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Guidelines

PROSPECT guideline for total hip arthroplasty: a systematic review and procedure-specific postoperative pain management recommendations

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Summary

The aim of this systematic review was to develop recommendations for the management of postoperative pain after primary elective total hip arthroplasty, updating the previous procedure-specific postoperative pain management (PROSPECT) guidelines published in 2005 and updated in July 2010. Randomised controlled trials and meta-analyses published between July 2010 and December 2019 assessing postoperative pain using analgesic, anaesthetic, surgical or other interventions were identified from MEDLINE, Embase and Cochrane databases. Five hundred and twenty studies were initially identified, of which 108 randomised trials and 21 meta-analyses met the inclusion criteria. Peri-operative interventions that improved postoperative pain include: paracetamol; cyclo-oxygenase-2-selective inhibitors; non-steroidal anti-inflammatory drugs; and intravenous dexamethasone. In addition, peripheral nerve blocks (femoral nerve block; lumbar plexus block; fascia iliaca block), single-shot local infiltration analgesia, intrathecal morphine and epidural analgesia also improved pain. Limited or inconsistent evidence was found for all other approaches evaluated. Surgical and anaesthetic techniques appear to have a minor impact on postoperative pain, and thus their choice should be based on criteria other than pain. In summary, the analgesic regimen for total hip arthroplasty should include pre-operative or intra-operative paracetamol and cyclo-oxygenase-2-selective inhibitors or non-steroidal anti-inflammatory drugs, continued postoperatively with opioids used as rescue analgesics. In addition, intra-operative intravenous dexamethasone 8–10 mg is recommended. Regional analgesic techniques such as fascia iliaca block or local infiltration analgesia are recommended, especially if there are contra-indications to basic analgesics and/or in patients with high expected postoperative pain. Epidural analgesia, femoral nerve block, lumbar plexus block and gabapentinoid administration are not recommended as the adverse effects outweigh the benefits. Although intrathecal morphine 0.1 mg can be used, the PROSPECT group emphasises the risks and side-effects associated with its use and provides evidence that adequate analgesia may be achieved with basic analgesics and regional techniques without intrathecal morphine.

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Recommendations

1 Pre-operative exercise and education are recommended.
2 The basic analgesic regimen should include a combination of paracetamol and a non-steroidal anti-inflammatory drug or a cyclo-oxygenase-2-selective inhibitor administered pre-operatively or intra-operatively and continued postoperatively.
3 Spinal or general anaesthesia is recommended.
4 A single intra-operative dose of intravenous dexamethasone 8–10 mg is recommended for its analgesic and anti-emetic effects.
5 A single-shot fascia iliaca block or local infiltration analgesia is recommended.
6 If the patient has received spinal anaesthesia for the surgery, intrathecal morphine 0.1 mg could be considered.
7 Opioids should be reserved as rescue analgesics in the postoperative period.

Why was this guideline developed?

Total hip arthroplasty is a common surgical procedure and is associated with significant postoperative pain. Pain control can facilitate early postoperative rehabilitation, which is being increasingly encouraged in recent guidelines. The aim of this guideline is to provide clinicians with an updated evidence-based approach to pain management for elective total hip arthroplasty.

What other guidelines are available on this topic?

Several guidelines have been published assessing peri-operative care in total hip arthroplasty. However, some are focused on enhanced recovery after surgery or anaesthetic technique, and those specifically assessing peri-operative pain management focus on the efficacy of single interventions, broad techniques (e.g. regional analgesic techniques) or specific opioid-sparing strategies.

How does this guideline differ from other guidelines?

The present guideline applies the updated procedure-specific postoperative pain management (PROSPECT) methodology that critically evaluates the available literature. It considers the analgesic benefit of interventions against the backdrop of basic analgesics (i.e. paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 (COX-2)-selective inhibitors) and balances the procedure-specific efficacy and benefits of an intervention against its general risks and invasiveness. In that sense, it is more clinically applicable and pragmatic than statistical analysis used in meta-analyses, as well as focused on pain rather than overall enhanced recovery after surgery (ERAS) pathways or anaesthetic techniques.

Introduction

Total hip arthroplasty is a common surgical procedure aiming to improve mobility and quality of life in patients suffering from hip pain [1]. Adequate analgesia with minimal side-effects allows for early postoperative mobility, optimal functional recovery and decreased postoperative morbidity [2]. Despite being a frequently performed surgical procedure, there is high variability in the peri-operative anaesthetic and analgesic management for total hip arthroplasty [3, 4]. Recent guidelines have focused on ERAS [4] or anaesthetic technique [5] and those specifically assessing peri-operative pain management do not address all possible analgesic interventions in a single document [6, 7]. Also, for some recommendations [3–7] a detailed approach to the systematic review of literature is not provided, and lacks scientific discussion on the design of included randomised controlled trials, such as the efficacy when evidence-based basic simple analgesia had been included as active comparators [2]. One guideline is not updated [6].

The PROSPECT Working Group is a global collaboration of surgeons and anaesthetists formulating procedure-specific recommendations for pain

management after common but potentially painful operations [8]. The recommendations are based on a procedure-specific systematic literature review of randomised controlled trials and systematic reviews. The methodology also considers clinical practice, efficacy and adverse effects of analgesic drugs and techniques in order to provide overall recommendations [9].

