Anesthesiology 2007; 106:189-90

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Coiling of Stimulating Perineural Catheters

To the Editor:—We read with great interest Dr. Boezaart's excellent review on continuous perineural catheters¹ and would like to comment on the optimal length of catheter to be threaded beyond the needle tip.

While Dr. Boezaart advocates inserting the catheter 5-10 cm past the needle tip for nonstimulating (blind) catheters and 3-5 cm for stimulating catheters, we would like to point out that the optimal length of catheter to be introduced beyond the needle tip still remains speculative. With blind catheters, some authors have inserted as little as 3 cm,² whereas others have threaded as much as 20 cm.^{3,4} The rationale behind introducing such a great length of catheter seems to rest for the most part on the belief that the perineural sheath can be dilated with a small amount of saline or local anesthetic to permit subsequent threading of a catheter toward the plexic roots.⁴ However, studies on femoral catheters reveal that only a minority (23-40%) achieve a position close to the lumbar plexus roots: In fact, most tend to course medially in the direction of the psoas muscle or laterally in the direction of the iliacus muscle.^{3,4} It is perhaps this unpredictability in (blind) catheter migration that is responsible for the 40% secondary analgesic block failure rate.5

Stimulating perineural catheters, by permitting real-time observation of muscular twitches, allow the operator to manipulate both needle and catheter until the desired length of catheter has been threaded alongside the nerve.^{6,7} Therefore, it should theoretically be easier to direct a stimulating a catheter toward the plexic roots. Thus, in our practice (which uses exclusively stimulating catheters), when catheterizing "toward the plexus" (axillary, femoral, subgluteal, and lateral popliteal sciatic blockade), we routinely introduce a greater length of catheter (5-8 cm) than when threading "away from the plexus" (interscalene, supraclavicular, and infraclavicular blockade), in which case we introduce only 2-4 cm beyond the needle tip.

Our clinical results have been highly satisfactory, and so far, few complications have been noted. However, we recently had a patient with a retained infraclavicular catheter (possibly due to coiling) that required surgical extraction.⁸ Furthermore, radiographic images of catheters that appear incidentally on postoperative control x-rays ordered by surgeons suggest that more than two thirds of catheters may in fact be coiled (unpublished data from case series: De Q. H. Tran, M.D., June 2005). It was thus decided by the regional anesthetists of our department to order a plain anteroposterior x-ray after stimulating perineural catheters placed during a 2½-month period for quality assurance purposes. Following institutional guidelines, approval from the Director of Professional Services and the Internal Review Board were obtained to review the charts and to perform the audit.

During the 10-week period, 81 catheters were placed in 74 patients. Seventy percent of the catheters were found to be coiled on x-ray examination. The average insertion distance was significantly greater in the coiled group (P = 0.012; table 1). Catheters threaded 3 cm or more showed a higher incidence of coiling, but after 4 cm, the latter did not seem to increase (fig. 1).

Because it is our practice to maintain constant stimulation during the advancement of the catheter beyond the needle tip, we explain the formation of loops by hypothesizing that, at some point during the catheter's progress, its tip stops migrating forward: Pushing on the proximal end of the catheter through the needle therefore leads to bending and coiling of its middle portion. This would result in a coiled catheter with preserved neurostimulation. This is clearly

David C. Warltier, M.D., Ph.D., served as Handling Editor for this exchange.

 Table 1. Distance and Minimal Stimulating Threshold for

 Noncoiled and Coiled Catheters

	Noncoiled	Coiled	P Value
n Distance, cm Threshold, mA	24 4.29 ± 1.72 0.57 ± 0.21	57 5.31 ± 1.60 0.51 ± 0.20	0.012 0.22

Data are mean \pm SD.

illustrated by figure 2: The body of the catheter forms a coil that is situated outside the dye-delineated perineural sheath. Therefore, only a fraction (the tip) of the catheter introduced beyond the needle is actually situated inside the nerve's sheath. This may explain the "all or nothing" phenomenon often seen with perineural catheterization: When the right combination of needle shaft angulation and bevel orientation has been found, the catheter can be easily and swiftly fed through the needle while preserving the same amplitude of motor stimulation. In all likelihood, the tip has been anchored and remains stationary while its shaft is being inserted (and looped) through the needle.

Although it can be argued that coils may contribute to anchor and stabilize perineural catheters subcutaneously, they could also in theory predispose to knotting during removal of the catheter. In the literature, cases of knotting have been reported after advancement of femoral and fascia iliaca catheters 10-20 cm beyond the needle tip.^{9,10} Coiling was thought to be the underlying mechanism. We have previously reported the case of a retained (and surgically extracted) stimulating infraclavicular catheter that was inserted only 4 cm beyond the needle tip.⁸ The risk of ensnaring the nerve is another possible complication of looping. In our series, despite a coiling rate of 70%, no kinking or knotting was noted. All catheters were removed uneventfully. Therefore, despite the high rate of catheter dislodgement (10.5%) reported by a recent series of 1,416 patients,¹¹ coiling cannot be used as a means of catheter stabilization. Subcutaneous catheter tunneling may offer a safer alternative.7,12

In summary, although the optimal distance of stimulating catheter to be threaded beyond the needle tip remains speculative, Dr. Boezaart's



Fig. 1. Distribution of coiled and noncoiled (straight) catheters according to the distance in centimeters threaded beyond the needle tip.



