

TOTAL KNEE ARTHROPLASTY (TKA)

SUMMARY RECOMMENDATIONS

Notes on PROSPECT recommendations

PROSPECT provides clinicians with supporting arguments for and against the use of various interventions in postoperative pain based on published evidence and expert opinion. Clinicians must make judgements based upon the clinical circumstances and local regulations. At all times, local prescribing information for the drugs referred to must be consulted.

Pain after TKA and aims of the PROSPECT review

TKA is a major orthopaedic procedure associated with significant postoperative pain that is difficult to treat, and which may lead to persistent pain in 15 to 20% of patients ([Grosu 2014](#); [Wylde 2018](#)). Effective pain control is essential for rehabilitation and to enhance recovery and long-term outcomes.

The aim of this PROSPECT review is to provide clinicians with recommendations for pain management after unilateral primary TKA, with particular attention to early rehabilitation and mobilisation.

This narrative review is based on published systematic reviews and meta-analyses, using modified PROSPECT methodology (details in the full publication: [Lavand'homme 2022](#)). It updates the previous review ([Fischer 2008](#)).

The PROSPECT approach is unique in that the available evidence is critically assessed for current clinical relevance, balanced with regards to the use of simple non-opioid analgesics, such as paracetamol and NSAIDs. This approach reports true clinical effectiveness by balancing the invasiveness of the analgesic interventions and the degree of pain after surgery, and also balancing efficacy and adverse effects. In addition, attention is paid to early rehabilitation and mobilisation.

Summary recommendations

Recommended: Pre- and intra-operative interventions

- ‘Pre-operative’ refers to interventions applied before surgical incision and ‘intra-operative’ refers to interventions applied after incision and before wound closure
- Analgesics should be administered at the appropriate time (pre- or intra-operatively) to provide sufficient analgesia in the early recovery period

Paracetamol and NSAIDs or COX-2-specific inhibitors

Paracetamol and NSAIDs or COX-2 specific inhibitors are recommended, administered either preoperatively or intra-operatively.

- The recommendation for **paracetamol** is based on evidence in TKA from two RCTs of paracetamol ([Murata-Ooiwa 2017](#); [O’Neal 2017](#)).
- A meta-analysis concluded that although paracetamol alone has limited analgesic and opioid-sparing efficacy, moderate evidence supports its use for peri-operative pain management after TKA ([Fillingham 2020](#)). It is a low-cost and low-risk option and it demonstrates an interesting opioid-sparing effect when combined with NSAIDs ([Martinez 2017](#); [Ong 2010](#)).
- Recommendations for **NSAIDs or COX-2 specific inhibitors** are based on evidence in TKA from six studies of COX-2 specific inhibitors, showing analgesic and opioid-sparing effects ([Zhu 2014](#); [Essex 2018](#); [Gong 2013](#); [Munteanu 2016](#); [Reynolds 2003](#); [Meunier 2007](#)).
- This is in agreement with the strong recommendation for NSAIDs and COX-2 specific inhibitors in a meta-analysis by [Fillingham 2020](#).
- COX-2-specific inhibitors possess similar analgesic efficacy to NSAIDs but with no effects on platelet function, and thus, could be administered preoperatively.
- A meta-analysis found that NSAIDs are unlikely to be the cause of postoperative bleeding complications ([Bongiovanni 2021](#)).
- No safety concerns were reported with NSAIDs and COX-2 specific inhibitors but prescribers need to remain vigilant as the typical older TKA population may be at a higher risk of adverse effects ([Fillingham 2020](#)).

Regional analgesia

Single shot adductor canal block (ACB) administered preoperatively and peri-articular local infiltration analgesia (LIA) administered intra-operatively are recommended. The combination of these two techniques is preferred.

- **ACB** demonstrates similar analgesic efficacy to FNB but seems to better preserve quadriceps function ([Kim 2014](#); [Grevstad 2015](#); [Memsoudis 2015](#); [Macrinici 2017](#)).
- As ACB have analgesic effects limited to the anteromedial aspect of the knee, leaving the lateral and posterior compartments untargeted, the use of complementary blocks, such as LIA is recommended.