The PROSPECT group has previously published a review on total hip arthroplasty in 2005 [10] that was updated in 2010 [11]. Of note, the previous update included the literature search from 1966 to July 2010 [11]. The aim of the present systematic review was to update the 2010 recommendations using the recently modified PROSPECT methodology [9], focusing on postoperative pain outcomes while assessing the effects of analgesic interventions in reference to the use of basic analgesics (paracetamol and NSAIDs or COX-2-selective inhibitors) and balancing risks and benefits of analgesic strategies.

Methods

The methods of this review adhered to the PROSPECT methodology as previously reported [9]. Specific to this study, the Embase, MEDLINE, PubMed and Cochrane Databases were searched for randomised controlled trials published between July 2010 and December 2019. The search terms related to pain and total hip arthroplasty included: "replacement" OR "prosthesis" OR "arthroplasty" AND "hip" AND "postoperative pain" OR "pain" OR "pain scale" or "rehabilitation" OR " pain management" OR "epidural" OR "spinal" OR "intrathecal anaesthesia" OR "peripheral nerve block" OR "nerve block" OR "local anaesthetics" OR "regional anaesthesia" OR "regional analgesia" OR "plexus block" OR "nerve block" OR "infiltration" OR "local infiltration analgesia" OR "lidocaine" OR "nonsteroidal anti-inflammatory drugs (NSAIDs)" OR "NSAIDs" OR "non-opioid analgesic" OR "opioid" OR "opioids" OR "dexamethasone" OR "gabapentin" OR "pregabalin" OR "ketamine" OR "paracetamol" OR "acetaminophen" OR "nefopam" OR "COX 2 selective inhibitor" OR "COX 2 inhibitor" OR "clonidine". We excluded any studies on acute hip fracture.

Only studies reporting either pain scores (verbal or numerical) or opioid consumption were included [9]. Systematic reviews and meta-analyses, when available, were used to check for studies not identified in our database search. Quality assessment of eligible studies was made according to PROSPECT methodology [9]. In brief, this involved a grading of allocation concealment (A–D); Jadad score (1–5); adequacy of statistical reporting (yes or no); and level of evidence (1–4). In the present report, we defined a change of more than 10 mm on the visual analogue scale (VAS) or one point on a numerical rating score as clinically relevant [12]. Also statistically significant differences in analgesic opioid rescue medication or in opioid induced side-effects were used as valid outcomes.

For recommending an analgesic, at least two randomised controlled trials have to show efficacy. In addition, the efficacy of the analgesic intervention over the use of basic analgesics (paracetamol and NSAIDs or COX-2-selective inhibitors) was also considered. Furthermore, adverse effects and clinical aspects were evaluated. A subgroup developed draft recommendations, which were then circulated amongst all the members for review and comments. A modified Delphi approach was utilised as previously described [9]. This included obtaining feedback from PROSPECT members via email, followed by revised drafts of recommendations. This was followed by face-to-face discussions with the aim of developing a consensus. For conflicting recommendations, members voted via email. Once the members had opined, the lead authors drafted the final manuscript, which was ultimately approved by the full PROSPECT group.

Results

A total of 108 randomised controlled trials and 21 meta-analyses were included for the final qualitative analysis (Fig. 1). Summary recommendations on analgesic interventions are given in Table 1 and interventions that are not recommended are listed in Table 2. The methodological quality assessments of the randomised controlled trials are summarised in online Supporting Information Table S1. The characteristics of the included studies are shown in online Supporting Information Tables S2 and S3.

Pre-operative interventions

A single study assessed the effects of carbohydrate loading on postoperative pain and fatigue in hip arthroplasty patients [13], demonstrating a significant reduction of postoperative pain for the first 20 h following surgery. In a study by Goyal et al., the effect of management status (i.e. inpatient vs. day-case total hip arthroplasty) with similar postoperative analgesic protocols was considered [14]. Postoperative pain was significantly lower in day-case patients but this was not clinically significant. Pre-operative exercise and education were both found to be beneficial in reducing postoperative pain and improving functional outcomes in a meta-analysis conducted by Moyer et al. [15].

