Continuous Peripheral Nerve Blocks: A Review of the Published Evidence

Brian M. Ilfeld, MD, MS

Continuous peripheral nerve blocks (CPNBs) are relatively simple in concept: a catheter is percutaneously inserted adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter (Fig. 1). Thus, the terms CPNB and “perineural local anesthetic infusion” are often used synonymously. Using currently available long-acting local anesthetics, the maximal duration of a single-injection peripheral nerve block is 8 to 24 hours. Therefore, CPNB provides an alternative option when a prolonged neural blockade is desired. Since its first description in 1946, CPNB has evolved from a needle inserted adjacent to a peripheral nerve, to a well-validated analgesic technique accepted by the medical community through a cork taped to a patient’s chest, to a well-validated technique’s most common application is providing analgesia after surgical procedures. However, additional indications include treating intractable hiccups; inducing a sympathectomy and vasodilation to increase blood flow after a vascular accident, digit transfer/replantation, or limb salvage; alleviating vasospasm of Raynaud disease; and treating peripheral embolism and chronic pain such as complex regional pain syndrome, phantom limb pain, trigeminal neuralgia, and cancer-induced pain. After trauma, perineural infusion can provide analgesia during transportation to a distant treatment center, or while simply awaiting surgical repair. Catheter insertion may be accomplished using many possible modalities, including nerve stimulation, ultrasound guidance, paresthesia induction, fluoroscopic imaging, and simple tactile perceptions (“facial click”). Either a nonstimulating epidural-type catheter may be used, or a “stimulating catheter” that delivers electrical current to its tip. Administered infusate generally includes exclusively long-acting, dilute, local anesthetic delivered as a bolus only, basal only, or basal-bolus combination. Documented benefits appear to be dependent on successfully improving analgesia, and include decreasing baseline/breakthrough/dynamic pain, supplemental analgesic requirements, opioid-related side effects, and sleep disturbances. In some cases, patient satisfaction and ambulation/functioning may be improved; an accelerated resumption of passive joint range-of-motion realized; and the time until discharge readiness as well as actual discharge from the hospital or rehabilitation center achieved. Lastly, postoperative joint inflammation and inflammatory markers may be decreased. Nearly all benefits occur during the infusion itself, but several randomized controlled trials suggest that in some situations there are prolonged benefits after catheter removal as well. Easily rectified minor complications occur somewhat frequently, but major risks including clinically relevant infection and nerve injury are relatively rare. This article is an evidence-based review of the published literature involving continuous peripheral nerve blocks. (Anesth Analg 2011;113:904–25)
patients with an intolerance to alternative analgesics (e.g., opioid-induced nausea). The surgical site dictates the anatomic location of catheter insertion (Table 1). Although not as thoroughly validated as in adults, CPNB has been described in hundreds of pediatric patients."

"CPNB has been used to provide analgesia during the subsequent infusion with an insulated needle adjacent to a peripheral nerve, followed by injection of local anesthetic and subsequent perineural catheter insertion. Although multiple prospective studies document the possible high success rate of this procedure, others have found an unacceptably high rate of "secondary block" failure, presumably when the catheter tip was unknowingly misplaced during insertion. To help counter this risk, the perineural catheter may be first inserted, followed by a local anesthetic bolus via the catheter itself. However, remaining unknown is whether a relatively large bolus of concentrated local anesthetic resulting in a successful nerve block guarantees that the catheter tip is close enough to the target nerve(s) to provide analgesia during the subsequent infusion with relatively small volumes of dilute local anesthetic. Regardless, even if prediction of successful perineural infusion is provided, the identification of those failed catheters requires waiting at least 15 minutes for block onset/failure, followed by removal of the catheter/dressing, repreparation, and catheter reinsertion, a process requiring a longer period of time than many practices permit. In addition, a partial block is possible, suggesting the catheter tip is not optimally located, but often precluding replacement using electrical current.

An option is the use of a "stimulating catheter" in which an electrical current is used with an insulated needle to locate the target nerve(s), followed by the insertion of a perineural catheter that conducts current to its tip. If muscle contraction intensity decreases during catheter advancement, it is presumed that the catheter tip is moving away from the target nerve. This provides real-time evidence of catheter-nerve distance. There are data to suggest that in the area of the popliteal fossa, using stimulation during catheter advancement results in the catheter tip being placed closer to the sciatic nerve. Although there are limited data suggesting a similar improvement for femoral and interscalene catheters, the clinical relevance is questionable for these anatomic locations.

"CATHETER INSERTION (NERVE STIMULATION)"

Historically, perineural catheters were inserted using induced paresthesia, a facial "click," or fluoroscopic guidance. However, after the introduction of portable nerve stimulators in the 1970s, the overwhelming majority of published CPNB reports involve this modality. Originally, this technique involved using electrical current to place an insulated needle adjacent to a peripheral nerve, followed by injection of local anesthetic and subsequent perineural catheter insertion. Although multiple prospective studies document the possible high success rate of this procedure, others have found an unacceptably high rate of "secondary block" failure, presumably when the catheter tip was unknowingly misplaced during insertion. To help counter this risk, the perineural catheter may be first inserted, followed by a local anesthetic bolus via the catheter itself. However, remaining unknown is whether a relatively large bolus of concentrated local anesthetic resulting in a successful nerve block guarantees that the catheter tip is close enough to the target nerve(s) to provide analgesia during the subsequent infusion with relatively small volumes of dilute local anesthetic. Regardless, even if prediction of successful perineural infusion is provided, the identification of those failed catheters requires waiting at least 15 minutes for block onset/failure, followed by removal of the catheter/dressing, repreparation, and catheter reinsertion, a process requiring a longer period of time than many practices permit. In addition, a partial block is possible, suggesting the catheter tip is not optimally located, but often precluding replacement using electrical current.

