Systematic Review of High-volume Multimodal Wound Infiltration in Total Knee Arthroplasty

PURNAJYOTI BANERJEE, DIPORTH, MSC, MRCSED; BENEDICT A. ROGERS, MA, FRCS(ORTH)

educational objectives

As a result of reading this article, physicians should be able to:

1. Understand the high-quality evidence regarding the use of multimodal high-volume local wound infiltration in total knee arthroplasty.
2. Understand the contents of the drugs used, intraoperative infiltration techniques, and postoperative placement and use of a wound catheter.
3. Explain the effects of using wound infiltration in immediate postoperative pain relief, early mobilization, and length of hospital stay after total knee arthroplasty.
4. Understand the safety and complications associated with this technique.

ABSTRACT

Pain relief following total knee arthroplasty (TKA) is challenging because early mobilization and rehabilitation are essential for a successful outcome. Postoperative pain can limit recovery, leading to reduced mobility and prolonged hospitalization. There are potential benefits of infiltrating high volumes of local anesthetics around the soft tissues of replaced hip and knee joints. The risk of systemic toxicity is minimized with diluted local anesthetic solution, which also allows a high volume to be used. One of the
The risk of systemic toxicity is unclear. There are few reports of complications, including falls and delayed mobilization, when femoral nerve blocks are used. Wound infiltration analgesia should be used at the preference of the surgeon and anesthetist provided regular review of their practice is undertaken to identify any untoward side effects. Further randomized trials with sufficient sample size comparing each outcome, including pain scores, opiate consumption, and length of hospital stay, should be undertaken.

Local infiltration analgesia uses a systematic infiltration of the periacrylic soft tissues with a mixture of ropivacaine (a long-acting local anesthetic with a superior cardiotoxicity profile), ketorolac (an NSAID), and adrenaline (a vasoconstrictor). In their series of 325 patients undergoing total hip and knee arthroplasty, Kerr and Kohan reported excellent pain control and just one overnight hospital stay in 71% of patients. Due to the simplicity and relative safety of the procedure, it has gained widespread acceptance and use. One of the principal advantages is that analgesia agents are administered intraoperatively by the surgeon and subsequently by the ward staff, thereby minimizing the need for additional invasive procedures. However, some methodological concerns have been expressed regarding the validity of comparing its efficacy with that of other analgesic modalities. The current systematic review was designed to synthesize the available clinical evidence on the efficacy of high-volume multimodal wound infiltration following TKA, in particular intraoperative administration with and without the supplemental dosage through a suitably placed wound catheter. The aim of this study was to evaluate whether high-volume multimodal wound infiltration reduces pain and opiate intake while enhancing early rehabilitation and discharge when used in patients undergoing TKA.

**Materials and Methods**

A literature search was conducted in June 2012. The databases reviewed included Medline and Embase. The search terms included pain, postoperative, wound infiltration, total knee replacement/arthroplasty, wound catheter, and intra-/extra-articular injection. All studies identified using these search terms were then integrated using the Boolean and, which was subsequently scrutinized manually by the authors to extract the studies that fit the inclusion and exclusion criteria. Studies were limited to randomized trials in English and available through the Internet studying adults between the years 2000 to 2012. Studies published in the past decade were searched to ensure current evidence and the latest perspective on the issue. Furthermore, randomized controlled trials were included to ensure that highest level of evidence. All published articles were identified with the above search strategy. They were first screened using the title and the abstract to extract relevant studies that could be included in a systematic review, which was restricted to patients undergoing TKA. A manual search of the reference lists from selected articles was also performed to further increase the number of publications with relevant data.

**Inclusion Criteria**

Inclusion criteria were the following:
1. Randomized controlled trials reporting results on perioperative wound infiltration in primary unilateral TKA
2. Use of wound catheters
3. Defined research questions
4. Adequately described methodology
5. Use of intermittent injections or continuous infusions
6. Well-defined outcome measures

Principal advantages is that analgesia agents are administered intraoperatively by the surgeon, thereby minimizing the need for additional invasive procedures. The authors conducted a systematic review to evaluate whether high-volume multimodal wound infiltration reduces pain and opiate intake while enhancing early rehabilitation and discharge when used in patients undergoing TKA. Only randomized controlled studies were included. Although better pain relief in the immediate postoperative period with wound infiltration is gained after TKA, there is no definite evidence that this leads to a reduction in opiate consumption, the achievement of early milestones, or a reduction in hospital stay. The roles of individual agents in achieving pain relief and the use of percutaneous wound catheter for postoperative doses are also unclear. There are few reports of complications, including falls and delayed mobilization, when femoral nerve blocks are used. Wound infiltration analgesia should be used at the preference of the surgeon and anesthetist provided regular review of their practice is undertaken to identify any untoward side effects. Further randomized trials with sufficient sample size comparing each outcome, including pain scores, opiate consumption, and length of hospital stay, should be undertaken.

