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CORR Insights®: No Difference in Pain After Spine Surgery with Local Wound Filtration of Morphine and Ketorolac: A Randomized Controlled Trial

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Where Are We Now?

Analgesia after spine surgery remains a challenge. Many patients have moderate or severe postoperative pain, and analgesic therapy is often opioid-based. Resultant opioid-related side effects range from common and treatable (such as nausea, vomiting, and itching) to infrequent and dangerous (such as respiratory depression). For these reasons, better pain control after spine surgery is desired. Goals include reducing pain scores, reducing opioid use, and improving patient-oriented outcomes. Injection of a local anesthetic into the operative site is widely used and has been shown to be helpful after knee arthroplasty [1]. This may be termed local infiltration analgesia, periarticular injection, or simply wound infiltration. Some surgeons inject local anesthetics with epinephrine, while others mix a local anesthetic with a number of additives (including opioids and nonsteroidal anti-inflammatory drugs) [8]. Singhatanadgige et al. [8] randomized patients undergoing lumbar spine surgery to receive either control wound infiltration (bupivacaine and epinephrine) or multimodal wound infiltration (bupivacaine, epinephrine, morphine, and ketorolac). There was no meaningful difference in analgesic outcomes, suggesting that spine surgeons who use wound infiltration should use the simpler injectate of a local anesthetic with epinephrine.

Where Do We Need to Go?

It is not universally accepted that wound infiltration provides a major benefit to patients undergoing spine surgery [2]. The first major question to address is whether surgical wound infiltration should be used for lumbar spine surgery. Is there a meaningful patient benefit? Singhatanadgige et al. [8] do not directly address this question, given that they did not include a no-injection control group, but their study raises the possibility that wound infiltration (of whatever composition) does not provide a meaningful benefit to patients undergoing lumbar spine surgery. The question remains as to whether the duration of analgesia that these injections provide is sufficient to matter.

Some form of wound infiltration may be beneficial to patients undergoing spine surgery. Perhaps a simple injection is not effective, but there could be a more complex mixture that is effective for wound infiltration. In other words, if a surgeon choses to infiltrate a lumbar spine wound, should the surgeon also inject other medications to prolong or improve the quality of the analgesia, as was investigated by Singhatanadgige et al. [8]? They showed that adding morphine and ketorolac was not helpful, but are there additives that provide clinical benefit? Are the additives working locally or is wound infiltration a cumbersome way to deliver the equivalent of an intramuscular injection?

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This leads to the next question: how do we decide if an analgesic intervention is truly beneficial? Statistical significance is not enough; in order for an intervention to be adopted into practice, the change brought about by it needs to be clinically meaningful [4]. In some cases, investigators have determined minimal clinically important differences (MCIDs). A MCID answers the question of how large a treatment effect needs to be for a patient to care about it [4, 10]. It is likely that MCIDs depend on the context (such as surgery or chronic illness), type of operation, and patient characteristics. MCID information from one country or region may not apply universally because of cultural factors, different expectations, and country-specific availability of opioids. The patient-acceptable symptomatic state (PASS) is a concept related to the MCID that converts a linear scale into a binary result by asking whether an intervention results in a state that the patient finds acceptable [10]. For example, a patient will likely feel better if a numerical rating scale pain score reduces from 10 to 7, but may still think that a pain score should be less than 4 to be truly acceptable [6]. Such patients would be considered responders to analgesic therapy if the numerical rating scale score changed from 5 (above the PASS cutoff) to 2 (below the PASS cutoff). Knowledge of responder rates can guide clinical decisions and allow for a determination of useful concepts such as the number needed to treat. MCID and PASS information is available for pain scores [6] and many orthopaedic questionnaires [5]. Unfortunately, MCID and PASS information is not readily available for many perioperative patient-oriented outcomes. The MCID and PASS have been determined for quality of recovery scales [7], but questions remain about whether this scale is sufficiently responsive to analgesic interventions for widespread use as a primary outcome in analgesic trials [9].

Speaking broadly, the main question is, how should trials aimed at improving analgesia after lumbar spine surgery be conducted and analyzed? As clinicians and researchers, what do we do with a well-designed and well-conducted trial yielding a statistically significant difference that is less than the MCID [10]? Statistically significant results without clinically important effect sizes should not change clinical practice.

How Do We Get There?

The first question—does surgical wound infiltration as currently practiced provide a benefit to patients undergoing lumbar spine surgery?—can be addressed with randomized trials that include placebo controls. Singhatanadgige et al. [8] did not address this issue directly but hint that wound infiltration may not provide a major benefit. Another approach would be to perform retrospective analyses of large databases. National databases may have insufficient information to address these questions, but institutional electronic medical records could be queried to see whether there is a clear association between the use of surgical wound infiltration and patient improvement. Database research provides information on a large scale, but it is difficult to fully address potential confounding factors. Additionally, preexisting databases may not include all of the desired data. A complementary approach would be to study patient outcomes prospectively, both before and after systematically adopting an intervention. This is not as rigorous as a randomized controlled trial, but can provide pragmatic real-world information about an intervention.

The second major question—the ideal composition of the injectate—is probably best addressed with carefully designed randomized controlled trials. Singhatanadgige et al. [8] showed that adding ketorolac and morphine to the wound infiltration mixture was not an improvement over bupivacaine with epinephrine, but other injectates can be evaluated. In such studies, a proper power analysis is essential. This requires an accurate idea of the mean and standard deviation of the control population (it is often best to use locally obtained data) and a defensible estimate of the projected difference. The MCID should be considered when the effect size is selected for a study, and studies should be powered so that they are large enough to detect clinically important differences. It may be acceptable for a study to be underpowered for smaller differences that are likely not to be perceptible to patients and so are unlikely to justify the intervention.

Further research is needed to define the MCID and PASS. For analgesic trials, it is crucially important to have patient-oriented outcome questionnaires that are responsive, meaning that clinically relevant changes in analgesic outcomes should lead to changes in outcomes scores that exceed the MCID.

It seems likely that the way forward is not with a single analgesic improvement, but with bundles of interventions. After a careful consideration of relevant evidence, pathways should incorporate a group of interventions thought to be incrementally helpful. A pathway may incorporate multiple studies with beneficial effects that are smaller in size than the MCID [3].

Combining multiple interventions may have additive effects, and such a pathway may provide a clinically meaningful benefit. The enhanced recovery after surgery approach is a codified technique for perioperative pathways. These pathways should be tested and shown to be beneficial before widespread adoption. Either randomized controlled trials [9] or before-and-after studies of the effects of adopted pathways are recommended. Eventually, large-scale surveillance studies need to be performed to evaluate whether there is a risk of rare side effects or complications.

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