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"CATHETER INSERTION (ULTRASOUND)"

Unfortunately, continuous muscle contraction guarantees neither surgical block nor postoperative infusion success. In addition, adequate muscle response cannot always be elicited with catheter advancement, and stimulating catheters take more time on average for placement and cost more than their nonstimulating counterparts, leading some to question their overall benefit. There is minimal, if any, benefit of injecting fluid via the needle before catheter insertion to "open" the perineural space, but D5W is recommended if a bolus is used. Lastly, there are few data to provide recommendations on the minimal acceptable current resulting in a muscle response.

The optimal distance to advance a perineural catheter past the needle tip remains unknown, but there are data to suggest that increasing the insertion distance is correlated with an increased risk of catheter coiling, and possibly the final nerve-to-catheter tip distance. Considering the multiple catheter knots reported with insertion >5 cm and the lack of data suggesting insertion lengths >5 cm is beneficial, recommending a maximal insertion of 5 cm seems warranted. Recently reported "self-coiling catheters" may render this issue moot in the future if they are found reliable and approved for human use. Similarly, the optimal minimum insertion distance remains unknown, with evidence that 0 to 1 cm results in a minimal risk of secondary block failure, but possibly an increased risk of subsequent dislodgement.

Figure 1. Illustration of a continuous peripheral nerve block involving the femoral nerve. This particular perineural catheter insertion technique employs electrical stimulation alone via a stimulating catheter.
Table 1. Catheter Locations

<table>
<thead>
<tr>
<th>Surgical site</th>
<th>Major approaches</th>
<th>Evaluated with RCT?</th>
<th>Comments</th>
<th>Comparative CPNB studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Mandibular and maxillary nerves</td>
<td>No 17,32,24,325</td>
<td>Validated with nerve stimulation 34,38,13,7,8,217,230,236–331 and ultrasound guidance 33,32,329</td>
<td>There are no studies comparing these CPNB techniques.</td>
</tr>
<tr>
<td>Shoulder and proximal humerus</td>
<td>Interscalene</td>
<td>Yes 34,39,71,73,78,217,230,236–331</td>
<td>Nearly all publications from a single group</td>
<td>Validated with nerve stimulation 34,38,13,7,8,217,230,236–331 and ultrasound guidance 33,32,329</td>
</tr>
<tr>
<td>Elbow, forearm, and hand</td>
<td>Suprascapular</td>
<td>No 334</td>
<td>Effectiveness of technique unclear without RCT</td>
<td>No benefit of ropivacaine 0.1% or 0.2% over placebo infusion</td>
</tr>
<tr>
<td>Thorax and breast</td>
<td>Paravertebral</td>
<td>Yes 337</td>
<td>For mastectomy: no infusion benefits over single injection 236 For open lung surgery: benefits over thoracic epidural 339</td>
<td>No benefit of ropivacaine 0.1% or 0.2% over placebo infusion</td>
</tr>
<tr>
<td>Abdomen, iliac crest, and inguinal region</td>
<td>Transversus abdominus plane</td>
<td>No 234,32,34,345</td>
<td>Relatively new technique with risks and benefits yet to be thoroughly investigated. Retrospective study suggests decreased opioid requirements and pain scores in renal transplant recipients 345</td>
<td>There are no studies comparing these CPNB techniques</td>
</tr>
<tr>
<td>Hip and thigh</td>
<td>Posterior lumbar plexus Femoral</td>
<td>Yes 13,33,21,73,78,230,34,345</td>
<td>Impact of various catheter insertion techniques remains uninvestigated.</td>
<td>For hip arthroplasty, patients with femoral (versus posterior lumbar plexus) catheters: no difference in resting pain scores, but ambulation suffered 13,34,35. Dynamic pain scores either higher 240 or no difference 331, and increased opioid-related side effects and satisfaction 340.</td>
</tr>
<tr>
<td>Knee and thigh</td>
<td>Posterior lumbar plexus Femoral</td>
<td>Yes 166,239,352</td>
<td>Surgery involving the posterior thigh: reliable analgesia for the posterior femoral cutaneous nerve distribution</td>
<td>For knee arthroplasty, no major analgesic differences found among approaches 166,239,353,354.</td>
</tr>
<tr>
<td>Leg, ankle, and foot</td>
<td>Fascia iliaca</td>
<td>Yes 353,354,358,359</td>
<td>Reliable analgesia for the posterior femoral cutaneous nerve distribution</td>
<td>No major analgesic differences found between subgluteal and popliteal 351,362</td>
</tr>
</tbody>
</table>

Only selected references are included because of publication limitations; similarly, only RCTs are included when at least 1 study with this design is available. RCT = randomized controlled trial; CPNB = continuous peripheral nerve block.

*Unpublished data, Mariano and Ilfeld (2011).
compared with a perpendicular orientation. There are few RCTs to help guide practice. One study suggests that for interscalene catheters, a needle with its long axis parallel to the nerve has distinct benefits compared with a perpendicular needle-to-nerve orientation.

Because of the multiple variables for various blocks/techniques (e.g., bolus via the catheter versus needle, catheter insertion distance, and catheter design), applying the results of one study to others’ practices will most likely prove difficult. For example, the results of the above-mentioned infracavicular catheter study will probably not be replicated with a single catheter injection of local anesthetic via a popliteal sciatic catheter because of differences in perineural anatomy between the 2 sites. Similarly, in the RCT comparing anterolateral and posterior approaches, a relatively rigid 3-orifice catheter was used, greatly increasing the chance that for the posterior approach all 3 orifices would fail to reside within the narrow facial (anterior-posterior) plane containing the brachial plexus. Evidence from other investigations suggests that the posterior approach is highly reliable using a relatively flexible single-orifice catheter, and that using a flexible catheter for other needle in-plane approaches may help avoid the catheter tip bypassing the target nerve during insertion.