**Pain relief following total knee arthroplasty (TKA) is challenging because early mobilization and rehabilitation are essential for a successful outcome.** Postoperative pain can limit recovery, leading to reduced mobility and prolonged hospitalization. Local anesthetic agents block impulse transmission from some, but not all, peripheral pain receptors following major surgery. In addition, if infiltrated in large quantities, universal local anesthetic sodium channel block may lead to detrimental cardiac and neurological effects. It has been proposed that the release of inflammatory mediators and proteins secondary to cytolysis induces a stress response in the brain and the spinal cord, stimulating pain, even with a full block of peripheral receptors.

Recent clinical evidence has highlighted the potential benefits of infiltrating high volumes of local anesthetics around the soft tissues of replaced hip and knee joints. The risk of systemic toxicity is minimized with diluted local anesthetic solution, which also allows a high volume to be used. The possible loss of efficacy resulting from this dilution can be compensated with the addition of adjuvant agents such as adrenaline and nonsteroidal anti-inflammatory drugs (NSAIDs). Analgesia may be prolonged up to 48 hours with long-acting local anesthetics and the administration of supplemental doses via a wound catheter at regular intervals.

**Local infiltration analgesia uses a systematic infiltration of the periacrylic soft tissues with a mixture of ropivacaine (a long-acting local anesthetic with a superior cardiotoxicity profile), ketorolac (an NSAID), and adrenaline (a vasoconstrictor).** In their series of 325 patients undergoing total hip and knee arthroplasty, Kerr and Kohan reported excellent pain control and just one overnight hospital stay in 71% of patients. Due to the simplicity and relative safety of the procedure, it has gained widespread acceptance and use. One of the principal advantages is that analgesia agents are administered intraoperatively by the surgeon and subsequently by the ward staff, thereby minimizing the need for additional invasive procedures. However, some methodological concerns have been expressed regarding the validity of comparing its efficacy with that of other analgesic modalities.
Exclusion Criteria

Exclusion criteria were the following:
1. Systemic reviews and meta-analyses
2. Nonrandomized trials
3. Studies not published in English
4. Studies published prior to 2000
5. Bilateral TKA with infiltration of both knees
6. Unicompartmental TKA
7. Studies on knee arthroscopic surgery, hip replacements, and nonorthopedic surgical procedures
8. No comparator group
9. Nonrandomized
10. Outcome measures not well defined
11. No validated patient-reported functional outcome scores

Data Extraction

Once the authors identified the studies that appeared to meet the inclusion criteria, they read through the abstracts of the studies to find those that were relevant and fulfilled all of the inclusion criteria. Ideally, at this stage, both authors independently read each article to assess the adequacy of the search results and extract data according to their defined inclusion and exclusion criteria to ensure that the evidence gathered was adequate and relevant. Dissenting opinions regarding a study’s inclusion were resolved with informal discussions between the authors.

The authors included data on pain intensity as measured by the visual analog scale (VAS) from 0 to 10, where 0 represents no pain and 10 represents the worst imaginable pain. Postoperative rehabilitation was recorded in hours, opiate consumption in milligrams, and length of stay in days.

Outcomes as Endpoints

The following 2 primary endpoints were used, and any study not providing either was excluded:

1. Visual analog scale score on at least 2 time points separated by more than 4 hours (ie, 4 and 24 and 48 hours)
2. Morphine equivalent consumption (in milligrams) during these time periods

In addition, a number of secondary endpoints were analyzed (if reported), including, but not limited to:
1. Length of hospital stay in days
2. Side effects, including nausea and/or vomiting, headache, dizziness, numbness, and infection
3. Complications, including infection, nerve injuries, and hematomas

RESULTS

A total of 344 studies were found in the Medline database, and 19 were found in Embase. Thus, a total of 363 abstracts were identified that fulfilled the initial search strategy. From these abstracts, 44 studies were considered to be relevant to the study’s design and had all of the inclusion criteria and none of the exclusion criteria described previously. Of these, 18 randomized prospective studies were included in this systematic review, which had the necessary data as outlined previously. All studies identified in Embase were included in Medline except one, which was separately analyzed. These studies are summarized in Tables 1 and 2.

