iPACK block vs. periarticular injection for total knee arthroplasty. A comprehensive review

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Systematic Review

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Abstract

Introduction

Total knee arthroplasty (TKA) is commonly performed in patients with end-stage osteoarthritis or rheumatoid arthritis of the knee to reduce joint pain, increase mobility and improve quality of life. However, TKA is associated with moderate to severe postoperative pain, which remains a significant clinical challenge. Surgeon-administered PAI and anesthesiologist-administered iPACK have proven viable alternatives to conventional peripheral nerve blocks. This review aims to discuss which IPACK block or periarticular injection, combined or not with different peripheral nerve blocks, has better effects on postoperative rehabilitation, patient satisfaction, and overall outcome.

Material and Method

The literature was reviewed through four electronic databases: PubMed, Cochrane Library, Google Scholar, and Embase.

Results

The initial search yielded 494 articles. Fifty-eight relevant articles were selected based on relevance, recentness, search quality, and citations. Six studies compared PAI to peripheral nerve block (PNB), and eight studies checked the effectiveness of adding PNB to PAI. Three studies compared iPACK to PNB, and ten studies checked the effectiveness of adding PNB to iPACK.

Conclusions

The best analgesic effect is obtained by combining PAI or iPACK with a peripheral nerve block, particularly with ACB, due to its analgesic and motor-sparing effect, and satisfactory analgesia.

Introduction

Total knee arthroplasty (TKA) is commonly performed in patients with end-stage osteoarthritis or rheumatoid arthritis of the knee to reduce joint pain, increase mobility, and improve quality of life. However, TKA is associated with moderate to severe postoperative pain (1), which remains a significant clinical challenge. Therefore, establishing optimal pain management requires a continuous reassessment of the available data (2). Following general or spinal anesthesia, analgesic regimens often consist of epidural anesthesia, intrathecal anesthesia, and patients-controlled analgesia (3). Oral and intravenous opioids also play an important role in postoperative pain relief due to their efficacy in relieving moderate to severe pain (4), (5). However, due to their unfavorable side-effect profile (6), newer alternative therapy combinations, primarily peripheral nerve blocks such as infiltration between the Popliteal Artery and Capsule of the Knee (iPACK) and periarticular injections (PAI), are being used instead of frequent opioid
usage (7). This review aimed to summarize data on the effectiveness of iPACK blockade and PAI on managing pain immediately after surgery, postoperative rehabilitation, patient satisfaction, and overall outcomes.

Innervation of the human knee is complex. Innervation of the posterior knee is provided by articular branches derived from the posterior branch of the sciatic, tibial, common peroneal, and obturator nerve. The articular branch of the tibial nerve is the primary source of innervation of the posterior knee capsule. They occur proximally or distally to the superior margin of the medial femoral condyles, where they branch further to form a network. The articular branches of the sciatic nerve and/or the common peroneal nerve divide further into anterior and posterior branches that innervate the anterolateral and posterolateral capsules. The articular branch of the posterior obturator nerve runs with the femoral artery and vein through the adductor hiatus and drains into the popliteal fossa. Finally, at the level of the femoral condyle, it divides into two to three terminal branches that supply the superior medial aspect of the posterior capsule.

Pain arising from the posterior knee after TKA can be alleviated by ultrasound-guided local anesthetic infiltration into the space between the posterior knee capsule and popliteal artery (iPACK) (8). The advantages of iPACK compared to other post-knee pain management modalities are enhanced analgesic efficacy, reduced postoperative opioid consumption, and improved functional measures. However, adverse complications during iPACK blockade include peroneal nerve block, intravascular injection, or risk of vascular injury to nearby popliteal vessels (9).

In contrast to iPACK, intraoperative PAI is the standard analgesic option for acute pain treatment after TKA. However, PAI is performed by an orthopedic surgeon using the Landmark technique. Therefore, its effectiveness depends on the technique and the analgesic regimen, but there is yet to be a consensus. Therefore, there is a potential pain relief benefit equivalent to the motor savings of the iPACK block (10).

This review aimed to compare iPACK block with routine PAI and hypothesize that iPACK is an effective technique to provide adequate pain management after TKA.

**Materials And Methods**

The literature was reviewed through four electronic databases: PubMed, Cochrane Library, Google Scholar, and Embase. This search was performed in November 2022. We evaluated studies published between 2017 and 2022 using the following search terms: “IPACK block” (title), “total knee arthroplasty” (title), and “local infiltration analgesia” (title). The titles, abstracts, and full texts of published studies were screened. As a result, trials were included in this review. This entire process is depicted in Fig.1

**Results**

The initial search yielded 494 articles. Fifty-eight relevant articles were selected based on relevance, recentness, search quality, and citations. Six studies compared PAI to peripheral nerve block (PNB), and
eight studies checked the effectiveness of adding PNB to PAI. On the other hand, only three studies compared iPACK to PNB, and ten studies checked the effectiveness of adding PNB to iPACK. The results are presented in several tables to facilitate the analysis of the collected material.