Simply visualizing the catheter tip in close relation to the target nerve intuitively seems to be an obvious solution; however, in practice, identifying the tip is often challenging because, unlike rigid needles, flexible catheters do not usually remain within the ultrasound plane of view. Although there are exceptions, many investigators observe the location of fluid, or simply air injected through the catheter. Unfortunately, the positive and negative predictive value of each of these methods remains unknown, and even what constitutes a “positive” or “negative” test has yet to be determined. Future technological developments in equipment such as 3-dimensional ultrasound may render this issue moot.

NERVE STIMULATION VERSUS ULTRASOUND GUIDANCE

Many RCTs suggest that for most anatomic locations, catheters inserted with ultrasound guidance provide at least similar analgesia, and often decrease insertion-related discomfort and insertion time, compared with an electrical technique using an insulated needle and nonstimulating or stimulating catheters. And while there are reports of combining nerve stimulation and ultrasound guidance for catheter insertion, the majority of these reports do not suggest much benefit—and often increasing difficulties compared with using one technique alone leading some to question the utility of stimulating catheters, and even insulated needles (while others disagree). Currently, insufficient data are available to determine the optimal techniques/equipment for these insertion modalities, and their associated risks and benefits.

There are some clinical situations in which ultrasound is a superior modality, at least theoretically, such as when limb amputation, when sensory nerves are solely targeted, with concomitant anticoagulation, or when an electrically induced muscle response is either undesirable or cannot be elicited. However, ultrasound nerve/plexus/needle-tip visualization/identification are often difficult for relatively deep targets, in which case nerve stimulation may prove beneficial. There are also situations, such as when placing a posterior lumbar plexus catheter, whereby prepuncture ultrasound visualization may aid subsequent electrical stimulation-guided catheter insertion. Lastly, the relative costs of each insertion modality must be accounted for, with 1 investigation suggesting that for single-injection peripheral nerve blocks, the use of ultrasound guidance is at least as financially competitive, and often becomes a “profit center,” depending on the clinical scenario, compared with electrical stimulation.
is needed (e.g., femoral perineural infusion–induced quadriiceps femoris weakness limiting ambulation, or an insonate extremity during infracavicular or popliteal sciatic infusion). Of note, data derived from laboratory animals suggest that both ropivacaine and bupivacaine induce tissue injury, but ropivacaine results in significantly less damage. The clinical implications of these data remain unknown.

It also remains unknown whether the primary determinant of CPNB effects is solely local anesthetic dose (mass), or if volume (rate) and/or concentration exert additional influence. For single-injection nerve blocks, volume and concentration primarily determine efficacy when dose is held constant. However, for continuous blocks, data from the only study that varied both the infusion rate and concentration in a static ratio so that the total dose was comparable in each treatment group suggest that local anesthetic concentration does not influence block effects as long as the total dose remains constant. Unfortunately, the results from this study of posterior lumbar plexus ropivacaine infusion may not be applicable to other anatomic locations, local anesthetics, infusion rates, local anesthetic concentrations, or bolus dose/volume combinations, and thus further investigation is required for a definitive answer.

To complicate the issue, in the clinical setting, patient-controlled bolus doses and/or an adjustable basal infusion rate are often provided, and therefore total local anesthetic dose varies depending on individual patient requirements. In these clinical cases, it seems that concentration and rate do influence infusion effects. Unfortunately, currently published studies provide widely conflicting data, probably because of the many variables influencing infusion effects and analgesic requirements. For example, studies involving interscalene ropivacaine infusion report increasing local anesthetic concentration results in increased, decreased, or no difference in postoperative analgesia. Similarly, increasing local anesthetic concentration has differing effects on the incidence of an insensate extremity depending on catheter site location: increased for infracavicular, decreased for popliteal, no difference for axillary, and variable for interscalene. Therefore, no optimal concentration/rate combination may be recommended for all anatomic locations, and further study is warranted. For bupivacaine/levobupivacaine and ropivacaine, the most frequently cited concentrations are between 0.1% to 0.125% and 0.1% to 0.2%, respectively.

Several medications are occasionally added to the local anesthetic during CPNB in an attempt to improve analgesia without increasing motor block. There are reports of the inclusion of opioid with perineural local anesthetic, but currently there are insufficient data to draw any conclusions regarding its efficacy. Although clonidine was often added in the earlier years of CPNB, 3 subsequent RCTs failed to demonstrate any clinically relevant benefits. An additional RCT found no benefit to adding epinephrine to perineural ropivacaine, and possible prolonged vasoconstriction places the safety of this practice into doubt. Additional possible adjuvants have been reported, but none is currently approved for perineural use in patients, and some may have unacceptable systemic effects.

LOCAL ANESTHETIC DELIVERY REGIMENS

Infuses may be administered with 3 main strategies: exclusively as a basal infusion or bolus dose, and a combination of these 2 modalities. Unfortunately, similar to the data involving local anesthetic concentration, studies of delivery strategy are somewhat mixed (Table 2). In general, RCTs involving femoral and fascia iliaca infusions have reported few differences in analgesia among the various delivery regimens (other than reduced local anesthetic use with bolus-only dosing). Conversely, for sciatic catheters, providing a basal infusion maximizes analgesia and other benefits, although the data regarding the benefits of adding patient-controlled bolus doses are less clear.