The search suggested that intraoperative wound infiltration with high-volume local anesthetic infiltration provides adequate pain relief for at least the first 6 to 12 hours. However, most of these studies suffer from methodological inadequacies and insufficient blinding (Table 3). The assessment of postoperative pain and opiate consumption is not fully described. Furthermore, data are lacking on the consumption and quality of peripheral analgesia or epidural (continuous/intermittent) analgesia techniques used in control groups. Data on the use of comparable systemic analgesia between groups are lacking in some studies. There is no conclusive evidence on the use of wound catheters and postoperative doses of local anesthetics imparting any significant analgesic effects after TKA. However, a similar conclusion cannot be drawn on the use of intra- or extra-articular/intracapsular administration of the drugs. There seems to be a distinct advantage in administering the local anesthetic agents

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Table 1

<table>
<thead>
<tr>
<th>Search Results From Medline Database on Wound Infiltration in Total Knee Arthroplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain=469,378</td>
</tr>
<tr>
<td>Postoperative complications (OR)=5,451,344</td>
</tr>
<tr>
<td>Wound infiltration (OR)=5,179,326</td>
</tr>
<tr>
<td>Knee replacement (OR)=427,335</td>
</tr>
<tr>
<td>Wound catheter (OR)=196,778</td>
</tr>
<tr>
<td>Injection (OR)=5733</td>
</tr>
<tr>
<td>1 and 2 and 3 and 4 and 5 and 6</td>
</tr>
<tr>
<td>(AND)=344</td>
</tr>
<tr>
<td>Manual search (AND)=32</td>
</tr>
<tr>
<td>Limits applied=17</td>
</tr>
</tbody>
</table>

*Parentheses contain the Boolean used while expanding each search term.*

Table 2

<table>
<thead>
<tr>
<th>Search Results From Embase on Wound Infiltration in Total Knee Arthroplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain=840,225</td>
</tr>
<tr>
<td>Postoperative complications (OR)=685,542</td>
</tr>
<tr>
<td>Wound infiltration (OR)=208,384</td>
</tr>
<tr>
<td>Knee replacement (OR)=12,420</td>
</tr>
<tr>
<td>Knee arthroplasty (OR)=23,419</td>
</tr>
<tr>
<td>Wound catheter (OR)=284,755</td>
</tr>
<tr>
<td>Injection (OR)=5625</td>
</tr>
<tr>
<td>1 and 2 and 3 and 4 and 5 and 6</td>
</tr>
<tr>
<td>(AND)=19</td>
</tr>
<tr>
<td>Manual search (AND)=19</td>
</tr>
<tr>
<td>Limits applied=1</td>
</tr>
</tbody>
</table>

*Parentheses contain the Boolean used while expanding each search term.*

Limits were randomized trials, adults, 2000-2012, in English, available from the Internet.

