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Practice Guidelines

Periarticular Injection in Total Joint Arthroplasty: The Clinical Practice Guidelines of the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society



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The American Association of Hip and Knee Surgeons (AAHKS), The American Academy of Orthopaedic Surgeons (AAOS), The Hip Society, The Knee Society, and The American Society of Regional Anesthesia and Pain Medicine (ASRA) have worked together to develop evidence-based guidelines on the use of periarticular injection in primary total joint arthroplasty (TJA). The purpose of

these guidelines are to improve the treatment of primary TJA in patients and reduce practice variation by promoting a multidisciplinary, evidence-based approach for the use of periarticular injection in primary TJA.

The combined clinical practice guidelines means to address common and important questions related to the efficacy and safety of periarticular injection in primary TJA. Utilizing the AAOS Clinical Practice Guidelines and Systematic Review Methodology, the committee members completed a systematic review and meta-analyses to support the clinical practice guidelines [1]. Direct meta-analyses were performed when the data allowed, but network meta-analyses were not performed. Network meta-analyses are limited in their ability to control for significant variation, particularly in the multimodal analgesic protocols utilized, and the timepoints outcomes were reported. The current clinical practice guidelines were based on the available evidence, so future updates may become necessary as additional literature becomes available with future research.

Guideline Question 1

For patients undergoing primary TJA, does intraoperative periarticular injection affect postoperative pain and/or opioid consumption?

Response/Recommendation

Intraoperative periarticular injection reduces postoperative pain and opioid consumption after primary total hip and knee arthroplasty.

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Strength of Recommendation

Strong.

Rationale

We reviewed thirty-four studies that evaluated the effectiveness of intraoperative periarticular injection on reducing postoperative pain and/or opioid consumption after primary TJA [2–35]. Thirty studies were high quality, and 4 were of moderate quality [2–35]. Due to heterogeneity in the outcomes reported, and the timepoints at which the outcomes were reported, a limited number of direct meta-analyses were performed.

All studies, except for one, evaluated the effectiveness of periarticular injection on postoperative pain after primary TJA [2–16,18–35]. Periarticular injection consistently reduced postoperative pain after primary TJA compared to control. The control group was opioids alone for several studies, but a majority of studies used a different type of control such as a variation on a multimodal analgesia program. Among the thirty-three studies, twenty studies found that periarticular injection reduced postoperative pain after primary TJA compared to control [2–4,6–13,16,17,19,20,23,26,31,33,35]. Five studies included in a direct meta-analysis with limited heterogeneity ($I^2 = 30.4\%$) found that patients who received periarticular injection reported reduced pain with activity at 24 hours postoperatively (-0.53 standardized mean difference [SMD]; 95% confidence interval [CI] -0.80 to -0.25) [3,5,8,19,35].

Twenty-five studies evaluated the effectiveness of periarticular injection on postoperative opioid consumption after primary TJA [2–5,7,9,11,12,14–24,26,28,30–32,35]. Only a qualitative analysis was performed due to the different timepoints at which opioid consumption was reported postoperatively. Similar to postoperative pain, periarticular injection consistently reduced postoperative opioid consumption after primary TJA. Seventeen studies reported reduced opioid consumption with periarticular injection administered during primary TJA [2–5,9,11,14,16–19,24,26,30–32,35]. The remaining eight studies found no difference in postoperative opioid consumption between periarticular injection and control [7,12,15,20–23,28].

Guideline Question 2

For patients undergoing primary TJA, do differences in the content of intraoperative periarticular injections affect postoperative pain, opioid consumption, and/or complications?

Response/Recommendation 2A

Long-acting local anesthetics in periarticular injection are effective at reducing postoperative pain and opioid consumption without an increase in adverse events after primary total hip and knee arthroplasty.

Strength of Recommendation 2A

Strong.

Response/Recommendation 2B

There is no difference between periarticular injections with liposomal bupivacaine or other long-acting local anesthetics (e.g. ropivacaine, bupivacaine) in postoperative pain, opioid consumption, or adverse events after primary total hip and knee arthroplasty.

Strength of Recommendation 2B

Strong.

Response/Recommendation 2C

Ketorolac in periarticular injection is effective at reducing postoperative pain and may reduce opioid consumption without an increase in adverse events after primary total knee arthroplasty (TKA).

Strength of Recommendation 2C

Moderate.