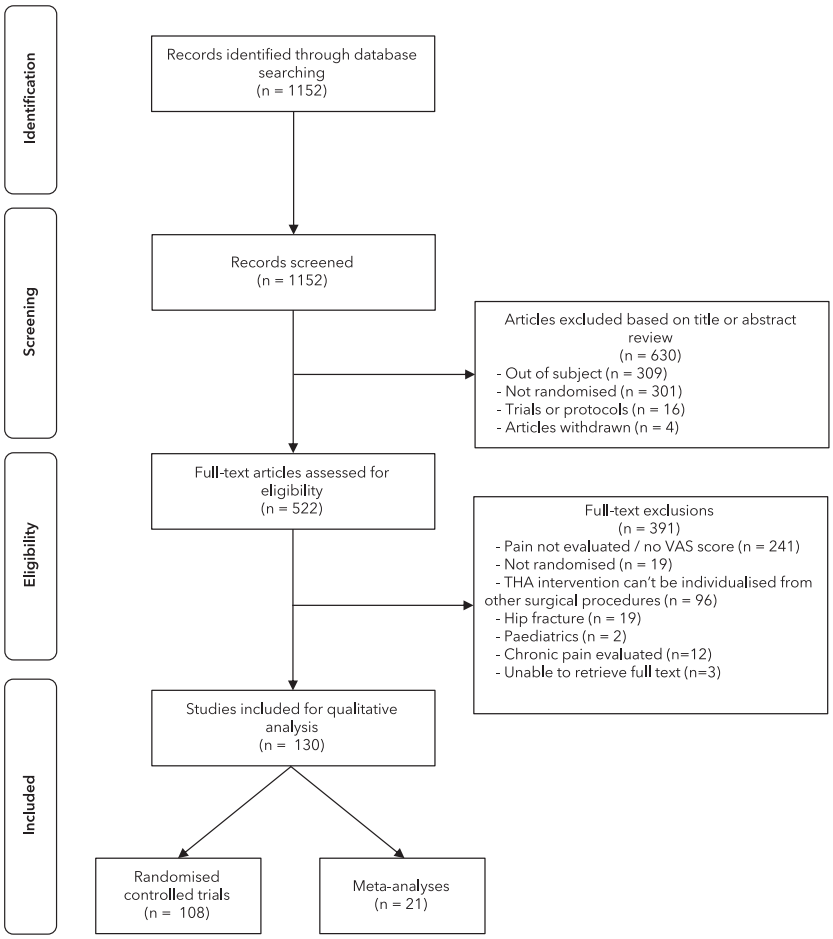

Figure 1 Flow diagram of studies identified, screened and included in this systematic review. VAS, visual analogue scale.

Table 1 Overall recommendations for pain management in patients undergoing total hip arthroplasty.

Pre-operative and intra-operative
Pre-operative exercise and education (Grade A)
General or spinal anaesthesia (Grade A)
Paracetamol (Grade A)
Non-steroidal anti-inflammatory drugs or cyclo-oxygenase-2-selective inhibitors (Grade A)
Dexamethasone 8–10 mg i.v. (Grade A)
Single-shot fascia iliaca block or local infiltration analgesia (Grade D)
If the patient has received spinal anaesthesia for the surgery, intrathecal morphine 0.1 mg could be considered (Grade D)
Postoperative
Paracetamol (Grade A)
Non-steroidal anti-inflammatory drugs or cyclo-oxygenase-2-selective inhibitors (Grade A)
Opioid for rescue (Grade D)

Basic systemic non-opioid analgesics

Intravenous (i.v.) paracetamol was compared with placebo in two studies [16, 17], which showed lower pain intensity scores over the first 24 h and lower morphine consumption in the paracetamol groups. Westrich et al. [18] found no difference between i.v. vs. oral administration of paracetamol on postoperative pain outcomes. Paracetamol, anti-inflammatory drugs and placebo were recently compared in two studies. When taken individually, both drugs improved postoperative pain outcomes, whereas parecoxib plus paracetamol did not improve pain scores over parecoxib alone in one study [19], and paracetamol combined with ibuprofen did not result in a clinically relevant improvement over ibuprofen alone [20]. This suggests a limited impact of paracetamol when added to a regimen including COX-2-selective inhibitors or NSAIDs, but paracetamol is recommended as part of basic postoperative analgesia in general, due to minor

Table 2 Analgesic interventions that are not recommended for pain management in patients undergoing total hip arthroplasty.

	Intervention	Reason for not recommending
Pre-operative or intra-operative	Carbohydrate loading	Limited procedure-specific evidence
	Outpatient status	Limited procedure-specific evidence
	Pre-incisional COX-2-selective inhibitor vs. post-incisional	Limited procedure-specific evidence
	Gabapentinoids	Inconsistent evidence for single-dose. Procedure-specific evidence for multiple peri-operative doses, but extra side-effects
	Ketamine	Limited procedure-specific evidence
	Lateral femoral cutaneous block	Limited procedure-specific evidence
	Anterior quadratus lumborum block	Limited procedure-specific evidence
	Femoral nerve block	Procedure-specific evidence, but side-effects
	Lumbar plexus block	Procedure-specific evidence, but side-effects
	LIA adjuncts to local anaesthesia drugs	Inconsistent procedure-specific evidence
	LIA infusion or repeated injections	Inconsistent procedure-specific evidence
	Epidural analgesia	Procedure-specific evidence, but side-effects
Postoperative	Tranexamic acid	Lack of procedure-specific evidence
	Partial weight bearing	Lack of procedure-specific evidence
	Topical fibrin sealant	Lack of procedure-specific evidence
	TENS	Limited procedure-specific evidence
Surgical technique	Anterior approach vs. posterolateral approach	Inconsistent procedure-specific evidence
	Minimally invasive vs. traditional incision	Inconsistent procedure-specific evidence, increased risks

LIA, local infiltration analgesia; TENS, transcutaneous electrical nerve stimulation.

side-effects. Finally, a single study compared i.v. paracetamol with i.v. metamizole and found clinically insignificant reductions in morphine consumption and pain scores with metamizole [21], although pain scores in both groups were always lower than 40 mm on a VAS.