	<ul style="list-style-type: none"> • LIA is an effective, simple and minimally-invasive analgesic technique, which should be considered as ‘basic’ analgesia in combination with paracetamol and NSAIDs/COX-2 specific inhibitors. • Overall, multiple meta-analyses demonstrated improved pain relief, reduced opioid requirements and earlier functional recovery with LIA compared with no injection or placebo (Andersen 2014; Xu 2014; Seangleulur 2016; Fang 2015; Zhang 2018). • LIA generally includes infiltration of different knee compartments with a cocktail consisting of local anaesthetic (typically, bupivacaine or ropivacaine) and one or more other drugs. However, the added benefit of drugs such as epinephrine or ketorolac is questionable. • The optimal site and volume for peri-articular administration of drugs remains unclear because of heterogeneity between the studies. • The NICE expert group reviewed evidence for best anaesthesia and analgesia techniques for knee replacement including costs involved with these techniques, and recommended LIA and peripheral nerve blocks (NICE guideline [NG157] 2020). • Continuous LIA or continuous intra-articular local anaesthetic infusion are not recommended because of inconsistent benefits and concerns of potential infection.
<p>Dexamethasone</p>	<p>Dexamethasone (≥ 10 mg, IV) is recommended, administered intra-operatively.</p> <ul style="list-style-type: none"> • The recommendation is based on three RCTs assessing a single preoperative dose of glucocorticoid (from 10 to 25 mg of dexamethasone equivalents) (Koh 2013; Xu 2018; Lunn 2011). These showed a reduction in pain, postoperative analgesic consumption and PONV, and no safety issues, even with concomitant use of paracetamol, NSAIDs/COX-2 specific inhibitors and LIA. • A single, intra-operative IV dexamethasone dose is simple, safe and effective with concomitant use of basic analgesics and LIA (Kehlet 2020). The optimal dose remains undetermined as the dose used in the different RCTs varied. • The safety of repeated doses of glucocorticoids to improve postoperative recovery remains questionable. • Although side effects of wound healing and infections are of potential concern, these have so far not been demonstrated, although more data are required in diabetic patients (Jørgensen 2017; Feeley 2021).

<p>Intrathecal morphine</p>	<p>Intrathecal morphine (100 µg) may be considered only in hospitalised patients when surgery is performed under spinal anaesthesia and in the rare situation wherein both ACB and LIA are not possible.</p> <ul style="list-style-type: none"> • Intrathecal morphine carries bothersome side effects (pruritus, nausea, urinary retention), which interfere with postoperative recovery (Tang 2017; Li 2016). • Although intrathecal morphine has been demonstrated to be more beneficial than placebo, it has not been shown to be superior to regional analgesic techniques (peripheral nerve blocks and LIA) (Sites 2004; Frassanito 2010; Olive 2015; Tarkkila 1998; Qi 2020). Interpretation of studies is hindered as most did not use LIA and had a variable use of basic analgesics. • Intrathecal morphine is not suitable for ambulatory TKA because of potential concerns of respiratory depression, albeit remote.
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ACB, adductor canal block; COX, cyclooxygenase; IV, intravenous; LIA, local infiltration analgesia; NSAIDs, non-steroidal anti-inflammatory drugs; PONV, postoperative nausea and vomiting; RCT, randomised controlled trial; TKA, total knee arthroplasty.

<p>Recommended: Postoperative interventions</p> <p>‘Postoperative’ refers to interventions applied at or after wound closure</p> <p>Analgesics should be administered at the appropriate time (pre- or intra-operatively) to provide sufficient analgesia in the early recovery period</p>	
<p>Paracetamol, NSAIDs, COX-2-specific inhibitors</p>	<p>Paracetamol and NSAIDs or COX-2 specific inhibitors are recommended.</p>
<p>Opioid</p>	<p>Opioids should be reserved as rescue analgesics in the postoperative period.</p>

COX, cyclooxygenase; NSAIDs, non-steroidal anti-inflammatory drugs.

Interventions that are NOT recommended

Analgesic interventions that are not recommended for pain management following primary TKA.

Intervention	Reason for not recommending
Gabapentinoids	Minimal analgesic and opioid-sparing effects and concerns of potential adverse effects, particularly when combined with postoperative opioids, which are typically high for total knee arthroplasty
Ketamine	Conflicting evidence
Dexmedetomidine	Inconsistent evidence
Epidural analgesia	Potential adverse effects precluding rapid recovery
Femoral nerve block	Negative impact on functional recovery
Sciatic nerve block	Negative impact on functional recovery

IV, intravenous; TENS, transcutaneous electrical nerve stimulation.

Overall PROSPECT recommendations

Overall recommendations for pain management following primary TKA

Pre-operative and intra-operative interventions	<ul style="list-style-type: none"> • Paracetamol and NSAIDs or COX-2 specific inhibitors, administered either pre-operatively or intra-operatively • Single shot adductor canal block administered pre-operatively and peri-articular local infiltration analgesia administered intra-operatively. Combination of these two techniques is preferred • Dexamethasone (≥ 10 mg, IV) administered intra-operatively • Intrathecal morphine (100 μg) may be considered only in hospitalised patients when surgery is performed under spinal anaesthesia and in the rare situation wherein both adductor canal block and local infiltration analgesia are not possible
Postoperative interventions	<ul style="list-style-type: none"> • Paracetamol and NSAIDs or COX-2 specific inhibitors • Opioids should be reserved as rescue analgesics

COX, cyclooxygenase; IV, intravenously, NSAIDs, non-steroidal anti-inflammatory drugs.

PROSPECT publication

Pain management after total knee arthroplasty: PROcedure SPECific Postoperative Pain Management recommendations.

Patricia M Lavand'homme, Henrik Kehlet, Narinder Rawal, Girish P Joshi, PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy (ESRA).

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