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Table 3
Randomized Controlled Trials in Wound Infiltration Analgesia Following Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Pain Score</th>
<th>Opiate Consumption</th>
<th>Treatment vs Control Length of Stay, d</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busch et al</td>
<td>Intraoperative wound infiltration vs no injection (n=64)</td>
<td>Reduced VAS immediately and 4 h postop</td>
<td>Reduced at 4, 12, and 24 h postop</td>
<td>Mean, 5.2 vs 5.2</td>
<td>Single-dose wound infiltration vs no injection; no ketorolac and epidural morphine in control group hinders exact interpretation of short-duration pain relief with wound infiltration; lack of wound catheter may explain relative short-term benefits achieved by treatment group patients</td>
</tr>
<tr>
<td>Toftdahl et al</td>
<td>Intra- and postop wound infiltration vs continuous femoral nerve block</td>
<td>Reduced NRS in treatment group vs femoral block on postop day 1; similar pain scores on day of operation</td>
<td>Reduced up to end of postop day 1</td>
<td>Median, 5 vs 6</td>
<td>No differences regarding side effects or length of stay seen between groups; small sample size; similar oral analgesia (NSAID/paracetamol/oxycodone) in both groups; femoral blockade group inferior to that reported in the literature; intra-articular bupivacaine (50 mg) and morphine (4 mg) administered with patients and research staff not blinded to patient groups</td>
</tr>
<tr>
<td>Vendittoli et al</td>
<td>Intra- and postop wound infiltration vs no injection (n=42)</td>
<td>Reduced at 24 and 48 h</td>
<td>Reduced up to 48 h postop</td>
<td>Mean, 4.8 vs 5.2</td>
<td>Not blinded; small sample size; effect predominant within the first 8 h of wound infiltration; similar systemic analgesia (COX-2 inhibitor/acetaminophen) and morphine PCA in both groups; lack of control for ketorolac in no injection group; no effect of 24-h postop administration in catheter</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration and postop intra- or extra-articular injection of local anesthetics (n=32)</td>
<td>No difference</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Double-blind placebo-controlled study; small sample size; no difference in pain scores, analgesia between the site of administration</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration with postop intracapsular vs intra-articular injection (n=60)</td>
<td>No difference</td>
<td>No difference</td>
<td>Mean, 3.0 vs 2.9</td>
<td>Double-blind study; intraop wound infiltration in both groups; intracapsular vs intra-articular injections 6 and 24 h with no difference</td>
</tr>
<tr>
<td>Gomez-Cardero et al</td>
<td>Continuous intra-articular 0.2% ropivacaine infusion vs placebo infusion with normal saline (n=50)</td>
<td>Reduced VAS score in first 3 postop d</td>
<td>Reduced opiate consumption for first 3 d in treatment group</td>
<td>Mean, 5.72 vs 7.3</td>
<td>Small sample size; blinding not clear; no NSAID or adrenaline used to enhance analgesic effects, indicating latter may not be needed; despite favorable results, unclear whether effect of pain relief was favorable during rest or motion; continuous infusion can hinder proper rehabilitation in the immediate postop period</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration with (treatment group) or without (control group) compression bandage (n=48)</td>
<td>NRS pain score at rest, during flexion, or on straight leg lift was lower for the first 8 h in patients with compression bandage vs noncompression bandage</td>
<td>Not reported</td>
<td>Mean, 2.8 vs 3.3</td>
<td>Compression bandage prolongs intraop analgesic effects after wound infiltration</td>
</tr>
<tr>
<td>Parvataneni et al</td>
<td>Intraop wound infiltration, not well-defined dose vs femoral nerve block (n=60)</td>
<td>No difference</td>
<td>No data</td>
<td>Mean, 3.2 vs 3.2</td>
<td>Not blinded; variable nonopioid analgesia on request; femoral nerve block not described; pain assessment insufficient</td>
</tr>
</tbody>
</table>
Table 3 (cont’d)