Three studies showed analgesic benefit of NSAID administration [22–24]. Regular i.v. diclofenac and orphenadrine infusions after surgery and at 12 h reduced morphine patient-controlled analgesia (PCA) consumption postoperatively [22]. McQuay et al. [23] showed that a combination of oral dexketoprofen 25 mg with tramadol 75 mg was superior to both medications alone for postoperative pain control. In a three-group study, ketorolac improved pain scores and morphine consumption compared with a novel protein kinase C-epsilon inhibitor and placebo [24].

Four studies [25–28] specifically assessed controlling postoperative pain with pre-incisional COX-2-selective inhibitor administration. Two studies found that oral etoricoxib 2 h before surgery [26], or i.v. parecoxib or oral celecoxib 1 h before surgery [27] were associated with significantly lower postoperative pain scores and morphine consumption when compared with placebo. These benefits were not found in another study with a 30-min pre-incisional i.v. parecoxib infusion [28]. Moreover, one study directly compared 30-min pre- vs. 30-min post-incisional i.v. 40 mg parecoxib administration [25] and found lower pain scores up to 6 h postoperatively and lower morphine consumption up to 24 h postoperatively with a pre-incisional protocol.

In conclusion, and in keeping with the PROSPECT basic analgesia recommendation [9], the administration of paracetamol in combination with NSAID or COX-2-selective inhibitors is recommended for total hip arthroplasty patients unless contraindicated. There is insufficient evidence to determine whether pre-operative COX-2 administration has an advantage over postoperative COX-2 administration. There is no procedure-specific evidence to choose a specific NSAID or COX-2-selective inhibitor.

Analgesic non-opioid adjuncts

Six studies showed a benefit on postoperative pain outcomes with glucocorticoid use [29–34]. Peri-operative 125 mg methylprednisolone compared with placebo reduced 24-h pain scores [31]. A second study showed analgesic benefit from 20 mg prednisolone pre-operatively followed by two postoperative doses of i.v. hydrocortisone

administered 8 h apart in patients with patient-controlled epidural analgesia, while pain scores did not differ [30]. Backes et al. [29] demonstrated that 10 mg of peri-operative dexamethasone had a significant effect, reducing mean VAS pain scores by > 20 mm, reducing opioid consumption in the first 24 h, with early ambulation and a shorter length of hospital stay. An additional dose of 10 mg dexamethasone at the postoperative 24-h mark showed continued effect, with lower morphine consumption on day two and a shorter length of stay when compared with a single dose. The efficacy of dexamethasone was demonstrated on top of adequate basic analgesia [32–34] showing improved postoperative pain outcomes with 8 or 10 mg, a lower incidence of postoperative nausea and vomiting and a shorter length of stay. Three meta-analyses showed benefits from glucocorticoids use on postoperative pain outcomes; time to discharge; and postoperative nausea and vomiting [35–37]; No major adverse events were described in these studies, other than a small but significant increase in blood glucose concentration in diabetic patients when dexamethasone was used [29,32]. The occurrence of postoperative infection did not differ [34, 35].

When considering gabapentinoids as the sole intervention, Paul et al. found no analgesic benefit when gabapentin 600 mg was administered pre-operatively followed up by a regimen of 200 mg three times daily for 3 days postoperatively [38]. However, Clarke et al. showed effectiveness of pre-operative pregabalin 150 mg administration continued postoperatively when added to a basic analgesic regimen of celecoxib and morphine PCA [39]. Carmichael et al. [40] investigated the combination of celecoxib and pregabalin (75 mg twice daily) for 2 weeks preceding and 3 weeks following surgery and found that patients in the treatment group experienced less acute pain on postoperative day one. However, morphine consumption did not differ, and there were more side-effects in the pregabalin-celecoxib group. The three meta-analyses included assessing the efficacy of gabapentin or pregabalin [41–43] in total hip arthroplasty found morphine-sparing effects, but reported side-effects such as dizziness, and were inconsistent regarding pain reduction. In conclusion, repeated doses of peri-operative gabapentinoids show evidence of pain reduction but are not recommended as routine medication due to clinically relevant side-effects.

The efficacy of intra-operative ketamine vs. pregabalin was compared in a four-group study consisting of ketamine alone, pregabalin alone, a combination of pregabalin and ketamine or placebo [44]. However, no basic analgesia was used. Both ketamine and pregabalin significantly reduced 48-h morphine consumption with no difference in pain scores and side-effects (nausea; pruritus; dizziness). This sole study is insufficient evidence to recommend peri-operative ketamine or single-dose pregabalin.