Fig. 2. Infractavicular catheter with a coil situated outside the dye-delineated perineural sheath. Only the catheter's tip is located inside the sheath. Minimal stimulating threshold = 0.5 mA; distance inserted = 4 cm.

intuition and foresight may in time prove to be correct as suggested by our small audit. Nonetheless, the true incidence of coiling (as well as its relation to stimulating threshold and length of catheter threaded beyond the needle tip) must be examined though a carefully designed prospective study. Means of reducing catheter coiling (such as dilation of the perineural sheath with a bolus of D5W before threading¹³ must be studied as well. Finally, any link between looping and knotting (or nerve ensnaring) during catheter removal should be reported. (Quang Hieu) De Tran, M.D., F.R.C.P.C.,* Juan Carlos De La Cuadra-Fontaine, M.D., Sher-Yi Chan, M.D., Garrett Kovarik, M.D, F.R.C.P.C., Juan Francisco Asenjo, M.D., Roderick Finlayson, M.D., F.R.C.P.C. *The Montreal General Hospital, McGill University Health Centre, Montreal, Quebec, Canada. de_tran@hotmail.com

References

1. Boezaart AP: Perineural infusion of local anesthetics. An esthesiology 2006; 104:872–80 $\,$

2. Ilfeld BM, Morey TE, Enneking K: Continuous infraclavicular brachial plexus block for postoperative pain control at home. Anesthesiology 2002; 96:1297-304

3. Ganapathy S, Wasserman R, Watson J, Bennett J: Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty. Anesth Analg 1999; 89:1197-202

4. Capdevila X, Biboulet P, Moreau D, Bernard N, Deschodt J, Lopez S, d'Athis F: Continuous three-in-one block for postoperative pain control after lower limb orthopedic surgery: Where do the catheters go? Anesth Analg 2002; 94:1001-6

5. Salinas FV: Location, location, location: Continuous peripheral nerve blocks and stimulating catheters. Reg Anesth Pain Med 2003; 28:79-82

6. Sutherland IBD: Continuous sciatic nerve infusion: Expanded case report describing a new approach. Reg Anesth Pain Med 1998; 23:496-501

7. Boezaart AP, deBeer JF, duToit C, Van Rooyen K: A new technique of continuous interscalene nerve block. Can J Anesth 1999; 46:275-81

8. Tran QHD, Gordon A, Asenjo JF, De la Cuadra-Fontaine JC: Retained and cut stimulating infractavicular catheter. Can J Anesth 2005; 52:998-9

9. Offerdahl MR, Lennon RL, Horlocker TT: Successful removal of a knotted fascia iliaca catheter: Principles of patient positioning for peripheral nerve catheter extraction. Anesth Analg 2004; 99:1550-2

10. Motamed C, Bouaziz H, Mercier FJ, Benhamou D: Knotting of a femoral catheter. Reg Anesth 1997; 22:486-7

11. Capdevila X, Pirat P, Bringuier S, Gaertner E, Singelyn F, Bernard N, Choquet O, Bouaziz H, Bonnet F: Continuous peripheral nerve blocks in hospital wards after orthopedic surgery. ANESTHESIOLOGY 2005; 103:1035-45

12. Ekatodramis G, Borgeat A: Subcutaneous tunneling of the interscalene catheter. Can J Anesth 2000; 47:716–7

13. Tsui B, Kropelin B, Ganapathy S, Finucane B: Dextrose 5% in water: Fluid medium for maintaining electrical stimulation of peripheral nerves during stimulating catheter placement. Acta Anaesthesiol Scand 2005; 49:1562-5

(Accepted for publication August 22, 2006.)

Anesthesiology 2007; 106:190 Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc. Ultrasound-guided Perineural Catheters Have Already Arrived

To the Editor:—I read with much dismay the article by Boezaart¹ regarding perineural infusion of local anesthetics. As a practicing anesthesiologist at a teaching hospital, it was concerning to see the flagship journal of our specialty present a review of perineural catheter placement with such little regard for emerging technology. Many who practice regional anesthesia on a daily basis consider ultrasound to be the most significant advance in several decades. Boezaart, however, dismisses ultrasound as a technique that "works well for superficial nerves (when it is not really needed) . . . [but] is not sufficient to identify deeper nerves, especially in very obese patients (where it is most needed)." The author goes on to say that ultrasound is "not likely to replace nerve stimulation for continuous nerve block."

I would encourage the author to review a number of quality publications by Marhofer *et al.*,²⁻⁴ Chan *et al.*,⁵ and Sandhu and Capal,⁶ to name a few, which demonstrate the superiority of ultrasound techniques when compared with nerve stimulation. At the University of Utah (Salt Lake City, Utah), we no longer use or teach nerve stimulator techniques. More than 2 yr ago, our techniques were completely transitioned to ultrasound guidance. Our residents perform more than 3,000 blocks per year (more than 1,000 indwelling catheters) using only ultrasound guidance, with satisfying results both for the resident and for the patient.