Interestingly, providing automated, hourly, 5-mL bolus doses of levobupivacaine via a popliteal sciatic catheter decreased pain scores compared with patients receiving a continuous, 5-mL basal infusion of 0.125% levobupivacaine (although a similar investigation involving femoral ropivacaine infusion failed to detect differences in sensory or motor effects). However, by adding patient-controlled bolus doses to these 2 regimens, the difference in pain scores disappeared. Importantly, all investigations report less total consumption of local anesthetic with regimens providing patient-controlled bolus doses, suggesting the desirability of including this modality for 3 main reasons: (1) decreasing the required basal infusion rate and thus theoretically decreasing motor block (inadequately investigated to date); (2) decreasing the incidence of an insensate extremity; and (3) increasing the duration of infusion/analgesia for ambulatory patients discharged with a finite volume of local anesthetic.

In contrast to the lower extremity, investigations of interscalene and infracavicular perineural infusion are more uniform and suggest that including a basal infusion improves baseline analgesia, decreases the incidence and severity of breakthrough pain, and decreases sleep disturbances and supplemental analgesic requirements. Furthermore, adding patient-controlled bolus doses to a basal infusion decreases total local anesthetic consumption and supplemental analgesic requirements, allowing block reinforcement during dressing changes or physical therapy, and may provide increased independent activity. Additional RCTs attempting to further refine interscalene dosing report somewhat conflicting results. One study provides evidence that a high basal rate combined with low-volume, patient-controlled bolus doses reduces baseline pain scores and sleep disturbances, and decreases the incidence and severity of breakthrough pain, but at a cost of increasing local anesthetic consumption. However, other similar investigations report few differences in varying the basal infusion rate.

Unfortunately, because of the heterogeneity of catheter types, insertion techniques, and a myriad of additional factors, there is little evidence for an “optimal” infusion regimen. Until recommendations based on prospectively collected data are available, health care providers may wish
<table>
<thead>
<tr>
<th>Treatment groups</th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter location</td>
<td>Infusate(s)</td>
<td>n</td>
<td>Basal (mL/h)</td>
<td>Bolus (mL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interscalene</td>
<td>Bupivacaine (0.125%)</td>
<td>20</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>• Nonstimulating catheter</td>
<td>Clonidine (1 µg/mL)</td>
<td>20</td>
<td>5</td>
<td>2.5</td>
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<tr>
<td>• Anterolateral approach</td>
<td>Sufentanil (0.1 µg/mL)</td>
<td>20</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>Interscalene</td>
<td>Ropivacaine (0.2%)</td>
<td>38</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>• Nonstimulating catheter</td>
<td>Ultrasound-guided posterior approach</td>
<td>43</td>
<td>5</td>
<td>5</td>
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<tr>
<td>Interscalene</td>
<td>Ropivacaine (0.2%)</td>
<td>12</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>• Stimulating catheter</td>
<td></td>
<td>12</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Interscalene</td>
<td>Ropivacaine (0.2%)</td>
<td>15</td>
<td>7</td>
<td>—</td>
</tr>
<tr>
<td>• Anterolateral approach</td>
<td>Ropivacaine (0.2%)</td>
<td>15</td>
<td>12</td>
<td>—</td>
</tr>
<tr>
<td>• Stimulating catheter</td>
<td></td>
<td>15</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>• Coracoid approach</td>
<td></td>
<td>15</td>
<td>—</td>
<td>9.9</td>
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<td>Axillary</td>
<td>Bupivacaine (0.25%)</td>
<td>10</td>
<td>10</td>
<td>—</td>
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<td>• Nonstimulating catheter</td>
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<td>—</td>
<td>10</td>
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<tr>
<td>Femoral</td>
<td>Bupivacaine (0.125%), clonidine (1 µg/mL), sufentanil (0.1 µg/mL)</td>
<td>15</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>• For hip arthroplasty</td>
<td></td>
<td>15</td>
<td>—</td>
<td>10</td>
</tr>
<tr>
<td>• Inguinal perivascular approach</td>
<td></td>
<td>15</td>
<td>—</td>
<td>5</td>
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<tr>
<td>• Nonstimulating catheter inserted 10–15 cm using Seldinger technique</td>
<td></td>
<td>15</td>
<td>—</td>
<td>10</td>
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<tr>
<td>Femoral</td>
<td>Bupivacaine (0.125%), clonidine (0.1 µg/mL)</td>
<td>15</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>• For knee arthroplasty</td>
<td></td>
<td>15</td>
<td>5</td>
<td>2.5</td>
</tr>
<tr>
<td>• Inguinal perivascular approach</td>
<td></td>
<td>15</td>
<td>—</td>
<td>10</td>
</tr>
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<td>• Nonstimulating catheter inserted 10–15 cm using Seldinger technique</td>
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</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Catheter location</th>
<th>Infusate(s)</th>
<th>n</th>
<th>Basal (mL/h)</th>
<th>Bolus (mL)</th>
<th>Lockout (min)</th>
<th>Primary findings</th>
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<tbody>
<tr>
<td>Fascia iliaca&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Ropivacaine (0.2%)</td>
<td>46</td>
<td>10</td>
<td>—</td>
<td>—</td>
<td>Least local anesthetic consumption versus other 2 groups</td>
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<tr>
<td></td>
<td>For knee surgery</td>
<td>46</td>
<td>5</td>
<td>5</td>
<td>60</td>
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<tr>
<td></td>
<td>Nonstimulating catheter inserted 10–15 cm</td>
<td>44</td>
<td>—</td>
<td>10</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without Seldinger technique</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subgluteal sciatic&lt;sup&gt;1,111&lt;/sup&gt;</td>
<td>Ropivacaine (0.2%)</td>
<td>25</td>
<td>10</td>
<td>—</td>
<td>—</td>
<td>Increased consumption of local anesthetic</td>
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<tr>
<td></td>
<td>Nonstimulating catheter inserted 3–4 cm</td>
<td>25</td>
<td>5</td>
<td>5</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Popliteal sciatic&lt;sup&gt;1,102&lt;/sup&gt;</td>
<td></td>
<td>10</td>
<td>12</td>
<td>—&lt;sup&gt;a&lt;/sup&gt;</td>
<td>—</td>
<td>Increased consumption of local anesthetic with a shorter duration of infusion and analgesia</td>
</tr>
<tr>
<td></td>
<td>Stimulating catheter</td>
<td>10</td>
<td>8</td>
<td>4</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Posterior approach</td>
<td>10</td>
<td>—&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.9</td>
<td>60</td>
<td>Increased baseline pain, breakthrough pain incidence and intensity, and sleep disturbances versus other 2</td>
</tr>
<tr>
<td>Popliteal sciatic&lt;sup&gt;1,74&lt;/sup&gt;</td>
<td>Levobupivacaine (0.125%)</td>
<td>22</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>Increased baseline and breakthrough pain intensity; a trend toward increased rescue analgesic requirement (&lt;i&gt;P = 0.055&lt;/i&gt;)</td>
</tr>
<tr>
<td></td>
<td>Nonstimulating catheter</td>
<td>22</td>
<td>—</td>
<td>5</td>
<td>60</td>
<td>Note that this group received automated hourly bolus doses of 5 mL without additional optional bolus doses</td>
</tr>
<tr>
<td></td>
<td>Posterior approach</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Popliteal sciatic&lt;sup&gt;1,75&lt;/sup&gt;</td>
<td></td>
<td>25</td>
<td>5</td>
<td>3</td>
<td>15</td>
<td>Increased local anesthetic consumption</td>
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<tr>
<td></td>
<td>Nonstimulating catheter</td>
<td>25</td>
<td>—</td>
<td>5</td>
<td>60</td>
<td>Note that this group received automated hourly bolus doses of 5 mL; and optional 3-mL bolus doses</td>
</tr>
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<td></td>
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<td>25</td>
<td>3</td>
<td>15</td>
<td></td>
<td></td>
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<tr>
<td>Popliteal sciatic&lt;sup&gt;1,73&lt;/sup&gt;</td>
<td>Levobupivacaine (0.125%)</td>
<td>15</td>
<td>7</td>
<td>—</td>
<td>—</td>
<td>Possibly increased assistance with daily activity and time until 10 min of ambulation (data combined with interscalene infusion; no &lt;i&gt;P&lt;/i&gt; value provided for ambulation)</td>
</tr>
<tr>
<td></td>
<td>Nonstimulating catheter</td>
<td>15</td>
<td>5</td>
<td>2</td>
<td>12</td>
<td>Possibly lower incidence of “slight paresthesia” (data combined with interscalene infusion)</td>
</tr>
</tbody>
</table>