Response/Recommendation 2D

In the absence of reliable evidence, it is the opinion of the workgroup that ketorolac may be used in periarticular injection to reduce postoperative pain and may reduce postoperative opioid consumption without an increase in adverse events after primary total hip arthroplasty (THA).

Strength of Recommendation 2D

Consensus.

Response/Recommendation 2E

Corticosteroid in periarticular injection is effective at reducing postoperative pain and may reduce opioid consumption without an increase in adverse events after primary TKA.

Strength of Recommendation 2E

Moderate.

Response/Recommendation 2F

In the absence of reliable evidence, it is the opinion of the workgroup that a corticosteroid may be used in periarticular injection to reduce postoperative pain and could reduce postoperative opioid consumption without an increase in adverse events after primary THA.

Strength of Recommendation 2F

Consensus.

Response/Recommendation 2G

Morphine in periarticular injection has no additive effect in reducing postoperative pain and opioid consumption and may increase postoperative nausea and vomiting after primary total hip and knee arthroplasty.

Strength of Recommendation 2G

Strong.

Response/Recommendation 2H

There is insufficient evidence on whether epinephrine in periarticular injection influences postoperative pain, opioid consumption, and adverse events after primary TKA.

Strength of Recommendation 2H

Limited.

Response/Recommendation 2I

In the absence of reliable evidence, it is the opinion of the workgroup that there is insufficient evidence on whether epinephrine in periarticular injection influences postoperative pain, opioid consumption, and adverse events after primary THA.

Strength of Recommendation 2I

Consensus.

Response/Recommendation 2J

There is insufficient evidence on whether clonidine in periarticular injection influences postoperative pain, opioid consumption, and adverse events after primary TKA.

Strength of Recommendation 2J

Limited.

Response/Recommendation 2K

In the absence of reliable evidence, it is the opinion of the workgroup that there is insufficient evidence on whether clonidine in periarticular injection influences postoperative pain, opioid consumption, and adverse events after primary THA.

Strength of Recommendation 2K

Consensus.

Rationale

We reviewed forty-seven studies that evaluated the contents of periarticular injections in primary TJA and the effects on postoperative pain, opioid consumption, and adverse events [17,19–29,31–34,36–49]. Direct meta-analyses were performed when the data allowed; however, only a few were completed due to heterogeneity in the outcomes and timepoints at which outcomes were reported.

Sixteen studies, including twelve high quality and four moderate quality studies, compared a local anesthetic periarticular injection alone vs control [19–29,31–34,36]. All sixteen studies evaluated postoperative pain and six studies found improved postoperative pain compared to control [19,20,23,26,31,33]. The remaining ten studies found no difference between local anesthetic and control in postoperative pain [21,22,24,25,27–29,32,34,36]. Eleven studies compared postoperative opioid consumption between a periarticular injection with local anesthetic and control [19–24,26,28,31,32,36]. Six studies found reduced postoperative opioid consumption when a periarticular injection was used with local anesthetic alone compared to control [19,24,26,31,32,36].

Eighteen high-quality studies compared a periarticular injection containing a local anesthetic with additional medications as an injection cocktail vs control [2–18,35]. All eighteen studies evaluated postoperative pain and fourteen studies demonstrated reduced postoperative pain with a periarticular cocktail injection. Only fourteen studies compared postoperative opioid consumption

between a periarticular injection cocktail and control, and twelve studies reported reduced opioid consumption with a periarticular injection cocktail. Although periarticular injection with only local anesthetic is an effective method of postoperative pain management, the use of a periarticular injection combined with additional agents appears to have a greater effect on reducing postoperative opioid consumption following primary TJA. The observed difference in the effectiveness of only local anesthetic and a combination of medications in the periarticular injection may represent a synergistic effect of the combined medications. As a result, the workgroup strongly recommends the use of periarticular injection cocktails with local anesthetic to reduce postoperative pain and opioid consumption. The effectiveness of common components of a periarticular injection cocktail was evaluated to provide guidance on best components to consider using in a periarticular injection. There were no differences between local anesthetic and control in adverse events reported in all studies except for nausea and vomiting. Of the three studies that reported postoperative nausea and vomiting, one study reported an increased nausea and vomiting with local anesthetic compared to control [33].