Anaesthetic technique

The PROSPECT Group has previously recommended that the anaesthetic technique should not be selected solely for its effects on postoperative pain or opioid consumption [11]. However, three studies examining the effect of choice of anaesthetic technique are included in this review. General anaesthesia with a total i.v. anaesthesia approach was compared with spinal anaesthesia in a 120-patient study using adequate basic analgesia [45]. Results showed that patients receiving general anaesthesia had significantly higher pain scores during the first 2 postoperative hours but lower after 6 h compared with the spinal anaesthesia group. A second study [46] showed lower VAS pain scores and morphine consumption up to 24 h postoperatively with spinal or epidural vs. general anaesthesia but adequate basic analgesia was not used. Mei et al. investigated the efficacy of dexmedetomidine or propofol as sedatives in addition to regional anaesthesia and found no difference in pain outcomes, but a lower risk of delirium in the dexmedetomidine group [47]. In a recent meta-analysis, Yang et al. [48] showed significantly less pain when dexmedetomidine was part of the anaesthetic protocol. However, the reduction in pain in the studies on total hip arthroplasty was small, and bradycardia was reported as a significant and frequent side-effect with dexmedetomidine.

In conclusion, there is insufficient evidence to support a specific anaesthetic technique in favour of another in terms of postoperative analgesic benefits, although spinal anaesthesia may positively influence other postoperative outcomes when compared with general anaesthesia [5].

Peripheral nerve block

Single-shot peripheral nerve blocks have previously been recommended by the PROSPECT Group for total hip arthroplasty without further specification regarding the type of blocks [11]. Twenty-six new studies were available for review on this topic: 22 randomised controlled trials and four meta-analyses. The interventions studied were: femoral nerve block; lumbar plexus block; psoas compartment block; fascia iliaca block; lateral femoral cutaneous nerve block; and anterior quadratus lumborum block.

Six studies [49–54] assessed femoral nerve block for postoperative analgesia. When compared with no block with adequate basic analgesia, Kratz et al. showed that single-shot femoral nerve block significantly improved pain scores and reduced analgesic consumption, despite a high dropout rate [52]. In another study, patients receiving a femoral nerve block met earlier post-anaesthesia care unit (PACU) discharge criteria, with lower pain scores and analgesic consumption [51]. Continuous femoral nerve block was also compared with lumbar plexus block [49] and with epidural analgesia [54]. Similar pain and analgesic requirements were reported. When femoral nerve block was compared with fascia iliaca block, pain scores were higher in the femoral nerve block group (but only by 5 mm with both groups being < 15 mm on the VAS) [50]. Kuchalik et al. [53] showed that femoral nerve block proved inferior to local infiltration analgesia (LIA) for the first 24 postoperative hours on pain scores and morphine consumption, and with significantly more motor blockade in femoral nerve block group.

Fascia iliaca block was evaluated in six studies [55–60]. Shariat et al. [55] used fascia iliaca block as rescue analgesia in PACU, reporting that it did not improve pain scores or morphine consumption vs. placebo. However, another study showed clinically relevant significantly lower morphine consumption at 24 and 48 h with a fascia iliaca block compared with no block on top of multimodal basic analgesia [56]. Comparing fascia iliaca block with alternative anaesthetic techniques, Kearns et al. [57] showed that morphine consumption was higher with fascia iliaca block when compared with 0.1 mg intrathecal morphine, with no difference in pain scores or side-effects apart from 2 h shorter time to mobilisation in the fascia iliaca block group. Perry et al. [60] found similar data between fascia iliaca block and psoas compartment block. When compared with LIA [58, 59], postoperative pain outcomes did not differ; however the fascia iliaca block group showed more muscle weakness at 6 h in one study [58]. Finally, three recent meta-analyses [61–63], combining the existing data, all concluded that there was lower pain scores, lower morphine consumption and even shorter length of stay when fascia iliaca block was used, with no greater risk of falls [61].

Thybo et al. performed two studies on lateral femoral cutaneous block compared with placebo with adequate baseline multimodal analgesia [64, 65]. One study did not show any difference in pain scores [65], the other showed that lateral femoral cutaneous block reduced movement-related pain [64]. A double nerve block of lateral femoral cutaneous block and subcostal nerves via infiltration had no effect on postoperative pain outcomes over placebo in a report from Bron et al. [66].

Six studies evaluated lumbar plexus block [67–72]. When compared with LIA [67, 68], lumbar plexus block did not show any benefit on postoperative pain and opioid consumption. Local infiltration analgesia had lower pain scores at 3 h postoperatively in one study [67]. Continuous lumbar plexus block was compared with paravertebral block performed at L2 by Wardhan et al. [70]. Morphine consumption during the first 24 h was higher in the paravertebral block group, but pain scores were similar. When lumbar plexus block was compared with 0.1 mg intrathecal morphine [72], patients in the latter group required less intra-operative opioids, less rescue morphine and had lower pain scores in PACU. However, they needed more rescue morphine in the subsequent 24 h and experienced increased pruritus. Also, ropivacaine 0.1% and 0.2% continuous lumbar plexus block have been compared [71], which demonstrated similar pain outcomes and motor block intensity. Lastly, Green et al. [69] considered an intra-operative, surgeon-delivered psoas compartment block performed during total hip arthroplasty vs. no block. Psoas compartment block prolonged the time to first request of rescue analgesia and reduced postoperative pain scores.

One study evaluated an anterior quadratus lumborum block compared with no block [73]. Patients in the treatment group showed lower morphine consumption and lower pain scores at 24 h, but not at other time-points.