Certainly, when discussing perineural local anesthetic infusions, ultrasound deserves a little more respect.

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References

1. Boezaart AP: Perineural infusion of local anesthetics. An esthesiology 2006; 104:872–80 $\,$

2. Marhofer P, Schrögendorfer K, Koinig H, Kapral S, Weinstabl C, Mayer N: Ultrasonographic guidance improves sensory block and onset time of three-inone blocks. Anesth Analg 1997; 85:854-7

3. Marhofer P, Schrögendorfer K, Wallner T, Koinig H, Mayer N, Kapral S: Ultrasonographic guidance reduces the amount of local anesthetic for 3-in-1 blocks. Reg Anesth Pain Med 1998; 23:584-8

4. Marhofer P, Sitzwohl C, Greher M, Kapral S: Ultrasonographic guidance for infraclavicular plexus anaesthesia in children. Anaesthesia 2004; 59:642-6

5. Chan VW, Perlas A, Rawson R, Odukoya O: Ultrasound guided supraclavicular brachial plexus block. Anesth Analg 2003; 97:1514-7

6. Sandhu NS, Capal LM: Ultrasound-guided infraclavicular brachial plexus block. Br J Anaesth 2002; 89:254-9

(Accepted for publication August 22, 2006.)

Anesthesiology 2007; 106:191

007; 106:191 Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc. Perineural Infusion of Local Anesthetics: "More to the Review"

To the Editor:-Dr. Boezaart's review article titled "Perineural Infusion of Local Anesthetics"1 represents a commendable attempt to educate the reader on a complex and evolving topic. In reading this article, we were surprised by the author's use of a study performed in volunteers to support the claim that the use of a stimulating catheter was associated with "around" 100% success compared with 65-85% for a nonstimulating technique. Studies conducted in patients certainly did not support this concept.² It is unfortunate that Dr. Boezaart did not acknowledge the value of continuous lumbar plexus blocks for hip primary replacement³ and acetabular fracture,⁴ especially when considering that some surgeons include the inguinal crease in their hip preparation, making impossible the preoperative placement of a femoral perineural catheter. Also, the recommended use of a posterior popliteal approach to the sciatic nerve for knee surgery or other procedures requiring a thigh tourniquet also deserves discussions. This practice has the potential for increasing the anesthesiologist's liability in the case of nerve injury. Therefore, the choice of the sciatic approach should facilitate the differentiation between the nerve block, the tourniquet, and/or surgery itself. When the site of the block is very close to the tourniquet or surgical field, electromyographic and conduction nerve studies cannot allow such a differentiation, and by default, the anesthesiologists is usually blamed. In our practice, we favor the use of approaches away from the tourniquet and the site of the surgery.5

The problem of continuous nerve blocks and anticoagulation is undoubtedly an important issue for regional anesthesiologists. In his article, the author referred to recommendations made by the American Society of Regional Anesthesiologists, but after going to the American Society of Regional Anesthesiologists Web site, we could not verify the source of these recommendations. Moreover, the authors of this letter have several thousand patient experiences with the combination of continuous lumbar plexus and thromboprophylaxis using various anticoagulants (aspirin, warfarin, low-molecular-weight heparin, and fondaparinux). As long as these anticoagulants are administered for the prevention of deep vein thrombosis and pulmonary embolism and not for their treatment, we found no reason to take any precaution when placing or removing the lumbar plexus catheter.⁶ For total knee arthroplasty,^{5,7} we also would like to stress the value of a continuous sciatic nerve block for postoperative analgesia. In our experience, 80% of patients undergoing total knee replacement report sciatic pain.⁷ Finally, although the author recommended the use of 0.2% ropivacaine for perineural infusion, he also recommend the use of 0.5% bupivacaine for the initial injection. Bupivacaine is recognized to be more toxic than ropivacaine.⁸ Therefore, it is surprising that the author would continue to recommend its use for the initial bolus injection. Certainly, in our practice, we have eliminated the use of bupivacaine.

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References

1. Boezaart A: Perineural infusion of local anesthetics. Anesthesiology 2006; 104:872-80

2. Casati A, Fanelli G, Koscielniak-Nielsen Z, Cappelleri G, Aldegheri G, Danelli G, Fuzier R, Singelyn F: Using stimulating catheters for continuous sciatic nerve block shortens onset time of surgical block and minimizes postoperative consumption of pain medication after hallux valgus repair as compared with conventional nonstimulating catheters. Anesth Analg 2005; 101:1192-7

3. Horlocker TT, Kopp SL, Pagnano MW, Hebl JR: Analgesia for total hip and knee arthroplasty: A multimodal pathway featuring peripheral nerve block. J Am Acad Orthop Surg 2006; $14{:}126{-}35$

4. Chelly JE, Greger J, Casati A, Al-Samsam T, Coupe K, Criswell A, Tucker J: Continuous lumbar plexus block for acute postoperative pain management after open reduction and internal fixation of acetabular fractures. J Orthop Trauma 2003; 17:362-7

5. Ben-David B, Schmalenberger K, Chelly JE: Analgesia after total knee arthroplasty: Is continuous sciatic blockade needed in addition to continuous femoral blockade? Anesth Analg 2004; 98:747-9