Due to publication limitations, includes only selected randomized, controlled trials specifically investigating varying local anesthetic delivery method.

— = not included for this treatment group.

<sup>a</sup> Nominal basal infusion rate or bolus volume provided to retain treatment group masking.
to consider that most published investigations report a basal rate of 4 to 10 mL/h (lower rates for catheters of the lower extremity; higher rates for the upper extremity), a bolus volume of 2 to 10 mL, and a bolus lockout period of 20 to 60 minutes. Similarly, the maximum recommended hourly total dose of local anesthetic during perineural infusion remains unknown, but a wide safety margin has been documented in numerous clinical trials, with 1 study reporting no toxicity signs or symptoms with perineural ropivacaine 0.2% administered at basal rates up to 14 mL/h and large, repeated boluses of ropivacaine 0.5% (10–60 mL) provided for up to 27 days.

**INFUSION PUMPS**

Although perineural local anesthetic may be provided using exclusively human-administered bolus doses, both clinical factors (e.g., basal infusion benefits) as well as logistical considerations usually dictate the use of an infusion pump. There is no single optimal device for all situations, given the multitude of clinical scenarios and practice requirements, so pump preference is usually based on the desired device characteristics. Infusion pumps may be (arbitrarily) categorized by their power source. Although spring- and vacuum-powered devices are available, neither is particularly desirable for the purpose of CPNB because of a multitude of factors, including highly variable basal infusion rates and relatively small local anesthetic reservoir volumes, respectively. Until recently, elastomeric infusion pumps were severely limited relative to the capabilities of electronic devices; however, with the advent of newer nonelectronic pumps, this is no longer the case.

In general, electronic devices provide very accurate and consistent (±5%) basal infusion rates over the entire course of infusion. In contrast, elastomeric pumps usually overinfuse (110%–130% expected) during the initial 3 to 8 hours of infusion and within the final hours before reservoir exhaustion, resulting in a shorter infusion duration than anticipated given the initial reservoir volume and set basal infusion rate. However, whether the increased variability is clinically significant, or in which clinical situations it is relevant, remains unknown. Unlike electronic devices, the basal infusion rate of most elastomeric devices increases with increasing ambient temperature and pump height relative to the catheter insertion site, although these changes are probably clinically relevant only at extreme values.

An adjustable basal infusion rate allows local anesthetic administration titration in case of an insensate extremity, undesired side effects (e.g., muscle weakness), inadequate analgesia, or desire to maximize infusion duration (e.g., ambulatory patients with a set reservoir volume). In addition, a patient-controlled bolus function often provides many clinical benefits. All electronic pumps provide an adjustable basal rate, patient-controlled bolus doses, and a variable bolus lockout period. Although most elastomeric devices provide a fixed basal infusion rate, a few now provide flexibility similar to their electronic counterparts. Nearly all electronic pumps use an external local anesthetic reservoir that allows for easy reservoir exchanges. In contrast, all elastomeric devices have an internal reservoir. Even though refilling such devices has been investigated, this procedure is not approved by manufacturers/governments for the majority of devices, requiring the use of an additional unit if continued infusion is desired after reservoir exhaustion. Regardless of reservoir type, filling the infusion pump/reservoir within the United States must now be executed within an isolation class 5 environment, essentially requiring local anesthetic compounding within a designated pharmacy with a laminar flow workbench.