In conclusion, femoral nerve block, lumbar plexus block, psoas compartment block, quadratus lumborum block and fascia iliaca block lowered postoperative pain scores and morphine consumption, whereas lateral femoral cutaneous block did not. At the time of our search, we only found one randomised controlled trial on quadratus lumborum block. The lumbar plexus block is a deep block with potential risks [74] and the femoral nerve block has a significant incidence of muscle weakness [74, 75], and are thus not recommended. The potential benefit of nerve blocks on postoperative pain should be balanced against the side-effects, such as delayed mobilisation, motor block or risk of falls. In recent meta-analyses, no more falls were reported with fascia iliaca block [61, 62], which is recommended as the preferred nerve block when a nerve block is indicated for total hip arthroplasty.

Local infiltration analgesia

Local infiltration analgesia was not part of previous PROSPECT recommendations, primarily due to inadequate

evidence. For the present review, single-injection LIA was directly compared with placebo or no injection in 15 randomised controlled trials [76–90]. Of these, five placebo-controlled randomised controlled trials showed lower pain scores, opioid consumption or shorter length of stay [83, 84, 86, 87, 89]. When compared with no injection, Busch et al. [85] showed significantly lower pain scores and morphine consumption, but basic analgesia was not used. Villatte et al. [88] reported a difference in pain scores, but this was not clinically meaningful. Another seven randomised controlled trials in which LIA was combined with adequate basic analgesia failed to show improvements in pain control [76–82]. In the meta-analyses of Ma et al., LIA resulted in significant benefits during the first 24 h in terms of less pain at rest and during movement, and a reduction in opioid consumption [92]. When bupivacaine was compared with liposomal bupivacaine for LIA, there were similar pain outcomes [93].

Two studies assessing multiple doses or continuous infusion of LIA compared with placebo [94, 95] found improved postoperative pain scores and morphine consumption at 48–72 h with a pericapsular infusion via a catheter. However, a systemic effect of local anaesthesia cannot be ruled out, and three studies with a similar design failed to show any benefit [96–98].

When comparing a multimodal pain regimen containing LIA and patient-controlled epidural analgesia, pain scores during movement favoured the epidural group. However, for the primary outcome of readiness for hospital discharge, there was no difference [99]. In a three-group study [100] comparing a multi-drug LIA regimen, morphine PCA and epidural analgesia, patients with LIA reported reduced pain scores and morphine consumption compared with those receiving morphine PCA. No difference was observed when compared with epidural. Yan et al. [101] compared LIA with epidural in a meta-analysis of nine studies and found no significant difference between the LIA and the epidural group 48–72 h after surgery for pain with movement, but less pain at 24 h in the epidural group [101].

Two studies compared LIA with intrathecal morphine 0.1 mg [102, 103]. One study [102], found no differences in pain scores or postoperative nausea and vomiting. Although patients in the LIA group required more rescue oxycodone, they mobilised better at 6 h after surgery as well as the following morning [102]. The second study [103] showed that intrathecal morphine was more effective in the first 24 h compared with multi-drug LIA, but patients in this group had higher morphine consumption after 24 h and experienced more postoperative nausea and vomiting and pruritus.

Three meta-analyses [104–106] indicated that multi-drug LIA had lower postoperative pain scores, lower opioid consumption and in one meta-analyses a shorter length of hospital stay [105]. Comparing LIA, peripheral nerve block and placebo in a network meta-analysis [107] including 35 randomised controlled trials and 2296 patients, the LIA treatment group had lower postoperative pain scores and opioid consumption at 24 h vs. placebo, whereas peripheral nerve block failed to do the same. However, there was no difference between peripheral nerve block and LIA on these outcomes. In conclusion, single-injection LIA has analgesic effect with no side-effects.

Epidural analgesia

Epidural levobupivacaine with sufentanil adjuvant was compared with oral controlled-release oxycodone [108]. Epidural analgesia provided better dynamic pain relief (mean VAS reduction from 3.0 to 1.7 on a 0–10 scale) and lower opioid consumption on day one postoperatively. However, oral oxycodone was more effective on pain control at rest on postoperative days two and three. The modest differences in pain reduces the impact of these results.

Adjuvant epidural therapies were addressed in three studies [109–111]. The following had beneficial effects on postoperative pain outcomes: 8 mg epidural dexamethasone [110], 75 mg epidural magnesium [109] and epidural ketamine [109, 111]; however, adequate basic analgesia was not used in these studies.

In conclusion, epidural analgesia is effective, but is not recommended due to well-recognised side-effects in lower limb surgery, such as limb weakness, bladder dysfunction and delayed mobilisation [112].

Spinal analgesia

Seven studies [58, 73, 102, 103, 113–115] evaluated the effectiveness of adding intrathecal analgesia for postoperative pain after total hip arthroplasty. Comparison of intrathecal morphine to peripheral nerve block [58, 73] or LIA [102, 103] is discussed in previous paragraphs. Evaluating intrathecal morphine doses of 0.05 mg vs. 0.1 mg showed that patients receiving 0.1 mg had lower pain scores and a longer duration of analgesia [113] but use of basic analgesia was not reported. Similar postoperative nausea and vomiting frequency was found in both groups, but patients receiving the higher dose experienced pruritus more often.