6. Chelly JE, Joshi R, Kandel A, Merman R, Ben-David B: Continuous lumbar plexus blocks are safe for total hip replacement (abstract). ANESTHESIOLOGY 2005; 103:A915

7. Pham Dang C, Gautheron E, Guilley J, Fernandez M, Waast D, Volteau C, Nguyen JM, Pinaud M: The value of adding sciatic block to continuous femoral block for analgesia after total knee replacement. Reg Anesth Pain Med 2005; 30:128-33

8. Graf BM, Abraham I, Eberbach N, Kunst G, Stowe DF, Martin E: Differences in cardiotoxicity of bupivacaine and ropivacaine are the result of physicochemical and stereoselective properties. ANESTHESIOLOGY 2002; 96:1427-34

(Accepted for publication August 22, 2006.)

Anesthesiology 2007; 106:191-2

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In Reply:—I thank Dr. De Tran *et al.* for sharing their experience and insights. With regard to their criticism: I did not advocate "inserting the catheter 5-10 cm past the needle tip for nonstimulating . . . catheters." Because I have little personal experience with nonstimulating catheters, I was merely reflecting what the authors who I cited typically do. I agree that the optimal distance of catheter advancement is speculative at this stage of our knowledge, but the catheter that I typically use (StimuCath; Arrow International, Reading, PA) is an armored catheter, which is floppy when the stylet is removed. The stylet goes down the catheter almost all the way but ends 5 cm from its tip. That, plus my experience of not having any problems with 3- to 5-cm catheter advancement, has led me to believe that 3-5 cm is probably appropriate. I am eagerly awaiting the results of the study planned by Dr. De Tran and colleagues in this regard.

The belief that the perineural sheath can be dilated with small amounts of saline has not yet been validated by research. In fact, we tried to demonstrate this on the perineural tissue of anesthetized pigs under direct vision and could only show that the tissue became edematous and the nerve stimulation was lost, making stimulation *via* the catheter useless. However, if practitioners still subscribe to this belief, I suggest that they use 5% dextrose in water to "open up the space" so that nerve stimulation is still possible.¹ Research is ongoing to evaluate this notion.

I share the author's sentiments regarding stimulating catheters.

It would be interesting to know for what blocks the 81 catheters of which 70% were found to be coiled up were placed. Based on my own experience, I share the belief that most catheters coil up, but like Dr. De Tran *et al.*, I do not have any objective data for my belief. It does seem that close to 100% of paravertebral catheters coil up, whereas a relatively small number of femoral catheters do. I am anxiously awaiting the results of their studies. I do believe, however, that the coiling is of no consequence as long as it does not involve too much of the catheter (advanced more than 5 cm), and its tip, where the drug comes out, is in the same fascia compartment as the nerve. This may be a problem with multiorifice catheters, because most of the drug comes out the most proximal orifice.

Ensnaring a nerve in the coil is at this stage only a theoretical possibility because, to the best of my knowledge, no such case has yet been reported in the literature.

We tunnel all catheters, and I agree with Dr. De Tran that it should probably be done routinely.

I share Dr. Swenson's enthusiasm for ultrasound as a promising "emerging technology" to aid in peripheral nerve blocks. I did not have any access to the unpublished results of Dr. Swenson and his students, and I am eagerly awaiting their publication. Surely, my omission of these results cannot be regarded as a flaw in my article.

I have reread the excellent articles by Marhofer *et al.*, Chan *et al.*, and Sandhu and Capal (Dr. Swenson's references 2–6), and I was again struck by the finding that all five of these reports were on singleinjection nerve blocks. Not unlike the rest of the literature, they do not address continuous nerve blocks by ultrasound guidance. I would respectfully remind Dr. Swenson that the title of my article was "Perineural *Infusion* of Local Anesthetics" and not "Perineural *Injection* of Local Anesthetics."

Based on the current state of our knowledge, it seems clear that for nerves that are "deep" (and it is not uncommon for us to do subgluteal sciatic nerve blocks where the nerve is 15 cm or deeper, although around 8 cm is the rule), the ultrasound technology simply does not help us much. I therefore believe that my statement that ultrasound helps us the most when the nerve is superficial, and the least when the nerve is deep, is factually correct. The experts cited by Dr. Swenson all restricted their studies to superficial nerve blocks.

With the equipment currently available to us, one needs at least three educated hands to place a catheter with ultrasound guidance: one to hold and maneuver the ultrasound probe, one to hold and maneuver the needle, and one to hold and maneuver the catheter. It is hoped that the emerging technology will address this problem soon.

Most ultrasound experts that I discussed this with (some cited above) agree that a combined technique of finding the nerve with the ultrasound and needle and then placing the catheter with a nerve stimulator is optimal at this stage of our development. Most would not rigidly transform to using only ultrasound guidance for catheters at this stage.

Finally, one of the experts cited by Dr. Swenson has as recently as July 2006 written, "Unfortunately ultrasound cannot help to guide the catheter into the sheath compartment. Because catheters generally curl up as they are advanced, multiple cross sectional views of the catheter are captured on ultrasound; thus the position of the catheter tip cannot be determined accurately."² With nerve stimulation, there is no problem in accurately determining the position of the catheter tip.