Table 1. Common cocktails of PAI
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Injection site</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Nicolino et al. (19)</td>
<td>Before cementation of the prosthesis: 30ml of the posterior capsule, 10ml of medial femoral and lateral periosteum on each side, and 10ml of tibial periosteum Before closing: 40ml the extensor apparatus, suprapatellar synovium, pes anserimus, cellular subcutaneous tissue</td>
<td>Before cementation of the prosthesis: 20ml 0,75% ropivacaine 8mg morphine 1mg/1ml in 0,3ml of epinephrine Before closing: 20ml 0,75% ropivacaine 20ml saline solution</td>
</tr>
<tr>
<td>2019</td>
<td>Kim at al. (57)</td>
<td>Posterior to the femur, beginning at the midline Deep injection before cementation: 30ml 0,5% bupivacaine with 1:3000,000 epinephrine plus methylprednisolone 40mg/l plus cefazolin 500mg in 10ml and normal saline 22ml The superficial injection before closure: 20ml 0,25% bupivacaine</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>Sankineani et al. (60)</td>
<td>Before the implant insertion- 30ml to the tissues around medial and lateral collateral ligaments And 30ml into the incision site after implant insertion 30ml 0,2% ropivacaine, 40mg ketorolac, 0,5ml of adrenaline, 4mg of morphine sulfate, and 30ml of distilled water</td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>Dannana et al. (61)</td>
<td>before implantation: 40ml infiltrated into the posteromedial and postero-lateral capsule, and PCL After implantation: 60ml was infiltrated into the medial and lateral gutters, quadriceps mechanism, vastus medialis obliquus, patella tendon, and the medial periosteum 20ml solution was infiltrated in the subcutaneous plane before wound closure</td>
<td>30ml 0,2% ropivacaine, 30mg ketorolac, inj adrenaline 0,5ml 1:1000 solution, inj morphine 5mg (10mg/ml) mixed with 88ml normal saline</td>
</tr>
<tr>
<td>Year</td>
<td>Author</td>
<td>Injection site</td>
<td>Components</td>
</tr>
<tr>
<td>------</td>
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</tr>
</tbody>
</table>
| 2020 | Altay et al. (62) | Periarticular:  
5ml posterior capsule  
5ml medial capsule/synovium/periosteum  
5ml quadriceps tendon, and 5ml lateral capsule/synovium/periosteum  
Incisional injection:  
Subcutaneous tissue around the midline incision before the wound closure | After implantation  
20ml 0,5% bupivacaine chloride  
Incisional injection of 10ml 0,5% bupivacaine chloride |
| 2018 | Zlotnicki et al. (63) | Before cementation:  
30ml into the posterior capsule (avoiding the midline) and the periosteum of the femur and tibia  
After cementation of implants:  
30 ml along the arthrotomy, including the quadriceps and patellar tendon  
20ml throughout the subcutaneous layer | 20ml 0,5% bupivacaine  
70ml normal saline |
| 2018 | Mont at al. (41) | Prior to cementation:  
Posterior capsule (8-10ml) and 8-10ml lateral; femur- medial and lateral periosteum, posterior periosteum, suprapatellar/quadriceps tendon; Tibia- fat pad, pes anserinus, medial collateral ligament and gutter (15ml); circumferential periosteum (15-20ml);  
After cementation:  
Medline quadriceps tendon (10ml); retinaculum, medial gutter, femoral to tibia (10ml); Lateral gutter, femoral to tibial (10ml), subcutaneous/closure (10ml) | 20ml 0,5% liposomal bupivacaine  
100ml normal saline |
| 2020 | Wang at al. (64) | Before the osteotomy:  
Periosteum of the distal femur and proximal tibia | Tranexamic acid, epinephrine, methylprednisolone, and ropivacaine diluted to a total volume of 100ml with normal saline |
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Injection site</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Cheng at al.(65)</td>
<td>Before the prosthesis installation: 20mL posterior capsule, including femoral attachments of anterior cruciate ligament and posterior cruciate ligament, posteromedial and posterolateral capsules. After prosthesis installation: 40mL medial and lateral collateral ligament, quadriceps tendon, patellar tendon, pes anserinus, fat pad, and subcutaneous tissues</td>
<td>200mg ropivacaine, 100ug fentanyl, 0,25mg adrenaline, 50mg flurbiprofen axetil, 1mg diprospan, addition of normal saline to a 60mL soliton</td>
</tr>
<tr>
<td>2021</td>
<td>Wang at al.(20)</td>
<td>Before prosthesis implantation: 20mL posterior aspect of the capsule, and 20mL medial and lateral collateral ligaments</td>
<td>0,2% ropivacaine, 2,0ug/mL epinephrine, and 0,1mg/m dexamethasone</td>
</tr>
</tbody>
</table>

Two authors used only 0,5% bupivacaine hydrochloride, and one used only 0,5% liposomal bupivacaine in their cocktails. The remaining seven researchers used cocktails consisting of the local anesthetic 0,5% bupivacaine hydrochloride (two) or 0,5% ropivacaine (five) along with epinephrine (seven) and other drugs, including opioids (four) and steroids (two).

