

epidural infusion, yet the title and abstract only mention the single-injection femoral nerve block (FNB) or adductor canal nerve block (ACB). The patient-controlled epidural analgesia contained 10 µg/ml hydromorphone combined with 0.06% bupivacaine set at 4 ml/h continuous infusion with 4 ml of patient-controlled boluses on demand every 10 min on the day of surgery (postoperative day 0 [POD 0]). This was reduced to 2 ml/h the next morning (POD 1), and continuous infusion was stopped at 5:00 PM that day (POD 1); however, the patient-administered boluses were not decreased, therefore the patients could still receive a total patient-controlled epidural analgesia infusion of up to 20 ml/h after the continuous infusion was stopped late on POD 1. Added to oxycodone/acetaminophen (5/325 mg) every 4 h and daily 7.5 to 15 mg meloxicam, this in and of itself represents an effective multimodal regimen. Any additional nerve block, when compared with FNB, would most probably have yielded similar results with this study design. With this level of multimodal analgesia, we agree with Mariano and Perlas<sup>2</sup> that "...[the block] *does not have to* [provide enough analgesia for total knee arthroplasty]."

Furthermore, pain and muscle strength were assessed at 6 to 8 h postanesthesia, as well as at 24 and 48 h. As neither single-injection FNB nor ACB could be expected to last to 24 h, the later measurements are a true testament to the efficacy of the epidural and the other multimodal analgesics.

Although the local anesthetic total doses used for the single-injection nerve blocks were the same, the ACBs were performed with 15 ml of 0.5% bupivacaine, whereas the FNBs were performed with 30 ml of 0.25% bupivacaine. The question of whether volume, concentration, or total dose has a more significant effect on analgesia, motor function, and spread of local anesthetic has not been conclusively answered, but this is a confounding factor.

Finally, the finding that the FNB was responsible for the "buckling" in three patients while ambulating on POD 1 is most probably a coincidental finding after the single-injection nerve blocks have long worn off, while the patients still had continuous epidurals in place. An article by Memtsoudis *et al.*,<sup>3</sup> of which Dr. Mariano, the principal author of the above-mentioned editorial,<sup>2</sup> is a coauthor, in the same issue of *ANESTHESIOLOGY* clearly demonstrated that peripheral nerve blockade is not a risk factor for falling after total knee arthroplasty.

The ACB may well have its effect simply by proximal spread of local anesthetic agent to the anterior and posterior divisions of the femoral nerve, as convincingly shown elsewhere.<sup>4-6</sup> If it did not, the ACB would block only one of the seven nerves that innervate the knee joint<sup>7</sup> and would most probably be ineffective. Due to this proximal spread, the lack of quadriceps muscle paralysis is not a constant characteristic of ACB.<sup>5,6</sup> Quadriceps muscle dysfunction due to FNB, however, is only a minor issue when compared with the dysfunction caused by the original disease and the surgery itself,<sup>8-10</sup> while effective postoperative analgesia is probably a major enabler of early ambulation.

## Competing Interests

Dr. Boezaart receives royalty payments from Teleflex (Wayne, Pennsylvania). Dr. Deloach declares no competing interests.

**Julia K. Deloach, M.D., André P. Boezaart, M.D., Ph.D.**

University of Florida College of Medicine, Gainesville, Florida (A.P.B.). aboezaart@anest.ufl.edu

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## Is Less than 50% More Narcotics Really Noninferior?

*To the Editor:*

I read with great interest the study by Kim *et al.*<sup>1</sup> presenting data on the superiority of an adductor canal block compared to a femoral nerve block preserving muscle strength and the noninferiority in analgesia. I believe the noninferiority "conclusion" deserves some discussion.

One of the most important aspects of designing a noninferiority study is the choice of the noninferiority margin\*—here a 50% increase in narcotic consumption. The validity

of any conclusion from the noninferiority study depends on the choice of margin.\* I do not think—statistically formulated but from a clinical perspective—that an intervention is noninferior if less than 50% more narcotics are used.

