knee arthroplasty patients in the United States (76.2%) receive general anesthesia alone, whereas only 12.1% receive any type of peripheral nerve block. Given these data, recommending a complex combination of both femoral and sciatic nerve blocks is totally impractical and does not improve access. Rather, introducing a single peripheral nerve block intervention in the context of multimodal analgesia may be more achievable.

Centers with an established multimodal analgesic total joint pathway have recently seen an essential shift in the application of peripheral nerve block for postoperative analgesia in the total knee arthroplasty patient with the implementation of the adductor canal block. Routine use of femoral[3] and sciatic nerve blocks for pain control conflict with the goals of early active mobility and may delay diagnosis of perioperative common peroneal nerve injury, which can occur in 0.3 to 4% of patients.[5] If patients are already receiving multimodal analgesia, peripheral nerve block, and periarticular injections,[6] sciatic block may not offer added benefit.[7]

Total knee arthroplasty clinical pathways that combine multimodal analgesics with continuous peripheral nerve block have already been shown to reduce hospital length of stay[3] and improve early participation in physical therapy.[8] It seems evident that the pathway, and perhaps not the individual items themselves, is most important. We believe the more critical question that still needs to be answered is how to best tailor a multimodal total knee arthroplasty clinical pathway to a specific institution and patient population to provide the best pain control, promote early ambulation, improve patient satisfaction, and facilitate timely discharge.

Competing Interests

Unrestricted educational program funding paid to Dr. Mariano's institution from Halyard Health (Alpharetta, Georgia). Dr. Horn is a consultant for Teleflex (Wayne, Pennsylvania) and Halyard Health. The other authors declare no competing interests.

Christopher A. J. Webb, M.D., Sarah Madison, M.D., Stuart B. Goodman, M.D., Ph.D., F.R.C.S.C., F.A.C.S., F.B.S.E., F.I.C.O.R.S., Edward R. Mariano, M.D., M.A.S., Jean-Louis Horn, M.D. Stanford University School of Medicine, Stanford, California (J.-L.H.). hornj@stanford.edu

References

1. Terkawi AS, Mavridis D, Sessler DI, Nunemaker MS, Doais KS, Terkawi RS, Terkawi YS, Petropoulou M, Nemergut EC: Pain management modalities after total knee arthroplasty: A network meta-analysis of 170 randomized controlled trials. Anesthesiology 2017; 126:923–37
2. Ilfeld BM, McCartney CJL: Searching for the optimal pain management technique after knee arthroplasty: Analgesia is just the tip of the iceberg. Anesthesiology 2017; 126:768–70
3. Webb CA, Mariano ER: Best multimodal analgesic protocol for total knee arthroplasty. Pain Manag 2015; 5:185–96
4. Memtsoudis SG, Danninger T, Rasul R, Poeran J, Gerner P, Stundner O, Mariano ER, Mazumdar M: Inpatient falls after total knee arthroplasty: The role of anesthesia type and peripheral nerve blocks. Anesthesiology 2014; 120:551–63
5. Park JH, Restrepo C, Norton R, Mandel S, Sharkey PF, Parvizi J: Common peroneal nerve palsy following total knee arthroplasty: Prognostic factors and course of recovery. J Arthroplasty 2013; 28:1538–42
6. Sawhney M, Mehdian H, Kashin B, Ip G, Bent M, Choy J, McPherson M, Bowry R: Pain after unilateral total knee arthroplasty: A prospective randomized controlled trial examining the analgesic effectiveness of a combined adductor canal peripheral nerve block with periarticular infiltration *versus* adductor canal nerve block alone *versus* periarticular infiltration alone. Anesth Analg 2016; 122:2040–6
7. Li J, Deng X, Jiang T: Combined femoral and sciatic nerve block *versus* femoral and local infiltration anesthesia for pain control after total knee arthroplasty: A meta-analysis of randomized controlled trials. J Orthop Surg Res 2016; 11:158
8. Duncan CM, Moeschler SM, Horlocker TT, Hanssen AD, Hebl JR: A self-paired comparison of perioperative outcomes before and after implementation of a clinical pathway in patients undergoing total knee arthroplasty. Reg Anesth Pain Med 2013; 38:533–8

(Accepted for publication October 27, 2017.)

In Reply:

Webb *et al.* note our conclusion that "the combination of femoral and sciatic nerve blocks provides the best analgesia"[1] and assert that it is "not surprising that anesthetizing multiple nerves is superior to blocking a single nerve." In fact, it was hardly a forgone conclusion that sciatic nerve blocks are necessary, because femoral nerve blocks alone work fairly well and might have proven sufficient, especially when combined with supplemental nonopioid systemic analgesics. Our results clearly show that sciatic nerve blocks significantly augment the benefit of femoral nerve blocks, and—importantly—quantify the effect magnitude.

Webb *et al.* comment that the incidence of transient peroneal nerve palsy was high in combined femoral-sciatic nerve blocks (7.6%). It is important to recognize that this fragile estimate was based on only six episodes in the femoral-sciatic group and was nearly the same as after periarticular infiltration (6.4%). Given how infrequently peroneal nerve palsy was reported in our underlying studies and the transient nature of the condition, it seems ill-advised to select analgesic strategy based on this minor and rare outcome.

Adding sciatic blocks to femoral blocks might slightly increase the incidence of falls, especially when a continuous infusion is used (we reported an incidence of 2.3%). However, it is important to recognize that falls are common (about 3%) even when patients are not given nerve blocks, presumably because of difficulty bearing weight on the painful joint. Patient and staff education might be more important than whether a block is used. For example, Clarke *et al.*[2] report that a simple patient education program almost eliminates postarthroplasty falls. Webb *et al.* suggest substituting adductor canal blocks for femoral nerve blocks to reduce the risk of falls. Quadriceps strength is generally preserved with adductor canal blocks, but it remains unclear whether these blocks reduce the risk of falls after knee arthroplasty[3] and

whether they speed discharge readiness[4] compared to femoral nerve block.