Drs. Chelly and Casati raised some interesting issues. The worst technique for continuous nerve block will have exactly the same outcome as the best technique, in terms of postoperative pain, if not all of the nerves that innervate that joint are blocked and the patients also receive effective multimodal analgesia. The studies that demonstrated no difference between stimulating and nonstimulating catheters were all performed on femoral nerve blocks for ${\rm knee^3}$ and ${\rm hip^4}$ surgery, ignoring the other nerves that innervate the knee and hip joints. Similarly, for example, the best continuous musculocutaneous nerve block will fare the same as the worst musculocutaneous nerve block if pain in the elbow is the measured outcome after elbow surgery and the patients receive effective multimodal analgesia. Therefore, it is not surprising that when stimulating and nonstimulating catheters were compared, the former have consistently been superior in studies where the block had a chance of being successful as the sole block, such as popliteal block for foot and ankle surgery.^{5,6} Finally, the volunteer study was pure and the results were valid, because it tested the motor and sensory functions of only the nerve that was blocked without the obscuring factor of pain due to other unblocked nerves. In the estimation of Dr. Chelly, up to 80% of patients have a sciatic nerve component after total knee arthroplasty.

Although continuous lumbar plexus block may be of value for acetabular fracture and primary total hip replacement, recent studies have shown that pain after the latter is mild (visual analog scale score 3–5 out of 10) and only significant for the first 24 h.⁷ That is probably because the entire joint capsule is typically destroyed during primary total hip replacement, which in effect denervates the hip and explains why patients commonly have more pain before than after the surgery. Furthermore, the hip joint gets its innervation from the entire lumbosacral plexus; therefore, blocking only the lumbar part of the plexus would clearly not be sufficient for painful hip surgery such as acetabular fracture, whereas any block should be sufficient for primary total hip replacement, because there is only mild and short-lived pain in the first place. Based on these two facts, I prefer to do a combined spinal-epidural for hip surgery. The epidural catheter is removed the day after surgery, because most patients usually do not need it anymore and that is typically when the warfarin or other anticoagulants are started. The epidural infusion can also block the entire lumbosacral plexus.

I agree with the sentiments of Drs. Chelly and Casati regarding anticoagulation and continuous peripheral nerve blocks. Unfortunately, when the consensus guidelines were formulated by the American Society of Regional Anesthesiologists task force, they stated, "... the Consensus Statements on Neuraxial Anesthesia and Anticoagulation may be applied to plexus and peripheral techniques."⁸ An important factor that stimulated the development of continuous nerve and plexus blocks was precisely the growing popularity of low-molecular-weight heparin, and I am eagerly awaiting the publication of the "several thousand patient experiences" referred to by Drs. Chelly and Casati to strengthen the overdue case against this statement in the American Society of Regional Anesthesiologists consensus document.

Even if the estimate of Drs. Chelly and Casati that 80% of patients need a sciatic block after total knee arthroplasty were correct (in my experience it is closer to 20%), it would mean that 20% of Drs. Chelly and Casati's patients (80% of my patients) would receive a nerve block that they do not need. I therefore offer our patients postoperative sciatic nerve blocks if they need it. That would mean that 100% of the patients who received the sciatic blocks actually need them. Furthermore, my experience is that single-injection sciatic nerve blocks are long-lasting blocks as opposed to the posterior knee pain of total knee arthroplasty, and surgeons get nervous if the inevitable "foot drop" persists.

Although I agree that ropivacaine is a better choice than bupivacaine, bupivacaine is much cheaper than ropivacaine and quite suitable when patients cannot afford the more expensive drug.

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References

1. Tsui BCH, Wagner A, Finucane B: Electrophysiologic effect of injectates on peripheral nerve stimulation. Reg Anesth Pain Med 2004; 29:189-93

2. Chan VWS: The use of ultrasound for peripheral nerve blocks, Anesthesia and Orthopaedic Surgery. Edited by Boezaart AP. New York, McGraw-Hill, 2006, pp $284\,\text{-}90$

3. Morin AM, Eberhart LHJ, Behnke HKE, Wagner S, Koch T, Wolf U, Nau W, Kill C, Geldner G, Wulf H: Does femoral nerve catheter placement with stimulating catheters improve effective placement? A randomized, controlled, and observer-blinded trial. Anesth Analg 2005; 100:1503-10

4. Malisse M, Basset P, Ferrant T, Fusier R, Singelyn F: The analgesic efficiency of continuous femoral nerve blockade after total hip arthroplasty is not improved by the use of a stimulating catheter. Reg Anesth Pain Med 2005; 30 (suppl):4

5. Rodríguez J, Taboada M, Carceller J, Lagunilla J, Bárcena M, Álvarez J: Stimulating popliteal catheters for postoperative analgesia after hallux valgus repair. Anesth Analg 2006; 102:258-62

6. Casati A, Singelyn F, Koscielniak-Nielsen Z: Stimulating catheters for continuous popliteal block (letter). Anesth Analg 2006; 102:1585-6

7. Viscusi ER, Martin G, Hartrick CT, Singla N, Manvelian G: Forty-eight hours of postoperative pain relief after total hip arthroplasty with a novel, extended-release epidural morphine formulation. ANESTHESIOLOGY 2005; 102:1014-22

8. Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, Mulroy MF, Rosenquist RW, Rowlingson J, Tryba M, Yuan CS: Regional anesthesia in the anticoagulated patient: Defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). Reg Anesth Pain Med 2003; 28:172-97

(Accepted for publication August 22, 2006.)