Randomized Controlled Trials in Wound Infiltration Analgesia Following Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Pain Score</th>
<th>Opiate Consumption</th>
<th>Treatment vs Control Length of Stay, d</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spreng et al</td>
<td>Intra- and postop wound infiltration vs epidural analgesia, NSAIDs, and opioids in injection group vs systemic analgesia (n=102)</td>
<td>Reduced NSAIDs and opioids in wound infiltration group, which was more effective than systemic analgesia group</td>
<td>Opiate consumption (72 h) was lowest for wound infiltration group (80 vs 101 mg [epidural analgesia group] vs 118 mg [wound infiltration and IV NSAIDs and opioids group])</td>
<td>Median, LIA 3.5 and 4 vs epidural 5.5</td>
<td>Well-designed trial; marginal differences in VAS during knee flexion and opioid consumption between wound infiltration vs wound infiltration and IV NSAIDs and opioids; wound infiltration group only compared with epidural analgesia and not with no-wound infiltration group; controlled epidural analgesia for 48 h not otherwise recommended due to side effects</td>
</tr>
<tr>
<td>Carli et al</td>
<td>Intraop and 24-h wound infiltration vs continuous femoral nerve block (n=40)</td>
<td>Reduced in femoral nerve block group</td>
<td>Reduced morphine PCA consumption in femoral nerve block group</td>
<td>Median, 5 vs 5; no difference</td>
<td>Double-blind; same multimodal nonopioid analgesia; preoperative walking capacity, physical activity, and early total walking time were independent predictors of early recovery; traditional recovery program with low activity limits interpretation on early analgesia and functional recovery</td>
</tr>
<tr>
<td>Essving et al</td>
<td>Intraop wound infiltration vs no injection, followed by 1 top-up dose 21 h postop (n=48)</td>
<td>Postop pain lower at rest in treatment group during the first 27 h and on movement during first 48 h; patient satisfaction higher on days 1 and 7 in same group</td>
<td>Median morphine consumption lower in group A during first 48 h</td>
<td>Median, 3 vs 5</td>
<td>Double-blind placebo-controlled study; good methodology; indicates wound catheter has a beneficial role in prolonging analgesia up to 48 h postop with minimal risk of infection</td>
</tr>
<tr>
<td>Joo et al</td>
<td>Intraop wound infiltration in patients undergoing bilateral TKA with 1 knee infiltrated (treatment arm) and other knee infiltrated with placebo (control arm) in same patient (n=286)</td>
<td>No difference</td>
<td>No difference</td>
<td>Not reported</td>
<td>Poor methodology; same patients used as treatment and control group; lack of favorable outcome explained by patients being subjected to severe pain in placebo-injected knee, which can mask relative pain relief in the injected knee</td>
</tr>
<tr>
<td>Fu et al</td>
<td>Patients undergoing unilateral TKA randomly assigned to receive a multimodal analgesia protocol (comprising oral celecoxib and tramadol preop and postop and intra-articular injection of large doses of morphine, ropivacaine, adrenaline, and betamethasone intraop [trial group]) or oral and intra-articular placebo (n=100)</td>
<td>Reduced VAS score at rest and with movement for up to 7 d postop</td>
<td>Reduced significantly in treatment group at 48 h postop</td>
<td>Not reported</td>
<td>Not blinded; no wound catheter used; unclear why effects were applicable after 7 d postop; methodology not robust; betamethasone used, which may have implications not seen in other trials</td>
</tr>
<tr>
<td>Affas et al</td>
<td>Compared local infiltration analgesia and femoral block with regard to analgesia and morphine demand during first 24 h after TKA (n=40)</td>
<td>Better pain relief in first 24 h in treatment group</td>
<td>No difference</td>
<td>Not reported</td>
<td>Not blinded; poor quality of randomization with unequal distribution of osteoarthrits and inflammatory arthritis in each group; although no difference seen, authors advocated wound infiltration because it is inexpensive and easy to use</td>
</tr>
</tbody>
</table>
The effects of perioperative local wound infiltration on length of hospital stay are variable. Although many studies reported a positive outcome, some studies did not report the same findings. The effects of perioperative local wound infiltration on length of hospital stay are variable. Although many studies reported a positive outcome, some studies did not report the same findings. The effects of perioperative local wound infiltration on length of hospital stay are variable. Although many studies reported a positive outcome, some studies did not report the same findings. The effects of perioperative local wound infiltration on length of hospital stay are variable. Although many studies reported a positive outcome, some studies did not report the same findings. The effects of perioperative local wound infiltration on length of hospital stay are variable. Although many studies reported a positive outcome, some studies did not report the same findings. 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cause most authors did not justify or explain these factors transparently enough to reach a satisfactory conclusion. Another recent well-designed study reported a reduction in opioid requirement and NSAID usage following local wound infiltration after TKA in 3 groups with (a) epidural analgesia or (b) wound infiltration with ropivacaine 150 mg and epinephrine 0.5 mg combined with ketorolac 30 mg and morphine 5 mg given either locally or (c) intravenously. Epidural analgesia was maintained for 48 hours. More importantly, the authors recorded a significant reduction in length of stay in the treatment group (median, 5 vs 3.5 vs 4 days, respectively).