Table 2. PAI vs. PNB
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Nicolino et al(27)</td>
<td>Controlled, double-blinded, randomized</td>
<td>70</td>
<td>LIA with a saphenous nerve block (SNB) vs intra-articular cocktail</td>
<td>LIA with SNB was more effective in reducing pain after TKA (p = 0.001)</td>
</tr>
<tr>
<td>2018</td>
<td>Tong et al(32)</td>
<td>a prospective single-center, double-blind, randomized controlled trial</td>
<td>40</td>
<td>LIA vs adductor canal block (ACB)</td>
<td>ACB was more effective in reducing total morphine consumption in the first 24 (p = 0.004) and 48 hours (p = 0.03)</td>
</tr>
<tr>
<td>2018</td>
<td>Runge et al(28)</td>
<td>a prospective single-center, double-blind, randomized controlled trial</td>
<td>82</td>
<td>PAI vs combined obturator nerve and femoral triangle blockade</td>
<td>Combined femoral triangle blockade was more effective in reducing morphine consumption (p &lt; 0.001)</td>
</tr>
<tr>
<td>2019</td>
<td>Cicekci et al(31)</td>
<td>a prospective single-center, double-blind, randomized controlled trial</td>
<td>79</td>
<td>PAI vs ACB</td>
<td>ACB was more effective in reducing morphine consumption (p &lt; 0.005)</td>
</tr>
<tr>
<td>2020</td>
<td>Lützner et al(29)</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>140</td>
<td>Femoral nerve block, continuous sciatic nerve block, and single-shot obturator nerve block vs LIA with a continuous intraarticular catheter with ropivacaine</td>
<td>Femoral nerve block, continuous sciatic nerve block, and single-shot obturator nerve block were more effective in reducing morphine consumption (p &lt; 0.05)</td>
</tr>
<tr>
<td>2019</td>
<td>Kostelnik et al(30)</td>
<td>Two-group randomized, controlled clinical trial</td>
<td>40</td>
<td>Single shot sciatic nerve block combined with adductor canal block with a catheter (CACB) vs LIA</td>
<td>Single-shot sciatic nerve block combined with CACB was more effective in reducing morphine consumption (p &lt; 0.01)</td>
</tr>
</tbody>
</table>

Two researchers compared femoral nerve block (FNB) to PAI, and another two authors looked at the impact of adductor canal block (ACB) compared to PAI. Only one trial concerned continuous adductor canal blockade with a catheter (CACB).

Table 3. LIA with PNB
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>Aso et al(1)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>40</td>
<td>PAI with a femoral nerve block (FNB) vs FNB alone</td>
<td>PAI with FNB was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2018</td>
<td>Fenton et al(33)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>80</td>
<td>PAI vs PAI with FNB catheter</td>
<td>PAI with FNB was more effective in reducing pain after TKA (p &lt; 0.005)</td>
</tr>
<tr>
<td>2019</td>
<td>Kampitak et al(34)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>90</td>
<td>PAI with continuous adductor canal block with 1) obturator nerve block vs 2) tibial nerve block vs 3) obturator and tibial nerve block</td>
<td>PAI with triple nerve block was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2018</td>
<td>Biswas et al(35)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>201</td>
<td>PAI with sham adductor canal block (ACB) vs PAI with adductor canal block vs PAI with intrathecal morphine</td>
<td>PAI with ACB was more effective in reducing pain after TKA (p = 0.007)</td>
</tr>
<tr>
<td>2022</td>
<td>Luo et al(36)</td>
<td>a prospective single-center, double-blind, randomized controlled trial</td>
<td>86</td>
<td>PAI vs PAI with ACB</td>
<td>PAI with ACB was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2018</td>
<td>Tziona et al(37)</td>
<td>a prospective single-center, double-blind, randomized controlled trial</td>
<td>40</td>
<td>PAI vs PAI with ACB</td>
<td>PAI with ACB was more effective in reducing morphine consumption (p &lt; 0.05)</td>
</tr>
<tr>
<td>2019</td>
<td>Lan et al(19)</td>
<td>Double-blind, randomized, placebo-controlled trial</td>
<td>46</td>
<td>PAI vs PAI with CACB</td>
<td>PAI with CACB was more effective in reducing pain after TKA (p &lt; 0.001)</td>
</tr>
</tbody>
</table>
Only one trial had over 200 participants. Two studies examined the effects of LIA combined with FNB. Three trials looked at the impact of adductor ACB with PAI. Finally, two trials concerned CACB with catheter and PAI.

Table 4. PAI with liposomal bupivacaine (LB)

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Dysart et al. (40)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>139</td>
<td>PAI with LB mixed with bupivacaine HCl vs PAI with bupivacaine HCl alone</td>
<td>PAI with LB mixed with HCl was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2017</td>
<td>Mont et al. (41)</td>
<td>a randomized, prospective study</td>
<td>140</td>
<td>PAI with liposomal bupivacaine vs PAI with bupivacaine HCl</td>
<td>PAI with LB was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
</tbody>
</table>

Only two trials consider using LB in PAI for pain management after TKA.

