative pain management, researchers must carefully select the patient population, specific regimens to be compared, pharmacology of agents used, and pain control metrics. Ultimately, the accumulation of data from studies like that of Qiu *et al.* helps direct physicians toward regimens that reduce opioid use while minimizing postoperative pain.

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