Twelve high-quality studies compared liposomal bupivacaine to other long-acting local anesthetics, including bupivacaine and ropivacaine [50–61]. Eleven of these studies compared postoperative pain between liposomal bupivacaine and other long-acting local anesthetics and seven studies found no difference between them [50,52,54–56,58,59]. Three other studies found reduced postoperative pain with liposomal bupivacaine, while one other study found no difference in pain at three timepoints, but reduced maximal pain with liposomal bupivacaine [53,57,60,61]. Three studies included in a direct meta-analysis with limited heterogeneity ($I^2 = 4.3\%$) found no difference in postoperative pain at 24 h between patients who received periarticular injection with liposomal bupivacaine versus other local anesthetics (-0.33 weighted mean difference [WMD]; 95% CI -0.79 to 0.13) [52,57,58]. All twelve studies compared post-operative opioid consumption after primary TJA between periarticular injection with liposomal bupivacaine and other long-acting local anesthetics [50–62]. Seven studies found no difference in postoperative opioid consumption between patients who received periarticular injection with liposomal bupivacaine and other long-acting local anesthetics [52,54,55,57–59,63]. Three studies reported decreased opioid consumption at all timepoints reported with liposomal bupivacaine compared with other long-acting local anesthetics [51,60,61]. Perets et al. reported decreased opioid consumption within the 12 hours postoperatively after primary THA with liposomal bupivacaine compared with bupivacaine, but there was no difference in opioid consumption at any other timepoints up to 72 hours and no difference in cumulative opioid consumption measured in morphine equivalents [50]. In their study of 165 primary TKA patients, Amundson et al. reported no difference in cumulative opioid consumption between liposomal bupivacaine and ropivacaine, but found that more of the patients that received liposomal bupivacaine required opioids for breakthrough pain [56]. Three studies included in a direct meta-analysis with no heterogeneity ($I^2 = 0.0\%$) found no difference in postoperative cumulative opioid consumption between patients who received periarticular injection with liposomal bupivacaine vs other local anesthetics (-0.18 SMD; 95% CI -0.43 to 0.07) [50,57,58]. Seven studies reported adverse events and reported no difference in all adverse events except for oversedation and muscle spasms [51,53,55,56,58,59,61]. Dysart et al. reported increased muscle spasms, and Hyland et al. reported oversedation with liposomal bupivacaine compared with other long-acting local anesthetics [58,61]. An additional study by Mont

et al. was evaluated, but excluded from this clinical practice guideline by the workgroup as it directly did not address our PICO question [62]. In their study, Mont et al. compared liposomal bupivacaine with 20mLs of 0.5% ropivacaine versus 20mLs of 0.5% ropivacaine alone. The workgroup study excluded this study because it did not directly answer whether there was a difference between other long-acting local anesthetics and liposomal bupivacaine. Second, it was the only study that evaluated a combination of liposomal bupivacaine with another long-acting local anesthetic and the workgroup determined including this different treatment would add too much heterogeneity when interpreting the results as any observed difference between the treatment groups could have been the result of a dose effect of local anesthetic instead of the result of the liposomal bupivacaine.

Three high-quality studies evaluated ketorolac in periarticular injection used intraoperatively during primary TKA and its influence on postoperative pain, opioid consumption, and adverse events [17,37,64]. Due to the limited number of studies on ketorolac in periarticular injection and the heterogeneity in the data and timepoints reported, no meta-analyses were able to be performed. The two studies that reported postoperative pain found reduced postoperative pain when periarticular injection contained ketorolac and local anesthetic compared to control with local anesthetic alone [37,64]. All three studies reported postoperative opioid consumption. Two studies reported no difference with the addition of ketorolac to periarticular injection and one study found reduced cumulative postoperative opioid consumption [17,37,64]. The workgroup downgraded the recommendation of ketorolac from strong to moderate for several reasons. First, the data on both postoperative pain and opioid consumption was mixed. Only two studies reported postoperative pain and one of those two reported no difference with activity and reduced postoperative pain with ketorolac at another timepoint. As discussed previously, the results on opioid consumption were also mixed. In addition, a strong recommendation implies that future research is unlikely to change the recommendation. The workgroup believes that further research will clarify the mixed results observed in the data and thus downgraded the recommendation to moderate.

The two studies that reported adverse events found no difference when ketorolac was added to periarticular injection compared to a long-acting local anesthetic alone [17,64]. The workgroup made a consensus recommendation regarding the role of ketorolac in periarticular injection for THA because there are no studies in the literature evaluating ketorolac in periarticular injection for THA. As a result, the workgroup extrapolated the results from TKA to make a similar consensus statement for THA regarding ketorolac in periarticular injection.