Table 5. iPACK block
Table 5
iPACK block

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Patterson et al. (46)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>69</td>
<td>iPACK vs CACB</td>
<td>iPACK was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2020</td>
<td>Akesson et al. (44)</td>
<td>a prospective single-center double-blind, randomized controlled trial</td>
<td>60</td>
<td>iPACK vs genicular nerve block vs placebo</td>
<td>iPACK was as effective as a genicular nerve block in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2020</td>
<td>Kampitak et al. (34)</td>
<td>A prospective, triple-blinded, randomized controlled trial</td>
<td>105</td>
<td>Proximal iPACK vs distal iPACK vs Tibial Nerve block</td>
<td>Proximal iPACK was less effective in reducing pain after TKA (p &gt; 0.05)</td>
</tr>
<tr>
<td>2021</td>
<td>Kampitak et al. (43)</td>
<td>a prospective, randomized, double-blind study</td>
<td>72</td>
<td>Selective sensory nerve blockade (ACB + anterior femoral cutaneous nerve block + iPACK) vs PAI</td>
<td>SSNB did not provide superior postoperative analgesia</td>
</tr>
</tbody>
</table>

Three trials considered iPACK vs. PNB, and one compared iPACK with PNBs vs. PAI.

Table 6. iPACK block with PNB
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>Sankineani et al. (60)</td>
<td>Prospective study</td>
<td>120</td>
<td>iPACK with ACB vs ACB alone</td>
<td>iPACK with ACB was more effective in reducing pain after TKA (p &lt; 0.005)</td>
</tr>
<tr>
<td>2021</td>
<td>Wang et al. (48)</td>
<td>a prospective, randomized, double-blind study</td>
<td>149</td>
<td>iPACK with ACB + sham obturator nerve block (ONB) + sham lateral femoral cutaneous nerve block (LFCNB) vs ACB + iPACK + ONB + LFCNB vs ACB + iPACK + ONB + sham LFCNB</td>
<td>iPACK + ACB + ONB + LFCNB was more effective in reducing morphine consumption after TKA (p &lt; 0.01)</td>
</tr>
<tr>
<td>2020</td>
<td>Ochroch et al. (55)</td>
<td>a prospective, randomized, double-blind study</td>
<td>119</td>
<td>iPACK + ACB vs sham block + ACB</td>
<td></td>
</tr>
<tr>
<td>2022</td>
<td>Wang et al. (49)</td>
<td>a prospective, randomized, double-blind study</td>
<td>70</td>
<td>Continuous ACB + iPACK vs CACB + sham block</td>
<td>ACB + iPACK was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2022</td>
<td>Mou et al. (50)</td>
<td>a prospective, randomized, double-blind study</td>
<td>120</td>
<td>ACB + iPACK vs ACB vs iPACK</td>
<td>ACB + iPACK was more effective in reducing pain after TKA (p &lt; 0.001)</td>
</tr>
<tr>
<td>2022</td>
<td>Et et al. (51)</td>
<td>prospective, randomized, double-blind study</td>
<td>105</td>
<td>ACB vs iPACK + ACB vs LIA + ACB</td>
<td>ACB + iPACK was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2022</td>
<td>Tak et al. (54)</td>
<td>a prospective, randomized, double-blind study</td>
<td>171</td>
<td>ACB vs continuous ACB vs ACB + iPACK</td>
<td>CACB was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>Year</td>
<td>Author</td>
<td>Type of Study</td>
<td>Sample size</td>
<td>Method</td>
<td>Results</td>
</tr>
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<td>------</td>
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<td>--------------------------------------------</td>
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<td>------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>2020</td>
<td>Li et al. (52)</td>
<td>a prospective, randomized, double-blind</td>
<td>200</td>
<td>ACB + iPACK + lateral femoral cutaneous nerve block vs ACB + iPACK vs ACB + lateral cutaneous nerve block vs ACB alone</td>
<td>ACB + iPACK + lateral femoral cutaneous nerve block was more effective in reducing pain after TKA (p &lt; 0.05)</td>
</tr>
<tr>
<td>2021</td>
<td>Kampitak et al. (43)</td>
<td>a prospective, randomized, double-blind study</td>
<td>72</td>
<td>Selective sensory nerve blockade (ACB + anterior femoral cutaneous nerve block + iPACK) vs LIA</td>
<td>SSNB did not provide superior postoperative analgesia</td>
</tr>
<tr>
<td>2022</td>
<td>Abdullah et al. (53)</td>
<td>A prospective, randomized controlled trial</td>
<td>80</td>
<td>iPACK with ACB vs ACB alone</td>
<td>ACB + iPACK was more effective in reducing pain after TKA (p &lt; 0.01)</td>
</tr>
</tbody>
</table>

One of the studied parameters in all ten trials was iPACK block with ACB compared with iPACK alone, or iPACK with ACB and different PNB.