Carli et al reported significant reduction in pain scores following intraoperative wound infiltration (intraoperatively and 24 hours postoperatively) vs a continuous femoral nerve block and both groups receiving the same multimodal nonopioid analgesia (COX-2 inhibitor and paracetamol) after TKA compared with traditional femoral nerve block. They found no difference in opioid requirement or attainment of early rehabilitation milestones in the treatment group. Both groups had a median length of stay of 5 days. However, the authors did not report the specific role of wound infiltration in length of stay. Patients in both groups were allowed to fully mobilize 3 days postoperatively, which may have affected the length of stay results in this study. Similar results were reported in another study that reported significant reduction in pain and opioid use in the group having wound infiltration along with early attainment of discharge criteria (3 vs 5 days). They had no serious side effects or complications with this technique.

Reeves et al found no difference in terms of pain score, opioid consumption, and subjective evaluation of patient satisfaction in 2 treatment groups with continuous infiltration of a high dose (0.375% ropivacaine) and a low dose (0.2% ropivacaine) vs a control group receiving saline. They had 2 cases of postoperative knee infection in the infiltration group, which was not reported in other studies. However, the continuous infusion may explain this complication rate compared with intermittent postoperative top-up doses. Another concern often raised was the result of using autotransfusion drains in TKA with wound infiltration. Two studies examined ropivacaine concentrations in the drain fluids and systemic side effects of local anesthetics after autologous blood transfusion following TKA. Both studies confirmed a safe blood level of ropivacaine in the drain blood and no side effects, confirming the safety of using drains and autotransfusion with wound infiltration. Furthermore, one study reported significant reduction in intraoperative blood loss along with reduced pain and need for rescue opioid analgesia in patients who received wound infiltration while undergoing TKA. This outcome might be explained by the local vasoconstriction caused by adrenaline. Other authors did not achieve such outcomes. It has also been reported that postoperative wound healing, infection, blood pressure, heart rate, rash, respiratory depression, urinary retention, and deep vein thrombosis were similar in patients with wound infiltration, but nausea and vomiting were significantly less frequent in the treatment group, probably secondary to reduced opioid uptake.

**DISCUSSION**

A systematic review is a powerful tool to assess the efficacy of interventions and of their likelihood to cause harm in a scientific and transparent manner. This estimates the relevance of interventions in a clinical context by gathering evidence from all relevant trials—and more commonly from high-quality randomized controlled studies when available. The systematic review is structured to reduce bias in the collection, appraisal, and interpretation of relevant studies using transparent methodology. This has proven to extract evidence that was not apparent in individual studies. This methodology includes the definition of a clear, often narrow, question to be answered; a structured literature search with well-defined inclusion and exclusion criteria; a quality assessment of retrieved reports; and standardized data handling and analysis. Poor pain management in the postoperative period can cause several long-term sequel, including chronic pain syndromes, increased postoperative morbidities, and poor quality of life. Novel pain management standard requires adequate postoperative pain management to be a key strategy to avoid any untoward long-time pain-related complication.

The inherent simplicity of the wound catheter technique is that it can easily be placed in situ by the operating surgeon. Furthermore, the postoperative top-up doses can be administered by the nursing staff, avoiding regular specialist medical input. This, combined with the ease of postoperative mobilization by patients, has led to the frequent use of wound catheters.

The current authors’ search has revealed a number of randomized controlled trials examining the efficacy of perioperative local wound infiltration in patients undergoing TKA. This illustrates the interest this approach has evoked among orthopedic surgeons and anesthesiologists. However, all of these studies have resulted in conflicting evidence. Although most studies were randomized, the sample sizes were often not adequate, allowing them to erroneously accept the null hypothesis (type 2 error). Moreover, the comparator groups were often heterogeneous (eg, femoral block, epidural, etc.), making a logical summation of their results virtually impossible. Some facts that have emerged from one study show that (1) wound infiltration does not cause dangerous levels of ropivacaine in the blood; (2) autologous transfusion is safe when combined with wound infiltration; and (3) systemic side effects related to opiates...
However, there is no definite evidence on more important aspects, including (1) postoperative pain scores, (2) postoperative opiate consumption, and (3) reduction in length of stay. The literature is highly divided in recommending wound infiltration for achieving these benefits. Furthermore, although most studies have reported no significant complications, one study mentions postoperative infection in the knee. 

Hence, no general recommendations can currently be made to support this technique. It is apparent that wound infiltration gives pain relief in the initial 6 to 12 hours postoperatively. However, the role of other drugs, like NSAIDs and adrenalin, has not been clearly evaluated. Few studies have addressed this role. 