Anesthesiology 2007; 106:193-4

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Safety of Parecoxib and Valdecoxib after Noncardiac Surgery: Lack of Demonstration

To the Editor:—In the context of the current debate around the deleterious effects of the cyclooxygenase-2 inhibitors in patients with increased risks for cardiovascular diseases, we read with great interest the study published by Nussmeier *et al.*¹

The authors have studied, as intended, a population that was certainly at low risk for cardiovascular disease, and, indeed, the number of cardiovascular events was small and identical in both groups (five events per group [table 3 from the original article¹]).

In the discussion section, the authors highlight the fact that the size of the studied groups is too small to show any statistically significant difference in the number of cardiovascular events, because the study was only powered to show a difference in a combined multisystem endpoint.

Nevertheless, we believe that readers should not be left with an impression of possibly false security and conclude that the administration of a cyclooxygenase-2 inhibitor in a low-risk population does not increase the occurrence of cardiovascular events. This has simply not been demonstrated in this study, partly because of two methodologic problems that should be addressed and have not been discussed in the article.

First, the analyses were performed on a modified intent-to-treat population, were the patients who did not receive the treatment were excluded from the analysis after randomization (four patients in the placebo group and eight patients in the parecoxib-valdecoxib group). The creation of a "modified intent-to-treat population" could lead to the destruction of the similarity of the groups after randomization. This problem is further increased by the fact that the reasons for not administering the treatment are not given in the article (as per the CONSORT statement²) and that twice as many patients were excluded from the parecoxib-valdecoxib group.

In both groups, patients were lost to follow-up (five in the parecoxib-valdecoxib group and two in the placebo group). Although this is never clearly stated in the article, the usual definition of lost to follow-up implies that the primary endpoint (the combined incidence of postrandomization adverse events) is not known.

We computed the maximal possible bias to judge the robustness of the statistical results. In this method, all of the missing patients (eight excluded from analysis and five lost to follow-up) in the parecoxibvaldecoxib group are considered to have presented a cardiovascular event, in contrast to none of four excluded and two lost to follow-up in the placebo group. This is done with inclusion of all of the randomized patients. The computation of the risk ratio for presenting a cardiovascular event is given in table 1.

In contrast, when none of the 13 patients in the parecoxib-valdecoxib group are considered to have presented a cardiovascular event, but the 6 patients in the placebo group are considered to have presented a cardiovascular event, the results are given in table 2.

We concentrated this analysis on the cardiovascular adverse events because they are currently the most feared and highlighted adverse events of the cyclooxygenase-2 inhibitors.

One can see from these results that, with the data from the article, it is impossible to eliminate, from a statistical point of view, that the parecoxib-valdecoxib combination does increase the frequency of cardiovascular events in a low-risk population. But one can easily eliminate, with a high probability, that the placebo administration increased the frequency of cardiovascular events.

This should be clearly stated in the discussion section, where we have the impression that more emphasis is given to the demonstration of analgesic efficacy, which was a secondary endpoint, than to the lack of demonstration within a certain statistical probability of the primary endpoint, which was clearly stated to be the safety.

The second problem of this article is the marginal statistical power of the study. The authors state that "The sample size of 500 patients per treatment arm provided at least 80% power to detect a doubling of the 4% estimated background incidence of all predefined adverse events combined." In fact, to provide this sort of power, you need at least 550 patients per treatment with the primary endpoint available. With the available data in the study, calculated on 525 patients per arm, you have, at best, a power of 74%, which leaves 26% of chance (or more exactly bad luck) to face a type II error of not being able to detect a difference of 4% that would really exist. This lack of power is further aggravated by the fact that the true incidence of the combined adverse event was even lower than expected, and demonstrating a doubling of the 3.2% event rate in the placebo group would necessitate 697 patients per treatment to maintain an 80% power. All of these power calculations are true if we suppose that the authors accepted a 5% risk of type I error, which in fact was never stated in the article.

The conclusion about the cardiovascular safety in a low-risk population, even after this study, is that we do not know with any certainty. And we should not be afraid to say so.

Table 1. Risk Ratio Computation Considering That All Missing Patients from the Parecoxib–Valdecoxib Group Have Presented a Cardiovascular Event, in Contrast to None in the Placebo Group

Adverse Event	Placebo $(n = 529)$	Parecoxib–Valdecoxib $(n = 533)$	Risk Ratio (95% Cl)	P Value
Cardiovascular event (%)	5 (0.9%)	18 (3.4%)	3.57 (1.34–9.55)	0.011

CI = confidence interval.

 Table 2. Risk Ratio Computation Considering That All Missing Patients from the Placebo Group Have Presented a Cardiovascular Event, in Contrast to None in the Parecoxib–Valdecoxib Group

Adverse Event	Placebo $(n = 529)$	$\begin{array}{l} {\sf Parecoxib-Valdecoxib}\\ (n=533) \end{array}$	Risk Ratio (95% Cl)	P Value
Cardiovascular event (%)	11 (2.1%)	5 (0.9%)	0.45 (0.16–1.29)	0.137

CI = confidence interval.