Table 7. iPACK or LIA
Table 7
IPACK or LIA

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Type of Study</th>
<th>Sample size</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Vichainarong et al. (56)</td>
<td>a prospective, randomized, double-blind study</td>
<td>72</td>
<td>LIA + CACB vs iPACK + LIA + CACB</td>
<td>IPACK + LIA + CACB does not reduce postoperative opioid consumption (p = 0,08)</td>
</tr>
<tr>
<td>2019</td>
<td>Kim et al. (57)</td>
<td>A triple-blinded, randomized controlled trial</td>
<td>86</td>
<td>LIA vs iPACK + ACB + modified LIA</td>
<td>IPACK + ACB + LIA significantly improved analgesia (p = 0,001) and reduced opioid consumption (p = 0,005)</td>
</tr>
<tr>
<td>2021</td>
<td>Kertkiatkachorn et al. (58)</td>
<td>A prospective, randomized controlled trial</td>
<td>66</td>
<td>Continuous ACB + iPACK vs continuous ACB + LIA</td>
<td>ACB with IPACK block provides a non-inferior analgesia</td>
</tr>
<tr>
<td>2021</td>
<td>Naranjo et al. (59)</td>
<td>A prospective, randomized controlled trial</td>
<td>80</td>
<td>iPACK + ACB vs LIA + ACB</td>
<td>IPACK + ACB was more effective in reducing pain after TKA (p &lt; 0,01)</td>
</tr>
</tbody>
</table>

Only four authors tried to answer how iPACK with PAI affects pain management after TKA.

Discussion

Periarticular injection

PAI has become an essential component of a multimodal approach to managing postoperative TKA pain (11). PAI is a popular and widely accepted method of multimodal analgesic regimens because of its postoperative opioid- and motor-sparing effects in patients undergoing TKA (12, 13)

Kopitko et al. (14) demonstrated that the PAI technique offers a rapid and safe treatment option for pain relief after TKA. None of the patients reported high-intensity pain (NRS > 8) (p < 0,008), and no clinically relevant muscle weakness was observed compared to peripheral nerve block and spinal anesthesia. Unver et al. (15) investigated the efficiency of PAI and the impact of TKA functional outcomes. He found that PAI was associated with lower pain scores on postoperative first and second days compared to spinal anesthesia alone (p = 0,027; p = 0,020). Furthermore, McCarthy et al. (16) concluded that PAI was significantly higher in VAS scores compared to intrathecal morphine 0,3 mg at rest (16,43 vs. 37,2; p = 0,029) and exercise (39,1 vs. 57,0; p = 0,037). VAS scores were also lower with exercise within 48 hours after TKA (25,9 vs. 40,5; p = 0,028). Ukai et al. (17) randomized 58 patients to receive PAI compared with epidural catheters and showed similar efficacy in pain control with epidural and faster functional recovery (p < 0,05).
However, there still needs to be a consensus on PAI’s optimal configuration and invasion technique. Table 1 shows standard PAI cocktails.

The PAI technique is based on the systematic infiltration of a mixture of a local anesthetic and adrenaline around all knee joint structures, usually in combination with a non-steroidal anti-inflammatory drug. PAI is a simple, blinded technique that orthopedic surgeons in postoperative knee pain alleviate without quadriceps weakness. However, it can be seen in the cited studies that the maximum doses of local anesthetics were often exceeded, which may expose the patients to the risk of side effects, including LAST syndrome.

Among patients who underwent TKA, those who underwent intraoperative PAI showed reduced early postoperative overall anesthetic use and improved pain scores compared with those who underwent placebo infiltration (18, 19).

In recent years, different researchers have added different adjuvants to PAI cocktails (3).

Not all are equally effective in relieving postoperative pain. Wang et al. (20) randomized 107 patients. They found that the addition of corticosteroids to the PAI analgesic cocktail modestly improved early pain relief (p < 0,05), and in the first 24h after TKA, the recovery may be accelerated (p < 0,05). Moreover, Chan et al. (21) showed that steroids combined with PAI provided additional benefits for pain control and rehabilitation after TKA (p < 0,05). Miyamoto et al. (22) evaluated that the efficacy of morphine added to periarticular multidrug injection (PMDI) was limited and that the efficacy of morphine added to spinal anesthesia disappeared within 20 h postoperatively. Adding morphine to PAI or spinal anesthesia did not improve functional recovery and caused several side effects. Various investigators (8, 20, 23) have reached similar conclusions, suggesting that adding morphine to the PAI analgesic cocktail did not improve early pain relief, accelerated functional recovery, or provide clinical benefit to TKA patients. Schotanus et al. (24) randomized 50 patients and found no benefit of using epinephrine in an LIA mixture compared with ropivacaine alone in pain relief after TKA. Similarly, Kong et al. (25) concluded that epinephrine use in PAI with ropivacaine does not affect acute postoperative pain and use. Haagen et al. (26) showed that PAI with 300mg ropivacaine was more effective than 150mg ropivacaine (p = 0,021).

PAI vs. PNB

In recent years, multimodal pain treatment strategies have become increasingly widespread. In particular, the use of peripheral nerve blocks (PNB) and PAI in total knee arthroplasty have surged. However, there is significant variability in the administration of both anesthesia modalities. A critical review of the current literature is therefore warranted to elucidate the strengths and weaknesses of each technique, with the goal of further refining current pain management strategies.