Nonelectronic infusion pumps are often favored for their relative simplicity in both initially setting and subsequently adjusting the basal infusion rate; for their light weight and smaller size; their lack of audible alarms (although there is no warning for a pause in the infusion); disposability; and for their silent operation (noise generated by electronic pumps may disturb patient sleep). In addition, elastomeric devices with a manufacturer-fixed basal rate and no bolus dose capability are usually relatively inexpensive. Conversely, reusable electronic pumps use inexpensive disposable “cassettes” to provide sterile infusion for individual patients. A limited number of single-use electronic devices are available. Lastly, although the reliability for most infusion pumps is high, regardless of power source, certain devices are more dependable than others for both electronic and nonelectronic pumps.

**AMBULATORY PERINEURAL INFUSION**

First described in 1997, CPNB may be provided to patients outside of the hospital using a portable infusion pump, and nearly every catheter type (i.e., anatomic location) has been reported in ambulatory patients. Perineural infusion is often provided for ambulatory surgery without an overnight hospital stay, but the technique may be used to shorten hospitalization and/or provide benefits after discharge either home or to a skilled nursing facility. Time constraints are often more restrictive in high-turnover ambulatory centers, making insertion techniques with documented time savings frequently desirable (e.g., ultrasound guidance). Because patients are rarely directly monitored outside of the hospital, and not all patients desire or are capable of accepting the additional responsibility of caring for the catheter and pump system, patient selection criteria are often more stringent for ambulatory CPNB. In an effort to avoid local anesthetic toxicity, patients with renal or hepatic insufficiency are often excluded from outpatient perineural infusion. For infusions possibly affecting the phrenic nerve and weakening the ipsilateral diaphragm (e.g., interscalene and paravertebral catheters), caution is warranted for individuals with heart/lung disease and in obese patients who may not be able to compensate for mild hypoxia and/or hypercarbia. Of note, age alone is not an absolute exclusion criterion, with hundreds of pediatric patients receiving at-home CPNB without complication rates or severity higher than for their adult counterparts.

Providing ambulatory CPNB often leads to a reduced time until discharge readiness and, in some cases, actual discharge. After tricompartmental knee arthroplasty, permitting early discharge with ambulatory femoral...
infusion results in decreased hospitalization-related costs. However, although ambulatory continuous femoral and posterior lumbar plexus nerve blocks decrease the time until important discharge criteria are met, an increased incidence of patient falls in patients receiving ropivacaine versus saline through their catheters suggests that increased risk is warranted before implementing early discharge. Nevertheless, relatively small published series demonstrate the feasibility of total joint arthroplasty with only a single-night hospital stay, or even on an outpatient basis, when patients are permitted to continue their hospital-based perineural infusion at home.

Although the benefits of home CPNB are well documented with many placebo-controlled RCTs, there are negligible published data regarding the optimal practice for multiple aspects of ambulatory infusion, such as the requirement of a patient caretaker; method/frequency of patient oversight (e.g., home nursing visits, telephone calls, or simply written instructions with sole patient-initiated contact); and catheter removal protocol (health care provider extraction, caretaker withdrawal with instructions provided by telephone, or simply written instructions). Of 40 patients with a hospital-based CPNB, 13% stated they would be unwilling to remove their catheter at home. However, of patients who previously removed a perineural catheter at home, 98% felt “comfortable” doing the procedure with instructions given by telephone, only 4% would have preferred to return to the hospital for health care provider catheter removal, and 43% would have felt comfortable with exclusively written instructions. Of note, at least within the United States, there are no national guidelines regarding the maximal safe CPNB duration.

**COMPLICATIONS**

As with all medical procedures, the potential CPNB benefits must be weighed against the potential risks. Fortunately, infusion-related serious and lasting injuries are uncommon, whereas relatively minor complications occur at a frequency similar to single-injection peripheral nerve blocks. Unfortunately, heterogeneous catheter insertion techniques, equipment, anatomic locations, and infusions render generalizations difficult. For example, various prospective studies report an incidence of secondary block (infusion) failure of 1%, 20%, and 50%. Thus, the specific complication rates provided in this section will not apply to all practices. CPNB-specific complications during catheter insertion include inaccurate catheter tip placement and/or liquid adhesive; and catheter-induced brachial plexus irritation. A CPNB-induced insensate ankle, may provide less than optimal analgesia without the concurrent use of additional analgesics. Of published reports, nearly all investigators provide a single infusion, often supplemented with a separate single-injection peripheral nerve block (e.g., sciatic block after knee surgery). Some individuals have proposed inserting a second catheter, although there are minimal and somewhat conflicting data to guide clinical practice. Whereas a lumbar epidural provides generally equivalent analgesia to femoral perineural infusion for hip and knee arthroplasty, CPNB results in a more favorable side-effect profile without the risk of epidural hematoma during concomitant anticoagulant administration.

Although the evidence for CPNB benefits during local anesthetic infusion is overwhelming, there are few data demonstrating benefits after catheter removal. Exceptions include improved analgesia after a few days or months, more rapid resumption of unassisted standing and laryvage use; increased health-related quality of life in 1 study (but not 5 others); and faster tolerance of passive knee flexion resulting in earlier discharge from rehabilitation centers. Conspicuously lacking is evidence of medium- or long-term improvements in health-related quality-of-life measures.