These studies showed some superiority of local infiltration with ketorolac (NSAID) compared with systemic infusion, although it is known that analgesia is obtained by administration of NSAIDs, either locally or systemically, with minor clinical difference in terms of pain relief. 

Most studies have not taken into account the effects of the optimized multiple oral analgesics often offered to patients in treatment and comparator groups in the immediate postoperative period. Another study reported a reduction in opiate consumption and better perioperative pain relief leading to a reduction in length of stay with wound infiltration and intra-articular administration of ropivacaine compared with systemic administration of NSAIDs and continuous epidural infusion. A recent trial reported similar opiate consumption and length of stay with wound infiltration following TKA compared with femoral nerve block. However, pain with movement of the knee in the immediate postoperative period was significantly lower in the treatment group. This is important because postoperative knee motion is a key rehabilitation step following TKA. The achievement of adequate knee joint movement determines how quickly patients can be safely discharged.

There are no clear beneficial effects of top-up doses with wound infiltration in the postoperative period. Furthermore, this can lead to potential introduction of infection in the joint. Hence, this area needs further research to determine the optimal number and duration of top-up doses that provide patients with the best pain relief without increasing the risk of infection secondary to prolonged catheter placement in the knee joint. The role of other emerging agents may be of interest. Apart from paracetamol and NSAIDs, COX-2 inhibitors, gabapentinoids, and glucocorticoid injections have been tried along with wound infiltration. 

The role of gabapentin and pregabalin in postoperative pain relief after joint replacement has been reported. A single high-dose methylprednisolone injection in the joint can provide additional analgesia and reduce opiate intake following TKA. The evidence favoring these agents is sparse. More randomized controlled trials with sufficient sample sizes need to be undertaken to assess the safety, efficacy, and side effects of these agents.

There is some evidence that when used in conjunction with femoral nerve blocks, a single intraoperative injection can result in significant pain relief in the immediate postoperative period. However, the nerve block technique has its own inherent problems, including nerve damage, delayed mobilization, and falls due to motor blockade. Furthermore, when used with wound infiltration, it becomes unclear which technique (nerve block or wound infiltration) actually resulted in pain relief. Thus, wound infiltration should be used in isolation to avoid the potential complications associated with femoral nerve block. The latter has the advantage of allowing patient mobilization on the day of surgery, resulting in fast-track rehabilitation.

A limitation of the current review is that the search was confined to Medline and Embase. Although the authors tried to manually search the references to ensure all relevant studies were included, it is possible some may have been missed. Furthermore, the authors did not search other databases, such as Cochrane and CINAHL. The authors did not include grey literature (e.g., conference presentations and abstracts) that might contain more evidence regarding this technique. However, it is unlikely that a seriously performed randomized controlled trial is confined to a presentation without being published. The authors made no attempt to statistically compare the results because this was beyond the scope of this article; hence, this article contains some elements of a narrative review. The authors have not assessed cost analyses because that was not a part of their research question.

**CONCLUSION**

This article summarizes the current evidence and the implications of using perioperative wound infiltration analgesia with multimodal high-volume local anesthetic agents combined with additional agents like adrenaline and NSAIDs in patients undergoing TKA. The studies are heterogeneous with different methods and comparators, making valid comparison among the studies difficult. However, almost all of the studies reported better pain relief in the immediate postoperative period with wound infiltration. It is unclear whether this actually leads to a reduction in opiate consumption, the achievement of early milestones, or a reduction in length of hospital stay. The role of individual agents in achieving pain relief and the benefits of using a percutaneous wound catheter is also unclear. No study compares the individual agents with each other; therefore, it is unclear whether NSAIDs or adrenaline are needed in the mixture for wound infiltration. The role...
of a wound catheter is also not well established in terms of frequency of administration of bolus doses, continuous infusion, and optimal duration of leaving it in a replaced knee postoperatively. Although few recent reviews have condemned this technique,\textsuperscript{47,48} the evidence is unclear on whether to accept or reject wound infiltration. Currently, wound infiltration analgesia should be used at the preference of the surgeon and anesthetist provided regular review of their practice is undertaken to identify any untoward side effects. Further randomized trials with sufficient sample sizes comparing each outcome, including pain scores, opiate consumption, and length of hospital stay, should be undertaken.

**References**


