Searching for the Optimal Pain Management Technique after Knee Arthroplasty

Analgesia Is Just the Tip of the Iceberg

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TOTAL knee arthroplasty (TKA) is among the most common and painful surgical procedures, with more than 700,000 performed annually within the United States alone. Due to the difficulty of providing adequate pain relief, practitioners have proposed and evaluated a plethora of analgesic techniques. Unfortunately, little consensus exists as to the optimal method, in no small part because most investigations have only compared two or three methods—or combinations of methods—at a time. It is therefore noteworthy that a study published in this issue of Anesthesiology by Terkawi *et al.*[1] uses an innovative technique—network meta-analysis—to simultaneously compare 17 different analgesic modalities after TKA and provide new insight into this important issue.

"Will there, then, finally be widespread consensus regarding the optimal post-[total knee arthroplasty] analgesic technique with this new analysis?"

Traditional *pairwise* meta-analysis combines the results of multiple randomized controlled trials (RCTs) that all investigate the *direct* comparison of two—and only two—interventions to produce an estimate of the relative net benefits of these interventions (fig. 1A).[2] In contrast, *network* meta-analysis synthesizes the results of multiple RCTs that do not necessarily include one common intervention but various possible treatments (fig. 1B).[2] Using a process similar to geometry's transitive property of equality, this technique allows *indirect* comparison of diverse modalities that might themselves never have been directly compared. For example, if one RCT demonstrates that treatment A is superior to B and a second RCT provides evidence that treatment C is superior to A, then "networking" the two we have evidence that treatment C is superior to B, even though these two interventions were not directly compared (fig. 1B).

Using network meta-analysis, Terkawi *et al.*[1] combined data from 170 RCTs that each compared two or more treatments for post-TKA pain in a total of more than 12,500 subjects. Using this statistical method, the authors were able to evaluate 17 different analgesic techniques and determine their relative benefits, even though many or most of the combinations have never been directly compared.[1] The main finding was that various combinations of peripheral nerve blocks minimized pain at rest and opioid consumption, while maximizing passive range of motion compared with individual peripheral nerve blocks, periarticular local anesthetic (plus or minus additives) infiltration, epidural analgesia, intrathecal morphine, auricular acupuncture, and intravenous opioids. The authors explain that the optimal modality should achieve effective pain control with less opioid consumption and the best rehabilitation profile, and ultimately conclude, "Considering only high-quality studies, **femoral/sciatic** [blocks] **seemed best**" (emphasis added).

The need to restrict analysis to "high-quality studies" indicates that many studies in this field do not fulfill even basic methodologic requirements, which is obviously concerning. Aggregating data of questionable quality does not improve the precision or validity of results, and the reliability of traditional *pairwise* meta-analysis has been questioned.[3–5] *Network* meta-analysis—with its far greater degree of complexity[2]—has not been immune to similar concerns.[6] However, a discussion involving this complicated yet important topic is outside of our purview here; for the purposes of this editorial, we will assume that the results of Terkawi *et al.*[1]

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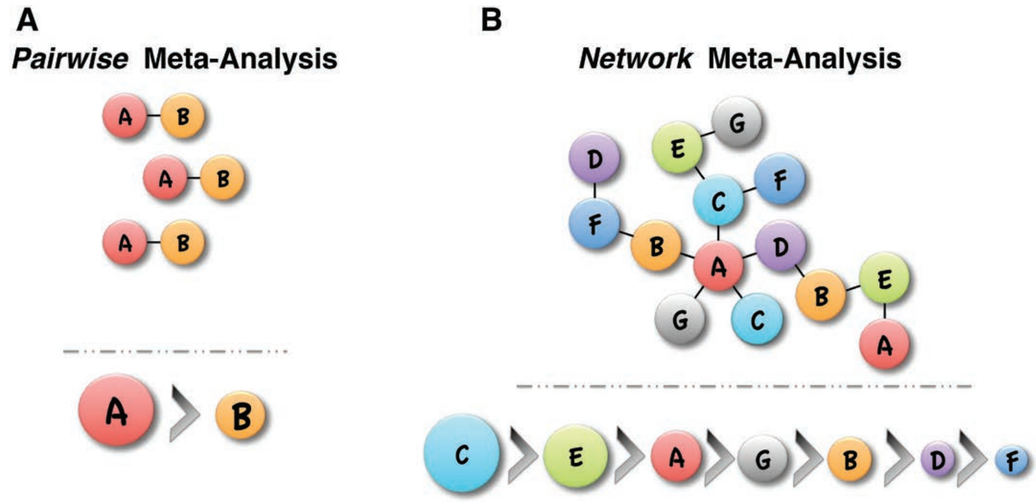

Fig. 1. A visual representation of two forms of meta-analysis. Each *circled letter* represents a distinct treatment, and each *line* represents a randomized controlled trial comparing two interventions. A traditional *pairwise* meta-analysis (*A*) compiles multiple trials comparing two treatments (*above dashed line*) and produces an estimate of the relative net benefits of the two (*below dashed line*). A *network* meta-analysis (*B*) uses a process allowing *indirect* comparisons of multiple, diverse treatments (*above dashed line*)—relatively few of which have been directly compared—to provide an estimate of the relative net benefits of all included interventions (*below dashed line*).

reflect a high degree of external validity—that is, they accurately reflect the experiences of most TKA patients.