Intrathecal adjuvants have also been evaluated in two other studies [114, 115]. Intrathecal ketorolac 2 mg showed no benefit on postoperative pain outcomes [114] but intrathecal or i.v. magnesium lowered pain scores and 24-h morphine consumption vs. no adjuvants [115].

In conclusion, when spinal anaesthesia is used for surgery, there is evidence for analgesic effect of intrathecal morphine 0.1 mg, which could be considered.

Operative techniques

We included 16 randomised controlled trials and three meta-analyses comparing surgical techniques. These interventions include drains [116–119]; different conventional surgical approaches [120–124]; and minimally invasive approaches to hip arthroplasty [125–133]. Pain was a secondary outcome in most of these studies, and a basic analgesic regimen was often inadequate or not specified. Considering the use of postoperative drains vs. no drains, pain scores were similar in both groups [116–118], but one study reported higher pain scores in the patients with a drain [119]. Thus, drains are not recommended to improve pain outcomes.

Comparing the direct anterior surgical approach with the posterolateral approach, three studies [120–122] found lower pain scores with the direct anterior surgical approach on the first postoperative day, but with less than 10-mm difference on the VAS. Pooling these results and others, a meta-analysis by Wang et al. [123], confirmed direct anterior surgical approach to be associated with less postoperative pain than a posterolateral approach to total hip arthroplasty, but was associated with a longer duration of surgery. Putananon et al. [124], showed that, despite experiencing lower postoperative pain with a lateral vs. anterior vs. posterior approach, surgical complications were seen more frequently in the same order, respectively.

Three studies supported improved postoperative pain outcomes with a minimally invasive operative approach vs. conventional approach [125, 126, 132], but surgical complications were more frequent in the minimally invasive approach group in one study [132]. However, five other studies did not show any difference on postoperative pain outcomes, comparing a minimally invasive approach to a conventional approach [127–130, 133]. Finally, a meta-analysis of 2849 patients [131] showed a clinically insignificant benefit on pain scores with the minimally invasive approach, but with a five-fold higher risk of iatrogenic nerve damage in this group when compared with a conventional approach.

One study showed similar pain scores and morphine consumption comparing a bipolar sealer and standard electrocautery [134].

In conclusion, there is inconclusive evidence in terms of postoperative pain for choosing a specific surgical approach. Thus, surgical technique should depend on surgeon and patient preference.

Postoperative interventions

Four studies evaluated postoperative opioid administration [135–138]. Rothwell et al. showed that PCA with i.v. morphine had no benefits over oral oxycodone [135]. One study found no differences in pain scores between i.v. morphine vs. a combination of i.v. oxycodone and morphine [137]; while i.v. fentanyl showed lower pain scores and lower morphine consumptions than i.v. oxycodone [138]. Lastly, Musclow et al. examined the effectiveness of adding 30 mg oral modified-release morphine every 12 h to a paracetamol/NSAIDs/morphine PCA regimen vs. placebo. Modified-release morphine did not prove effective on pain scores but was associated with significantly more opioid-related side-effects [136].

Analgesic effects of several other postoperative interventions have been examined. There were no clinical differences in pain outcomes between partial weight-bearing compared with full weight-bearing after cementless total hip arthroplasty [139]. Further, dressing type [140] or topical administration of fibrin sealant [141] did not make any difference. A single study [142] examining transcutaneous electrical nerve stimulation showed a reduction on postoperative fentanyl consumption at 24 h, but no effect on pain scores. Despite a reduction in blood loss, tranexamic acid administration proved inconsistent on improving pain outcomes [143, 144].

Discussion

This systematic review of total hip arthroplasty examined the effects of peri-operative analgesic, anaesthetic and surgical techniques, as well as other interventions, on postoperative pain. The updated recommendations are presented in Table 1. The strength of this study stems from the PROSPECT methodology [9], which goes beyond making recommendations based on the simple statistical analysis of the available evidence. The included studies are interpreted preferably based on the use of basic analgesics (paracetamol with NSAIDs or COX-2-selective inhibitors) and balancing the benefits and adverse effects of the intervention, as well as assimilating this information in a clinical context. More importantly, significant attention is given to the modern approach of early ambulation after total hip arthroplasty as well as performance of total hip arthroplasty on a short-stay or day-case basis. Furthermore, the changes in surgical

techniques, which have allowed for reduced postoperative pain and more rapid recovery, are also considered.

We would like to emphasise that the previous literature searches were performed between 1966 and July 2010, while this one is performed between July 2010 and December 2019. Of note, the databases searched and the inclusion criteria for the reviews are identical, although the PROSPECT methodology of interpretation of included studies has changed.

There are significant differences between these updated recommendations and our previous recommendations [11]. For example, previously recommended approaches such as femoral nerve block, lumbar plexus block and epidural analgesia are no longer recommended due to the availability of evidence supporting better and safer alternatives such as fascia iliaca block and LIA. In fact, even in the previous recommendation it was emphasised that lumbar plexus block provides superior pain relief to femoral nerve block, and that femoral nerve block may have negative effects on postoperative ambulation [11].