When we conducted our study, there were no randomized clinical trials that evaluated combinations of peripheral nerve block with periarticular injection. There is thus little evidence to support the assertion of Webb *et al.* that combining peripheral nerve blocks with periarticular injection offers advantages over other modalities. In fact, the reference they provide to support their assertion is a review article rather than original research.[5]

We restricted our rehabilitation analyses to passive range of motion because it was the only functional outcome reported sufficiently often to be analyzed. We agree that there are probably better methods of assessing functional recovery, and this point was conceded in the limitations section of our discussion. That said, it remains unknown which "newer" rehabilitation outcomes best predict good long-term recovery.

Including multiple analgesic approaches in recovery pathways is prudent and increasingly routine; however, it is also clear that peripheral nerve blocks substantially reduce the need for systemic analgesics and should be included in multimodal pathways when practical. For example, a recent cohort study found that patients given peripheral nerve blocks (including major plexus and femoral nerve blocks) for knee arthroplasty had shorter hospital stays and fewer readmissions, with no differences in emergency department visits or falls.[6]

Our network meta-analysis included multiple sensitivity analyses, such as excluding low-quality studies. It was based on the balance of pain control, opioid use, and passive range of motion of the prosthetic joint throughout the initial 72 postoperative hours and not at just at 72 h or any single time point.[1] We were thus able to strongly conclude that "the combination of femoral and sciatic nerve block appears to be the overall best approach," whereas "rehabilitation parameters remain markedly understudied."

Competing Interests

The authors declare no competing interests.

Abdullah Sulieman Terkawi, M.D., Edward C. Nemergut, M.D., Daniel I. Sessler, M.D. University of Virginia, Charlottesville, Virginia (A.S.T.). asterkawi@gmail.com

References

1. Terkawi AS, Mavridis D, Sessler DI, Nunemaker MS, Doais KS, Terkawi RS, Terkawi YS, Petropoulou M, Nemergut EC: Pain management modalities after total knee arthroplasty: A network meta-analysis of 170 randomized controlled trials. Anesthesiology 2017; 126:923–37
2. Clarke HD, Timm VL, Goldberg BR, Hattrup SJ: Preoperative patient education reduces in-hospital falls after total knee arthroplasty. Clin Orthop Relat Res 2012; 470:244–9
3. Elkassabany NM, Antosh S, Ahmed M, Nelson C, Israelite C, Badiola I, Cai LF, Williams R, Hughes C, Mariano ER, Liu J: The risk of falls after total knee arthroplasty with the use of a femoral nerve block *versus* an adductor canal block: A double-blinded randomized controlled study. Anesth Analg 2016; 122:1696–703
4. Machi AT, Sztain JF, Kormylo NJ, Madison SJ, Abramson WB, Monahan AM, Khatibi B, Ball ST, Gonzales FB, Sessler DI, Mascha EJ, You J, Nakanote KA, Ilfeld BM: Discharge readiness after tricompartment knee arthroplasty: Adductor canal *versus* femoral continuous nerve blocks: A dual-center, randomized trial. Anesthesiology 2015; 123:444–56
5. Webb CA, Mariano ER: Best multimodal analgesic protocol for total knee arthroplasty. Pain Manag 2015; 5:185–96
6. McIsaac DI, McCartney CJ, Walraven CV: Peripheral nerve blockade for primary total knee arthroplasty: A population-based cohort study of outcomes and resource utilization. Anesthesiology 2017; 126:312–20

(Accepted for publication October 27, 2017.)

Solvent Matters!

To the Editor:

We gladly read the article by Xing *et al.*[1] suggesting that lidocaine may exert potent antitumor activity in hepatocellular carcinoma. We would like to congratulate the authors for this *in vitro* and *in vivo* trial bringing new information to the subspecialty of onco-anesthesia.

However, we would like to point out a bias in the methodology. According to the Materials and Methods section, the authors purchased Lidocaine from Sigma-Aldrich (USA). The authors did not specify how it was diluted. It can be assumed that they followed the product specification sheet indicating that the powder is soluble in ethanol, absolute. This solvent could have an effect on cancer cells, *per se*. Indeed, percutaneous ethanol injection therapy is commonly used to treat hepatocellular carcinoma,[2,3] and ethanol is also combined with transarterial chemoembolization.[4] Ethanol causes tumor destruction by dehydrating tumor cells, thereby denaturing the structure of cellular proteins. As lidocaine must be solubilized at a maximal concentration of 0.21 M, ethanol is present in a range varying from 0.00446 to 4.46% in the *in vitro* experiments of Xing *et al.* Moreover, according to preclinical and clinical studies, quantifying ethanol regimens depending on the tumor size improves its curative effect.[3] Therefore, the effects shown by the authors could be a consequence of the addition of ethanol to the lidocaine. To be strictly rigorous in terms of methodology, the authors should have added another control group using only the solvent.

Furthermore, as onco-anesthesia is an emergent research field, we believe it is important to promote exhaustive and clean methodology to enhance reproducibility of experiments for further research in this area.

Research Support

The authors received funds from the French Society of Anesthesia and Intensive Care Medicine (SFAR; Paris, France). Thiên-Nga Chamaraux-Tran is an Institute of Genetics and Molecular and Cellular Biology (IGBMC; Illkirch, France) International PhD Program fellow supported by LabEx INRT