Will there, then, finally be widespread consensus regarding the optimal post-TKA analgesic technique with this new analysis? Will the more than 20% of practitioners providing epidural analgesia and nearly 60% of providers affording no regional analgesic whatsoever begin offering femoral and sciatic nerve blocks to their TKA patients?[7] The answers are probably related to Terkawi *et al.*'s reflection that pain, opioid use, and passive range of motion are but three factors defining the preferred analgesic technique and that "All these factors need to be balanced when choosing the optimal modality."[1]

To illustrate the importance of this concept, consider the results if a 72-h continuous spinal technique had been included as a postoperative analgesic modality in the meta-analysis. Without doubt, this analgesic technique inducing bilateral insensate extremities would have been found to provide the best pain control, minimize opioid requirements, and maximize passive range of motion and would therefore likely have been found to be highly effective by the definitions of the current study. However, the total motor, sensory, or proprioceptive block would completely preclude ambulation and *active* range-of-motion exercises, both considered crucial for adequate rehabilitation (not to mention the risks of infection, postdural puncture headache, bed sores due to inactivity, among others), and make the technique entirely impractical.

Clearly, there is a great deal more to evaluating postoperative analgesic modalities than pain scores, opioid use, and passive range of motion. Terkawi *et al.*[1] commendably attempted to collect much of this additional information but found that due to a lack of dependable data or other factors, they could not reliably assess with meta-analysis quadriceps strength, straight leg raises, maximum walking distance, the Timed Up and Go test; the incidence of wound infection, falls, postoperative delirium, nerve injury, intervention failure, or study withdrawal; as well as patient satisfaction. All meta-analyses are restricted to data reported in the underlying studies. A consequence is that the findings of Terkawi *et al.*[1] are heavily weighted toward three factors that, while indisputably important (and the focus of most anesthesiology-based investigations), do not reflect the full range of priorities of patients, surgeons, physical therapists, nursing staff, administrators, insurance companies, and government institutions.

To illustrate the impact of stakeholder priorities, consider the relatively simple question of whether to use a sciatic nerve block.[8] Some practitioners avoid any type of sciatic nerve block to enable identification of a possible intraoperative injury immediately after surgery (the incidence of sciatic nerve palsy is as high as 2.4% even without regional anesthesia or analgesia).[9,10] In contrast, a single-injection and continuous sciatic nerve block are often provided when opioid avoidance or potent analgesia are prioritized.[11] Some clinicians emphasize postoperative ambulation and favor a preoperatively administered single-injection sciatic block to provide intense analgesia when it is needed most—immediately after surgery—but no subsequent perineural local anesthetic infusion due to the possible foot drop's negative effects on ambulation.[12] Yet others who similarly prioritize mobilization refuse even a single-injection block as it inhibits weight bearing in the immediate postoperative period and yet want a continuous block to decrease pain and improve patient tolerance for physical therapy.[13] And, finally, there are some who advocate avoiding any peripheral nerve block due to concern about an increased risk of falls with either—in this case femoral—single-injection[14] or continuous infusion[15] (evidence suggests there is no increased risk with single-injection but added risk with continuous femoral blocks).[16] It is impossible to truly ascertain the optimal analgesic method for TKA without accounting for any increase in the risk of falling, effects on standing or ambulation ability, and adverse events such as myocardial infarction due to uncontrolled pain or apnea due to opioid-induced respiratory depression.

Therefore, the investigation by Terkawi *et al.*[1] is important not only because of the information it provides—combinations of peripheral nerve blocks minimize pain and opioid requirements while maximizing passive knee range of motion—but also in that it documents enormous deficits within the existing literature. Perhaps, with high-quality data from future clinical trials, a general consensus regarding the optimal post-TKA analgesic technique will emerge. Most likely, however, even with such knowledge, the myriad institution-specific characteristics, practitioner priorities, and other stakeholder preferences will preclude the determination of a single, optimal analgesic technique for all patients after TKA. Perhaps, a more realistic goal is providing all stakeholders and institutions with enough objective information that they can determine the optimal pain control modality and protocol for their individual situation. In this respect, the study by Terkawi *et al.*[1] is a superb addition to our knowledge involving post-TKA analgesia in that it provides actionable information for clinicians and other stakeholders and guidance for future clinical trials.

Competing Interests

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