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References

1. Nussmeier NA, Whelton AA, Brown MT, Joshi GP, Langford RM, Singala NK, Boye ME, Verburg KM: Safety and efficacy of the cyclooxygenase-2

Anesthesiology 2007; 106:194

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2006; 104:518-24

In Reply:—We wish to thank Drs. Engelman and Salengros for their comments. They correctly state that our analyses were performed on a modified intent-to-treat population, in which the patients who did not receive the treatment were excluded from analysis after randomization. The following paragraph of the International Conference on Harmonisation guidance on the use of statistics in clinical trials¹ makes it clear that the practice of removing patients who do not receive treatment is not without merit:

In some situations, it may be reasonable to eliminate from the set of all randomized subjects any subject who took no trial medication. The intention-to-treat principle would be preserved despite the exclusion of these patients provided, for example, that the decision of whether or not to begin treatment could not be influenced by knowledge of the assigned treatment. In other situations it may be necessary to eliminate from the set of all randomized subjects any subject without data post randomization. No analysis should be considered complete unless the potential biases arising from these specific exclusions, or any others, are addressed.

Regarding the current study,² it should be kept in mind that we are discussing only 12 patients who did not receive treatment (8 in the parecoxib-valdecoxib group and 4 in the placebo group) in a study that included more than 1,050 patients—approximately 1% of the randomized population. It is highly unlikely that the treatment responses of these few patients would have differed from the responses of the patients included in the analysis.

Drs. Engelman and Salengros also state that "this problem is further increased by the fact that the reasons for not administering the treatment are not given in the article . . . and that twice as many patients were excluded from the parecoxib-valdecoxib group as from the placebo group." However, given that there were 12 patients, the fact that 8 were assigned to one treatment and 4 to the other is not at all unlikely; in fact, it has more than a 19% probability of occurring by chance alone. It should also be understood that the number of patients not treated could just as easily have been 8 placebo and 4 parecoxib-valdecoxib patients. If one used this distribution in the sensitivity analysis suggested by the authors, one would conclude that parecoxib is actually cardioprotective. This scenario shows that the suggested analysis is inappropriate.

Drs. Engelman and Salengros then compute the risk ratio for a cardiovascular event if those patients in the parecoxib-valdecoxib intent-to-treat group who never received the treatment (n = 8) plus the 5 patients lost to follow-up in the parecoxib-valdecoxib group had all experienced a cardiovascular event. This sensitivity analysis is based on the premise that the patients who were not treated or lost to follow-up could have had vastly greater risk than the patients included in the analysis. That is, although the percentage of patients having a cardiovascular event in both placebo and parecoxib-valdecoxib groups was actually 1%, this sensitivity analysis assumes that 100% of the excluded patients in the parecoxib-valdecoxib group could have had an event,

which is not even remotely consistent with the observed data. In fact, we have gone back to look at the raw data from patients who did not receive treatment or were lost to follow-up and determined that none of these in either group experienced any cardiovascular thromboembolic events during the limited time that they were under observation.

inhibitors parecoxib and valdecoxib after noncardiac surgery. ANESTHESIOLOGY

SORT statement: Revised recommendation for improving the quality of reports of parallel-group randomised trials. Lancet 2001; 357:1191-94

(Accepted for publication August 17, 2006.)

2. Moher D, Schulz KF, Altman DG, for the CONSORT Group: The CON-

Drs. Engelman and Salengros also state that they concentrated this analysis on the cardiovascular adverse events and could easily eliminate the possibility that placebo administration increased the frequency of cardiovascular events. This is simply not true, as shown by the confidence intervals and P values produced by these two extreme analyses. Again, the results would change dramatically with a slight change in the number of missing data points in the placebo group.

Drs. Engelman and Salengros also mention that the risk of a type I error was never stated in the article. Certainly, we agree that this information should have been included. However, the considerable breadth of the confidence interval of the risk ratio (0.3-3.5) that we reported² makes it highly unlikely that increasing the power of the study would reveal a significant difference in cardiovascular event rates between the treatment and placebo groups. In addition, we have already acknowledged this limitation in the Discussion, in which we state,

Another limitation of the study is the sample size. Although this was the largest trial of any nonsteroidal antiinflammatory drug in patients undergoing noncardiac surgery, the number of adverse events was relatively small and possibly inadequate to detect a particular safety signal. This is especially true for cardiovascular thromboembolic events, given the low level of risk in this population compared with CABG [coronary artery bypass graft] surgery patients. Nevertheless, this population was representative of the majority of patients who undergo major surgery.

In summary, we appreciate Drs. Engelman and Salengros' thoughtful comments and speculations. Nonetheless, our interpretation of the results of our study—the largest such clinical trial yet performed worldwide—and the conclusions we draw from them remain unchanged.