Previously [11] LIA was not recommended due to inconsistent evidence. In contrast, single injection LIA may now be considered based on supportive studies. The PROSPECT Group emphasises the considerable heterogeneity and variability of published LIA studies with regard to analgesic effect, technique, volume and dose of local anaesthetic used and the drug combinations used [77–92]. In addition, the studies are inconsistent with regard to the comparator groups (placebo vs. no injection vs. other analgesic technique) and single-shot or catheter techniques. Also, in most studies of multi-drug LIA, there was no control for potential systemic effects of the additives in the mixtures. The PROSPECT Group emphasises that with modern surgical techniques and the correct implementation of basic analgesia and multimodal analgesia (paracetamol, NSAIDs and dexamethasone) the added value of LIA techniques still warrant further validation [145, 146]. Therefore, the PROSPECT Group strongly encourages further well-conducted studies in this area.

There was significant conflict amongst the PROSPECT members regarding the use of intrathecal morphine 0.1 mg, and a consensus could not be reached. Delphi voting revealed four members to be in favour of recommending the use of intrathecal morphine and nine members against. Therefore, if intrathecal morphine is used, the PROSPECT Group reminds clinicians of the risks and benefits associated with its use. In favour of intrathecal morphine is the documented analgesia it provides for at least 24 h postoperatively and the limited adverse effects with small doses (≤ 0.1 mg morphine) [147, 148]. However, pruritus and postoperative nausea and vomiting are associated with intrathecal morphine [103, 113]. It was thought that even if the incidence of these adverse events may be relatively lower with intrathecal morphine 0.1 mg, they may still delay ambulation and oral intake, and influence patient satisfaction [103, 113]. Indeed, adequate multimodal analgesia with paracetamol, NSAIDs and dexamethasone, without intrathecal morphine, together with more recent surgical techniques, may be sufficient to provide patients with good pain relief [145, 146, 149].

Dexamethasone was not recommended in the previous guidelines due to limited procedure-specific evidence. However, based on recent evidence, dexamethasone 8–10 mg i.v. is recommended. The safety of a single dose of steroids is well documented [150, 151]. Equipotent doses of alternative glucocorticoids seem to be equally effective, whereas multiple doses beyond 24 h are not recommended due to insufficient studies and concern related to the potential side-effect profile. Gabapentinoids have shown opioid-sparing effects but can cause sedation; blurred vision; dizziness [41]; interfere with early mobilisation; and cause orthostatic intolerance [152], and thus are not recommended. Intra-operative ketamine is not recommended due to limited procedure-specific evidence and potential psychotropic side-effects [153]. Neuraxial anaesthesia has been recommended because it is associated with improved postoperative outcomes compared with general anaesthesia [5]. However, its benefits with regard to postoperative pain control remains inconclusive.

The limitations in this review are, among others, related to those of the included studies. Many of the analgesic interventions were not evaluated against a control group that included an optimised multimodal analgesic regimen such as paracetamol and NSAIDs or COX-2-selective inhibitors. There was considerable heterogeneity between studies such as unstandardised anaesthetic techniques, variable analgesic dosing regimens, variable methods of administration, variable control groups, as well as variable time-points of pain assessments. Heterogeneous control groups were also documented by Karlsen et al. [154]. Other limiting factors include selection bias by the primary reviewers. Selection bias could have developed because all studies fulfilling the search requirements were split between two reviewers, and then included or excluded based on Jadad score requirements. This method also allows for

human error, where an appropriate study could have been missed by a reviewer and excluded. Unfortunately, none of the included studies assessed patients at high risk of excessive postoperative pain (e.g. chronic opioid use, chronic pain states or significant psychiatric disorders). It is possible that analgesic approaches not recommended in this review due to limited analgesic efficacy and/or concerns of adverse effects may be appropriate in situations where one or more of the primary recommendations are contraindicated or otherwise not appropriate to use. Also, it may be appropriate to use additional analgesic interventions beyond the primary recommendations in patients with an anticipated higher than average risk of strong postoperative pain (e.g. chronic opioid use, chronic pain states or significant psychiatric disorders).

In summary, this review has identified an analgesic regimen for optimal pain management after elective total hip arthroplasty (Table 1). We have also identified analgesic interventions that are not recommended for routine pain management in this patient population (Table 2). Future studies should be adequately powered with standardised anaesthetic regimens and use adequate basic analgesia to account for discrepancies between treatment and control groups. Focus should be on pain and appropriate analgesic treatment in a short-stay context, as this is evolving as the method of choice in terms of rapid rehabilitation. Outcomes, such as time to ambulation, hospital length of stay and the occurrence of chronic pain or chronic opioid consumption should be included in the scope of future studies, as these are closely related to the degree of postoperative pain.

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Appendix 1. PROSPECT Working Group

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1 Quality assessment and level of evidence assigned to the randomised trials included in this review.

Table S2 Summary of key results from randomised controlled trials evaluating systemic analgesics, systemic analgesics adjuncts, regional analgesia and surgical procedures in patients undergoing total hip arthroplasty.

Table S3 Summary of key results from studies evaluating systemic analgesics, regional analgesia, perineural analgesic adjuncts and surgical procedures used to support interventions that are not recommended for analgesic benefit in patients undergoing total hip arthroplasty.