From a statistical perspective, the margin was chosen based on a small study with the risk of overestimation of a treatment effect.<sup>2</sup> Further, as discussed in the same article, there are conflicting results of the narcotic-sparing effect of a femoral nerve block.<sup>2</sup> A conservative adjustment would have been necessary—choosing a smaller margin to accommodate this uncertainty.\* The upper limit of the CI is 1.3–1.4 depending on the time interval examined.<sup>1</sup> This means a more conservative margin of 30% (30% increase in narcotic consumption) would have failed to show noninferiority at all time intervals.

Another factor deserves illustration: the constancy assumption.\* In a noninferiority study, you are trying to compare the treatment group indirectly to a historical placebo group. But there are substantial differences in both studies, namely, epidural analgesia and small-dose acetaminophen, that make comparison difficult. These confounding interventions can reduce differences between study (adductor canal block) and control (femoral nerve block), making it “easier” to show noninferiority.

Also influencing the interpretation of the results is the substantial loss or simply the variability of treatment effect of the femoral nerve block. In the study by Allen *et al.*,<sup>2</sup> approximately 18 mg morphine equivalent dose was used (only a figure provided) compared to 36 mg in the current study. This could lead to the incorrect result of “proving” noninferiority when in fact there could be inferiority or potentially no effect at all.

Additionally, in a noninferiority study, the power analysis becomes crucial—the smaller the margin, the greater *n* has to be. In a superiority trial, you bias toward a type 2 error if you “under power” a study; in a noninferiority trial, a type 1 error is introduced. As discussed above, there are strong clinical and statistical arguments to choose a more conservative margin. This would have required a greater number of patients for adequate power.

I agree with the authors that the superiority conclusion is very sound (muscle strength), but a noninferiority conclusion cannot be drawn from the data at hand—so it remains to be determined if an adductor canal block is noninferior to a femoral nerve block with regard to analgesia. Here, the margin needs to be reevaluated using more than one small study, adjusted and clinically evaluated, answering the question: How much more narcotics are you willing to give to provide greater muscle strength and call it noninferior knowing now that there is at present no evidence for an increased fall risk with regional anesthesia after total knee arthroplasty?<sup>3</sup>

\* Available at: <http://www.fda.gov/downloads/Drugs/Guidances/UCM202140.pdf>. Accessed April 20, 2014.

## Competing Interests

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**Patrick Ziemann-Gimmel, M.D.**, Coastal Anesthesiology, St. Augustine, Florida. [pziemann@yahoo.com](mailto:pziemann@yahoo.com)

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## In Reply:

We thank Dr. Schwenk and Dr. Gandhi for their insightful comments to our article.<sup>1</sup> We agree that the dynamometer readings do seem variable in the adductor canal block group. It possibly could be due to the block techniques. Although we standardized the approach to the adductor canal block (mid-thigh, depositing 15 ml of the local anesthetic to spread around the lateral, anterior, and medial portions of the superficial femoral artery), having different anesthesiologists perform the block can lead to some interoperator variability. However, more likely, we think it is due to variability in the patient strength and effort in performing the dynamometer examination. It would have been interesting to present patients' change from baseline values to help eliminate the effect of baseline variability between patients' strength. By recording percentage of difference of strength within each patient, we would have been able to examine the blocks (true) ability to preserve or weaken quadriceps strength. Reasons why there is less variability in the femoral nerve block group may be that significant weakness among most of the group prevented stronger patients (*e.g.*, younger male patients) from performing the examination better in comparison to others (*e.g.*, older female patients). In other words, the femoral nerve block effectively shut down the quadriceps muscles to a point that it no longer depended on patients' efforts to perform the examination.

We do agree that an alternative study design for our study would have been to enroll patients with an intravenous patient-controlled analgesia and/or to include a control (no block) group. But given that our institutional standard