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References

1. ICH harmonised tripartite guideline E9: Statistical principles for clinical trials. Stat Med 1999; 18:1905-42

 Nussmeier NA, Whelton A, Brown MT, Joshi GP, Langford RM, Singla NK, Boye ME, Verburg KM: Safety and efficacy of the cycoloxygenase-2 inhibitors parecoxib and valdecoxib after noncardiac surgery. ANESTHESIOLOGY 2006; 104: 518-26

(Accepted for publication August 17, 2006.)

Anesthesiology 2007; 106:195

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Ultrasound Guidance for Peripheral Venous Access: A Simplified Seldinger Technique

To the Editor:—Occasionally, patients for ambulatory surgery present with difficult peripheral venous access. Because only short-term access is needed, I prefer to avoid central venous cannulation and the associated risks. In these cases, I have begun using ultrasound guidance and a simplified Seldinger¹ technique for upper extremity peripheral venous access. A description of the technique and the results of a series of 10 procedures follows.

In this technique, a tourniquet is applied to the upper arm. Alcohol or povidone iodine is used to prepare the antecubital fossa and distal upper arm. Disposable, nonsterile gloves are worn, and draping is unnecessary. A 10-5 MHz ultrasound probe (Sonosite Titan, L38; Sonosite, Bothell, WA) is covered with gel, an occlusive dressing (3M Tegaderm 10×12 cm; 3M, St. Paul, MN), and then additional sterile gel. Using a transverse view, an appropriate, nonthrombosed vein is identified. This may be the cephalic, basilic, or brachial vein. The brachial artery and median nerve are identified, so they can be avoided. Lidocaine is infiltrated 1-2 cm distal to the planned insertion site. I then use a spring-wire guide/catheter over needle assembly, usually used for arterial catheterization (Arrow arterial catheterization set FA-0420; Arrow International, Reading, PA). It consists of a 10.8-cm, 20-gauge catheter over a 22-gauge thin wall needle with an integral 0.46-mm-diameter spring wire guide. Using a transverse or longitudinal view and a free hand technique, the needle is inserted into the selected vein under real-time imaging. When ultrasound imaging shows the needle in the vein and venous blood flashback appears, I ask an assistant to advance the spring wire guide. Alternately, I drop the ultrasound probe and advance the wire myself. Next, the catheter is advanced over the wire, the tourniquet is released, and the needle/ wire assembly is removed.

Table 1 shows the results of a series of 10 consecutive ultrasoundguided peripheral venous access procedures performed by the author. Patients were included in this series if at least two attempts at standard peripheral venous access failed or no adequate sized veins were visible or palpable in the upper extremity. Success was defined by the ultrasound view of the catheter in the vein and free flow of venousappearing blood from the catheter. Each separate skin puncture was considered an attempt. Time was defined as the interval from initial skin puncture until success was achieved or the procedure was aborted. Nine of 10 catheter insertions were successful. There was an average of 1.3 attempts per procedure. The time required for a procedure averaged 140 s.

Ultrasound guidance is used commonly for peripherally inserted central catheters² and occasionally for standard peripheral venous access. In emergency medicine applications, Keyes *et al.*³ found that a

Support was provided solely from institutional and/or departmental sources.

Table 1. Series of 10	Ultrasound-guided	Peripheral	Venous
Access Procedures			

Vein	Success	Attempts	Time, s
Cephalic	Yes	1	89
Basilic	No	2	483
Brachial	Yes	1	65
Cephalic	Yes	2	201
Brachial	Yes	1	62
Basilic	Yes	1	135
Cephalic	Yes	1	110
Basilic	Yes	1	45
Brachial	Yes	2	162
Cephalic	Yes	1	48
Mean average		1.3	140

5-cm catheter over needle infiltrated 8% of the time, and therefore, a longer catheter might be useful for these deeper veins. Sandhu and Sidhu⁴ recommended long needle-mounted catheters or a Seldinger technique for deep veins. Using a guide wire may help to ensure that an advancing catheter enters the vein properly. However, a standard Seldinger technique takes more time and requires sterile gloves, draping, and a table to hold the wire, tissue dilator, and catheter.

Ultrasound guidance for peripheral venous access may be improved by the use of a simplified Seldinger technique. The Arrow catheter set is commonly used for arterial catheterization, so anesthesiologists should be familiar with its use. The series described here demonstrates that this technique has a good success rate and the procedure takes a relatively short time to complete. Ultrasound guidance using this catheter may prevent multiple puncture attempts and decrease the use of unnecessary central venous catheters.

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References

1. Seldinger SI: Catheter replacement of the needle in percutaneous arteriography: A new technique. Acta Radiol 1953; 39:368-76

2. Chrisman H, Omary R, Nemeck A, Ryu R, Saker M, Vogelzang R: Peripherally inserted central catheters: Guidance with use of US *versus* venography in 2,650 patients. J Vasc Interv Radiol 1999; 10:473-5

3. Keyes L, Frazee B, Snoey E, Simon B, Christy D: Ultrasound-guided brachial and basilic vein cannulation in emergency department patients with difficult intravenous access. Ann Emerg Med 1999; 34:711-4

 $4.\,$ Sandhu N, Sidhu D: Mid-arm approach to basilic and cephalic vein cannulation using ultrasound guidance. Br J Anaesth 2004; 93:292–4

(Accepted for publication September 20, 2006.)