Nicolino et al. (27) rated complementary saphenous nerve blocks as more effective than LIA in reducing pain after TKA (p = 0,001). In addition, Runge et al. (28) randomized 82 patients combined with triangular femoral block to reduce morphine use over LIA after TKA (6 vs. 20; p < 0,001). Finally, Lützner et al. (29)
found that a combination of a continuous femoral nerve block, a continuous sciatic nerve block, and a single-shot obturator nerve block slightly improved pain control (NRS 3.0 vs. 4.2; p < 0.05) but should it be avoided due to association with motor block.

Additionally, Kastelik et al. (30) demonstrated improved pain control (VAS: 0.3 vs. 2.3; p = 0.01) and reduced opioid use with the combination of single sciatic nerve block and CACB. It allowed both regiments to mobilize earlier than the LIA alone (78 vs. 107; p < 0.01). Cicekci et al. (31) randomized 79 patients. They found that ACB was superior to LIA in terms of pain control (p < 0.05), but the postoperative range of motion (ROM) and ambulation LIA was superior to ACB (p < 0.05). Tong et al. (32) concluded that adductor canal block (ACB) compared with LIA in the first 24 (6 vs. 17.5; p = 0.004) and 48 hours (14.5 vs. 24; p = 0.03) significantly reduced morphine consumption, and there was no difference in functional outcome in TKA patients.

Resume, PNBs appear more effective than PAI in treating postoperative pain after TKA.

PAI with PNB

There has been a strong push in the orthopedic community and elsewhere to provide opioid-sparing analgesia to surgical patients. As a result, there has been a focus on providing care related to multifaceted pain management, with periarticular injections and nerve blocks critical components of many protocols. PNB and PAI play an essential role in relieving postoperative pain. Adding PAI to PNB can reduce morphine consumption and improve pain relief and functional recovery.

Aso et al. (1) showed that adding local analgesic infiltration to the femoral nerve block promoted postoperative pain relief and knee recovery more than the femoral nerve block alone (p < 0.05). Adding FNB to PAI significantly decreased C-reactive protein levels (p < 0.01). Fenten et al. (33) randomized 80 patients to combine PAI with FNB. FNB with PAI resulted in lower pain scores and less opioid use but lower accelerometer activity than PAI alone. However, it is worth noting that subjects in the FNB group had lower peak pain scores at 3 and 12 months after surgery. Even more interesting is that they were less likely to take pain medications at 12 months postoperatively (p < 0.005).

Kampitak et al. (34) randomized 90 patients to evaluate that a triple nerve block (obturator and tibial nerve block) combined with PAI was associated with improved analgesia and functional outcomes in the postoperative period immediately after TKA. It was evaluated to be superior to double nerve blocks. Also, Biswas et al. (35) randomized 201 patients to receive PAI plus ACB and low-dose intrathecal morphine (100ug), improved resting analgesic profile (VAS: 4 vs. 4 vs. 3; p = 0.007), and during exercise (VAS: 6 vs. 6 vs. 4; p = 0.002) than PAI or ACB or intrathecal morphine alone.

Recent studies have shown that PAI and ACB combined have addictive effects on analgesia and opioid use after TKA. For example, Luo et al. (36) randomized 60 patients receiving ACB in combination with PAI, had significantly lower rest and activity VAS pain scores, and better ROM within 72 h postoperatively than LIA alone, with higher sleep quality and satisfaction (p < 0.05). In addition, Tzionas et al. (37) showed that
in addition to multimodal anesthesia with an ACB regimen, PAI reduced morphine consumption (6, 12, 18, 24 h; p: 0,035; 0,008; 0,015; 0,003).

Many researchers have shown that single-shot PNB provides adequate analgesia in the first 24 hours after TKA. However, the duration of analgesia does not cover the entire period of pain with VAS≥4. Recent studies have highlighted continuous PNB, which may compromise recruitment capacity. Lan et al. (19) showed that adding CACB to single-dose PAI improved analgesia (NRS: 3 vs. 5; p < 0,001) and promoted walking without motor weakness (p = 0,002) compared to LIA alone. On the other hand, Gudmundsdottir et al. (38) evaluated that the addition of CACB to single-dose PAI had no advantage compared to PAI alone.

Current evidence indicates that combining ACB with the addition of analgesic posterior capsule coverage with PAI may yield optimal results.

LIA with liposomal bupivacaine (LB)

Many attempts have been made to prolong the duration of local action (39). For example, bupivacaine loaded into multivesicular liposomes prolongs the duration of local anesthetic effects due to sustained release from the liposomes and delays peak plasma concentrations compared to simple administration of bupivacaine (4).

Dysart et al. (40) found that PAI with LB 266mg plus bupivacaine HCl significantly reduced demand for opioids (91% reduction in opioid use; p = 0,009) and intensification of pain (19% reduction; p = 0,0142) and significantly improved readiness for discharge (p = 0,0449) and contentment (p = 0,0306) 0–24 hours after TKA compared with bupivacaine HCl alone. In addition, Mont et al. (41) provided data on PAI with LB significantly reduced pain after surgery (VAS: 180,8 vs. 209,3; p = 0,381), opioid requirements 0–48 hours post-surgery (18,7 vs. 84,9; p = 0,0048), and time to first opioid rescue dose (p = 0,0230) and there were no unexpected safety concerns.