**COMPLICATIONS**

As with all medical procedures, the potential CPNB benefits must be weighed against the potential risks. Fortunately, infusion-related serious and lasting injuries are uncommon, whereas relatively minor complications occur at a frequency similar to single-injection peripheral nerve blocks. Unfortunately, heterogeneous catheter insertion techniques, equipment, anatomic locations, and infusions render generalizations difficult. For example, various prospective studies report an incidence of secondary block (infusion) failure of 1%, 20%, and 50%. Thus, the specific complication rates provided in this section will not apply to all practices. CPNB-specific complications during catheter insertion include inaccurate catheter tip placement too far from the target nerve to provide postoperative analgesia, and in exceptionally rare cases, epidural, intrathecal, intravascular, intraneural, and even interpleural catheter insertion. Catheter migration after accurate placement has been suggested, but also doubted, and the dearth of published events suggests that it is an exceptionally rare event, if it even occurs at all.

During the perineural infusion, more common (and benign) complications include catheter dislodgement or obstruction and fluid leakage at the catheter site. Although not prospectively investigated, subcutaneous catheter tunneling, application of liquid adhesive, use of a catheter anchoring device, and applying 2-octyl cyanoacrylate glue may decrease the incidence of dislodgement and leakage.

Additional possible complications include infusion pump malfunction, undesired pause, or disconnection; skin irritation or allergic reactions to the catheter dressing and/or liquid adhesive; and catheter-induced brachial plexus irritation. In addition, a CPNB-induced insensate extremity may prove disconcerting to patients.
Table 3. Benefits of Continuous Peripheral Nerve Blocks Documented in Randomized Controlled Trials Including at Least One Treatment Group Without a Regional Analgesic

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Brachial plexus</th>
<th>Femoral nerve</th>
<th>Sciatic nerve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia (improved)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Resting</td>
<td>RCT173,217,326,329,331,a</td>
<td>RCT13,2,38,346,b</td>
<td>RCT1,73,2,37,2,38,a,b</td>
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<td></td>
<td>MPC227</td>
<td>MPC222</td>
<td>MPC222</td>
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<tr>
<td>Breakthrough</td>
<td>RCT239</td>
<td>RCT230,b</td>
<td>RCT230,b</td>
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<tr>
<td></td>
<td>RCT237,240</td>
<td>RCT237,240,b</td>
<td>RCT237,240,b</td>
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<td></td>
<td>MPC32</td>
<td>MPC32</td>
<td>MPC32</td>
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<td></td>
<td>MPC1,78</td>
<td>MPC1,78</td>
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<td>Supplemental analgesic requirements (decreased)</td>
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<tr>
<td>Oral opioids</td>
<td>MPC23,93,178</td>
<td>MPC2,34</td>
<td>MPC2,34</td>
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<tr>
<td></td>
<td>RCT329,331</td>
<td>RCT161,242,248,346,356</td>
<td>RCT1,73,a</td>
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<tr>
<td></td>
<td>MPC2,38,346,b</td>
<td>MPC2,38,346,b</td>
<td>MPC2,38,346,b</td>
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<tr>
<td>Opioid-related side effects (decreased)</td>
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<tr>
<td>Pruritus</td>
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<td>RCT1,73,2,38,346</td>
<td>RCT1,73,2,38,346</td>
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<td>MPC227</td>
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<td>RCT346</td>
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<tr>
<td>Sleep</td>
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<tr>
<td></td>
<td>MPC23,93</td>
<td>MPC2,34</td>
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<td></td>
<td>RCT329,331</td>
<td>RCT161,242,248,346,356</td>
<td>RCT1,73,a</td>
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<tr>
<td>Nathan's vomiting or antiemetic rescue</td>
<td>MPC2,38,346,b</td>
<td>MPC2,38,346,b</td>
<td>MPC2,38,346,b</td>
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<tr>
<td>Sleep disturbance</td>
<td>RCT173,a</td>
<td>RCT1,73,a</td>
<td>RCT1,73,a</td>
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<td></td>
<td>MPC227</td>
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<td></td>
<td>RCT346</td>
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<td>Discharge (decreased time until...)</td>
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<tr>
<td>Discharge readiness</td>
<td>MPC23,93</td>
<td>MPC2,34</td>
<td>MPC2,34</td>
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<td></td>
<td>RCT329,331</td>
<td>RCT161,242,248,346,356</td>
<td>RCT1,73,a</td>
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<td>MPC2,38,346,b</td>
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<td>Resumption of passive joint range of motion</td>
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<tr>
<td>resumption (accelerated)</td>
<td>MPC23,93</td>
<td>MPC2,34</td>
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<td></td>
<td>RCT329,331</td>
<td>RCT161,242,248,346,356</td>
<td>RCT1,73,a</td>
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<tr>
<td>Resumption of ambulation or other functioning</td>
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<tr>
<td>(accelerated)</td>
<td>MPC23,93</td>
<td>MPC2,34</td>
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<td>RCT329,331</td>
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<tr>
<td>Inflammation or proinflammatory markers (decrease)</td>
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<td>MPC352</td>
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</tbody>
</table>

Only selected references are included because of publication limitations. RCT = randomized controlled trial (either no placebo control or at least 1 clinical group unmasked to treatment allocation); MPC = RCT with all clinical groups masked to treatment allocation and including a placebo control; NSAID = nonsteroidal antiinflammatory drug.

* The study by Capdevila et al.1,73 did not separate results for interscalene and popliteal sciatic catheters, and therefore one or both of these anatomic locations may account for all of the difference between treatment groups.

* Studies by Bagry et al.,238 Mistraletti et al.,237 and Blumenthal et al.240 compared 2 concurrent continuous peripheral nerve blocks versus no regional intervention, and therefore one or both of these anatomic catheter locations may account for all of the difference between treatment groups.
physical therapy and/or ambulation, and be considered a risk factor for injury by some investigators. In these cases, the infusion pump is usually paused until sensory perception begins to return, after which the infusion is restarted at a lower basal rate. Conversely, inadequate analgesia or breakthrough pain may occur, and is often treated by increasing the basal infusion and providing patient-controlled bolus doses, respectively.

More serious (but very rare) complications include myonecrosis with repeated large boluses of bupivacaine; systemic local anesthetic toxicity; Horner syndrome; and catheter knotting. Although infusions potentially affecting the phrenic nerve may have minimal pulmonary effects for relatively healthy patients, dyspnea is somewhat common, and lower lobe collapse has occurred. There is limited evidence that the risk of nerve injury from prolonged local anesthetic exposure may be increased in patients with diabetes and/or preexisting neuropathy.

There are case reports of peri-catheter hematoma formation, often with concurrently administered low-molecular-weight heparin for thromboprophylaxis. Most are self-limiting, but more dramatic cases require surgical evacuation. The most recent (Third) American Society of Regional Anesthesia consensus statement on neuraxial anesthesia and anticoagulation explicitly recommends precautions for neuraxial techniques and that anticoagulation be exercised for “deep” perineural catheters (undefined); specifically, that any catheter be removed before administration of various anticoagulants, although this practice has been questioned by various investigators.

Also concerning is the association between perineural infusions affecting the femoral nerve and patient falls after hip and knee arthroplasty, possibly because of CPNB-induced sensory, proprioception, and/or quadriceps weakness. Correlation does not prove causation; however, until further evidence is published, practitioners should consider interventions that may decrease the risk of falls, such as limiting the local anesthetic dose/mass; providing crutches/walker and a knee immobilizer during ambulation; and educating surgeons, nurses, and physical therapists of possible CPNB-induced deficits and fall precautions.

The reported rates of inflammation are seemingly high, clinically relevant infection is relatively rare (incidence 0%–3%); but most reports are <1%. Risk factors include admission to an intensive care unit, absence of perioperative antibiotic prophylaxis, and male sex. Although a multicenter study found a higher risk with axillary and femoral catheters, others have reported the interscalene location as the most problematic.

Risk of infection is also correlated with infusion duration. Nonetheless, infusions provided during extended medical transport for up to 34 days and provided at home for up to 83 days have been reported with a minimal incidence of infection. There is limited evidence that subcutaneous catheter tunneling may decrease the risk of bacterial colonization and infection. Abscesses have occurred, although the incidence remains unknown, and occasionally require surgical treatment, but often do not if timely antibiotic coverage is provided. Although life-threatening catheter-related infections/sepsis have been reported, there is currently no case of permanent injury due to CPNB-related infection within the English-language literature.

Perhaps the most feared postinfusion complication is neurologic injury. It is often difficult to determine how much of a neurologic deficit, if any, is attributable to CPNB because all surgical procedures are associated with a variable incidence of nerve injury, regardless of the application of a regional anesthetic/analggesic. For example, hip arthroplasty without a regional anesthetic is associated with an incidence of femoral neuropathy as high as 2.3%. So, if a study with a regional anesthetic/analggesic in the same patient population found a 1% incidence of femoral neuropathy, it would suggest that the perineural infusion is actually protective; but such an uncontrolled study would seem alarming with such a high incidence of nerve injury “associated” with CPNB. With this critical limitation in mind, the incidence of transient adverse neurologic symptoms associated with CPNB is 0% to 1.4% for interscalene, 0.4% to 0.5% for femoral, and 0% to 1.0% for sciatic catheters. An additional investigation found a 0.2% incidence of neurologic deficits lasting longer than 6 weeks in nearly 3500 catheters from multiple anatomic locations. In this latter study, it remains unknown whether the deficits resolved after the 6-week study period, but multiple prospective investigations report that the overwhelming majority of neurologic symptoms present at 4 to 6 weeks resolve spontaneously within 3 months of surgery.

There are reported cases of long-term and/or permanent nerve injury in patients with perineural infusion. Five large, prospective series that followed patients for at least 3 months found 3 cases of unresolved adverse neurologic events: a brachial plexus lesion after interscalene infusion (followed 9 months); a femoral neuropathy presumably the result of a retroperitoneal hematoma (cause undetermined; months followed not reported); and a persistent paraesthesia after a popliteal sciatic catheter (followed through 18 months). Combining the results of these studies (4148 subjects) suggests that the risk of neurologic injury lasting longer than 9 months associated with CPNB is 0.07%. It remains unknown whether CPNB contributed to these cases, or if they would have occurred without the addition of a regional analgesic. Although ultrasound guidance may decrease the incidence of many/most of these reported complications, there are few data supporting this proposition, and case reports suggest that completely abolishing such events is unlikely (quite possibly because postoperative neuropathy may occur without any regional anesthetic/analggesic).

CONCLUSIONS

Although the published literature presented in this review article provides a plethora of information involving CPNB, many aspects of perineural infusion have yet to be fully elucidated, including the optimal catheter insertion modality and technique; infusate(s) and adjuvants; local anesthetic delivery regimen; details of optimizing ambulatory...
infusion; possible infusion benefits; and the incidence of all possible risks. Furthermore, although CPNB seems to provide far more potent analgesia than wound catheters, \(^23\)–\(^30\) and often fewer undesirable side effects than epidural infusion, \(^23\)–\(^31\) many questions remain regarding the optimal analgesic technique for many surgical procedures. \(^31\),\(^32\) Last, perineural infusion must be adequately compared with possible new analgesic techniques. \(^24\),\(^33\)

Only through prospective research will we fully reveal and maximize the potential benefits, while minimizing the potential risks, of CPNB for our patients.

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