LB appears to provide better pain control than bupivacaine HCl when used in PAI for pain treatment in TKA. However, an extensive systematic review and meta-analysis failed to yield a true clinical benefit to using liposomal bupivacaine in PAI or PNB (42).

iPACK block

A novel technique for treating posterior knee joint pain is the infiltration of local anesthetics between the popliteal artery-capsular space (iPACK) of the knee joint, targeting the terminal sensory nerve endings in the posterior knee joint. The iPACK block is a motor-sparing analgesic modality that targets the distal sensory branches of the knee joint. Kampitak et al. (43) showed in their cadaver study that in the distal portion of the popliteal fossa, the tibial nerve and popliteal vessels run superficially and closely together lateral to the popliteal vasculature and plexus towards the posterior capsule of the knee under the medial aspect of the superior eminence of the lateral femoral condyle.
Akesen et al. (44) randomized 60 patients to receive that both IPACK and genicular block effectively improve patient comfort during and after TKA surgery, decreasing the need for systemic analgesics, including opioids. Kampitak et al. (45) compared IPACK with a tibial nerve block and found that IPACK preserved the motor function of the common peroneal and tibial nerves (p = 0.001). However, distal iPACK failed to demonstrate complete motor blockade of the common peroneal and tibial nerve while maintaining effective posterior knee pain relief. Furthermore, Kampitak et al. (43) concluded that ultrasound-guided selective sensory nerve blockade (SSNB) of the knee, including an ACB, anterior femoral cutaneous nerve block, and iPACK did not provide superior pain relief after surgery or better functional performance. However, it may result in lower opioid use after surgery than intraoperative PAI. Finally, Patterson et al. (46) randomized 69 patients to receive that IPACK improves pain control at rest (p = 0.0122), but pain scores during physical therapy were similar (p = 0.2080). Also, there was no difference in opioid demand (p = 0.7928) and walking distance (p = 0.5197) compared to CACB.

IPACK block with PNB

PNBs have been incorporated into most multimodal analgesia protocols for TKA. The sciatic nerve block provides optimal analgesia in the posterior part of the knee, and lower extremity motor dysfunction hinders early rehabilitation and masks intraoperative peroneal nerve (CPN) injury, discouraging the use of this analgesic modality. The iPACK block targets the articular sensory branch of the sciatic nerve while sparing the motor branches of the tibial nerve (TN) and CPN, thereby avoiding the foot drop that occurs with the sciatic nerve block. iPACK is an alternative analgesic adjuvant to femoral or adductor canal block for posterior knee pain.

Sankineani et al. (47) randomized 180 patients whose VAS scores (p < 0.005) and ROM of the knee and walking ability were significantly superior with ACB + IPACK block compared with ACB alone. Wang et al. (48) explored the efficacy of two unique combinations of nerve blocks on pain after surgery and functional outcome after TKA. He concluded that adding a sham obturator nerve block, sham lateral femoral cutaneous nerve block, and sham lateral femoral cutaneous block to ACB and IPACK block reduced morphine use (11.2 vs. 17.2; p = 0.001) compared with ACB and IPACK alone. However, absolute changes in morphine consumption, VAS scores, and QoR-15 scores did not exceed the minimal clinically significant differences.

Wang et al. (49) showed that the combination of CACB and iPACK reduced pain (p < 0.05) and promoted recovery of motor function (p = 0.001). Furthermore, Mou et al. (50) assessed that blockade of the adductor canal with IPACK block could improve early analgesia (p < 0.001) compared to ACB alone. Et al. (51) randomized 105 patients to receive IPACK with ACB, improved postoperative analgesia (p < 0.05), decreased opioid use (p < 0.001), and enhanced mobilization (p < 0.001) compared to LIA with ACB or ACB alone. Li et al. (52) randomized 200 patients. They found that a combination of ACB with iPACK and lateral femoral cutaneous nerve block effectively reduced early pain after TKA surgery (p < 0.05) without increasing early rehabilitation complications. Finally, Abdullah et al. (53) evaluated that the addition of iPACK to the ACB significantly reduced postoperative opioid use (20.93 vs. 9.68; p < 0.001) and pain score
after surgery (p < 0.01) compared to the ACB alone without significant difference in movement ability (p > 0.05) in patients undergoing TKA.

On the other hand, Kampitek et al. (43) proved that IPACK combined with ACB and anterior cutaneous nerve block did not provide superior postoperative analgesia or improvement in immediate functional capacity but reduced opioid use compared to LIA alone (0.0 vs. 0.2; p = 0.008). Also, Tak et al. (54) found that CACB was associated with improved pain control (p < 0.05) and reduced opioid consumption (p < 0.05) in the postoperative period immediately after TKA compared with ACB alone or ACB with IPACK providing more efficient ambulation and rehabilitation.

The ACB has gained popularity due to its quadriceps muscle sparing. In addition, the iPACK blocks, like ACBs, have been described as providing analgesia and motor-sparing properties (55).

IPACK or PAI

iPACK and PAI supply the same innervation area of the knee joint. Therefore, they can be used interchangeably.

Some studies have attempted to combine motor-sparing iPACK block with PAI as mandatory multimodal analgesia for TKA. Vichainarong et al. (56), in their double-blinded randomized controlled trial, revealed that the addition of an iPACK block to the LIA and CACB did not improve the postoperative opioid use (p = 0.08) or analgesia but did improve immediate clinical performance and shorter hospital stay (p < 0.05). However, Kim et al. (57) assessed that IPACK and ACB dependence on LIA significantly improved post-TKA analgesia (p = 0.001) and opioid use (p = 0.005) compared to LIA alone. Further studies evaluating IPACK with LIA for TKA are now required.

Other studies have attempted to assess whether IPACK, or LIA are superior for pain relief, opioid use, and recovery from TKA. Kertkiatkachorn et al. (58) demonstrated that ACB with IPACK block provided non-inferior analgesia compared to PAI when with CACB (pain scores at movement −0.66 vs. -0.19). However, morphine requirements were significantly higher at 48 hours postoperative (p < 0.05), indicating a significant decrease in quadriceps strength at 0 and 45 degrees on postoperative day 0 (p = 0.006 and 0.04 respectively) in the ACB + IPACK group. On the other hand, Narejo et al. (59) compared LIA with IPACK block and revealed that after surgery (p < 0.01). No significant difference was seen at 24 or 48 hours. The timed up-and-go test lasted much longer for patients in the LIA group at 4, 24, and 48 hours compared to those in the IPACK group (p < 0.001; p < 0.01; p < 0.01).

IPACK and PAI are potent in reducing immediate postoperative pain in patients undergoing major knee surgery. However, IPACK may be better than PAI for acute pain control in patients after TKA.

Conclusions

As the population ages, the number of elderly patients undergoing TKA will increase. Optimal pain management is a crucial component of rapid recovery and hospital discharge. Multimodal pain
management is incorporated into most clinical pathways to facilitate early ambulation and improve patient comfort and satisfaction. Using multiple analgesic strategies such as IPACK and PAI as a motion-preserving block can improve patient recovery by promoting early postoperative ambulatory ability, improving pain scores, and reducing opioid use. Changing market conditions, such as expanding outpatient joint replacement centers, represent additional premiums for exercise-sparing pain relief and early ambulation.

For this reason, surgeon-administered PAI and anesthesiologist-administered IPACK have proven to be worth using. They can be viable alternatives to conventional peripheral nerve blocks. However, considering the presented studies, the best analgesic effect is obtained by combining PAI or iPACK with a peripheral nerve block, particularly with ACB, due to its analgesic, motor-sparing effect, and satisfactory analgesia. Both PAI and iPACK blocks are infiltration techniques. Unfortunately, PAI is associated with high volumes of local anesthetics, which carries the risk of a drug overdose, which may limit its use.

Nonetheless, the superiority of both approaches still needs to be determined. In addition, the optimal protocol for multimodal analgesia requires further investigation.

**Abbreviations**

TKA - Total knee arthroplasty

PAI - Periarticular injection

PNB - Peripheral nerve block

ADC - adductor canal block

CACB – continuous adductor canal block

FNB – femoral nerve block

LB – liposomal bupivacaine

ROM – range of motion

SSNB - selective sensory nerve blockade

CPN – peroneal nerve

TB – tibial nerve

**Declarations**

Ethics approval and consent to participate
Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

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Authors' contributions

MD – conception, design of work, acquisition, analysis, interpretation of data,

KWT – conception, design of work, acquisition, analysis, interpretation of data,

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MG - acquisition, analysis, interpretation of data

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References


28. Runge C, Jensen JM, Clemmesen L, Knudsen HB, Holm C, Børglum J, et al. Analgesia of combined femoral triangle and obturator nerve blockade is superior to local infiltration analgesia after total


38. Gudmundsdottir S, Franklin JL. Continuous adductor canal block added to local infiltration analgesia (LIA) after total knee arthroplasty has no additional benefits on pain and ambulation on postoperative day 1 and 2 compared with LIA alone: a randomized, double-blind, placebo-controlled trial with 69 patients. Acta Orthop. 2017;88(5):537–42.


40. Dysart SH, Barrington JW, Del Gaizo DJ, Sodhi N, Mont MA. Local infiltration analgesia with liposomal bupivacaine improves early outcomes after total knee arthroplasty: 24-hour data from the


61. Dannana C, Apsingi S, Ponnala V, Bollavaram V, Boyapati G, Eachempati K. Comparative study of the influence of adductor canal block plus multimodal periarticular infiltration versus combined adductor canal block, multimodal periarticular infiltration and intra-articular epidural catheter ropivacaine


Figures
Figure 1

Flow chart of the search for published reports showing the process of inclusion and exclusion. TKA, total knee arthroplasty.