Eight high-quality studies evaluated corticosteroid in periarticular injection used intraoperatively during TKA and its influence on postoperative pain, opioid consumption and adverse events [17,38–44]. Due to the limited number of studies on corticosteroid in periarticular injection and the heterogeneity in the data and timepoints reported, no meta-analyses were able to be performed. A majority of the studies found that the addition of corticosteroid to periarticular injection reduced postoperative pain after TKA. Of the seven studies that compared postoperative pain after TKA between patients who received periarticular injection with and without corticosteroid, four studies reported reduced postoperative pain when corticosteroid was added to the periarticular injection [39,40,42,43]. The other three studies reported no difference in postoperative pain between patients who received periarticular injection with and without corticosteroid [38,41,44]. Four of the five studies that reported postoperative opioid consumption after

primary TKA found no difference with the addition of corticosteroid to the periarticular injection compared to control [17,38,43,44]. Sean et al. in their study of 100 primary TKA patients found reduced cumulative postoperative opioid consumption when triamcinolone was added to the periarticular injection compared to ropivacaine alone [42]. There were no differences in any adverse events in the five studies that compared adverse events after primary TKA between patients who received periarticular injection with and without corticosteroid [17,38–41]. Despite the number of high-quality studies, the workgroup downgraded the recommendation on corticosteroid in periarticular injection, similar to ketorolac, to a moderate recommendation for several reasons. First, the data on both postoperative pain and opioid consumption was mixed with some studies reporting reduced postoperative pain and opioid consumption with corticosteroid and others reporting no difference. In addition, a strong recommendation implies that future research is unlikely to change the recommendation. The workgroup believes that further research will clarify the mixed results observed in the data and thus downgraded the recommendation to moderate. The workgroup made a consensus recommendation regarding corticosteroid in periarticular injection for THA because there are no studies in the literature evaluating corticosteroid in periarticular injection for THA. As a result, the workgroup extrapolated the results from TKA to make a similar consensus statement for THA regarding corticosteroid in periarticular injection.

Five high-quality studies evaluated the addition of morphine to periarticular injection and the effects on postoperative pain, opioid consumption and adverse events after primary TJA [17,45–48]. Meta-analyses were performed, but were excluded due to the significant heterogeneity between the studies in the outcomes and timepoints reported. The addition of morphine consistently did not have an impact on postoperative pain after primary TJA compared to periarticular injection without morphine. Of the four studies that reported postoperative pain, three studies found no difference in postoperative pain with the addition of morphine to periarticular injection compared to periarticular injection without morphine [45–47]. Only two studies reported postoperative cumulative opioid consumption [17,48]. Kim et al. reported decreased opioid consumption with the addition of morphine to periarticular injection while Mauerhan et al. found no benefit to the addition of morphine in postoperative opioid consumption [17,48]. Four studies reported adverse events and there were no differences in adverse events with the addition of morphine to periarticular injection except for postoperative nausea and/or vomiting [17,45–47]. Two of the four studies reported increased rates of postoperative nausea and/or vomiting with the addition of morphine to periarticular injection [45,47].

There was limited evidence on clonidine and epinephrine in periarticular injection. One study evaluated clonidine in periarticular injection and one study evaluated epinephrine in periarticular injection [37,49]. Both high-quality studies only included primary TKA patients. As a result, the workgroup made a limited recommendation for TKA and a consensus recommendation for THA that there is insufficient evidence to make a recommendation on whether clonidine or epinephrine in periarticular injection influences postoperative pain, opioid consumption, and adverse events after primary TJA.

Areas for Future Research

This clinical practice guideline was formulated with the best available evidence which includes high quality data, however there are several limitations. It is clear that periarticular injection is effective in reducing pain and opioid consumption in primary TJA

without an increase in adverse events. In terms of the contents of periarticular injection, long-acting local anesthetics, corticosteroids and ketorolac are beneficial. However, it is unclear at what dose/concentration these medications should be used in combination. The benefit of epinephrine and clonidine, which are often added to modern periarticular injection cocktails, remain unknown and require future study. In addition, the workgroup was unable to make a recommendation regarding the amount of periarticular injectate that should be injected, where it should be injected, and at what point during the primary TJA. Future research should be focused on further understanding the dosing and volume of contents, and the location and timing of periarticular injection used during primary TJA.

Peer Review Process

Following the committee's formulation of the Clinical Practice Guideline draft, it underwent a peer review by the board of directors from AAHKS, ASRA, and the Hip and Knee Societies. The AAOS Evidence-Based Quality and Value Committee reviewed the Clinical Practice Guideline draft for endorsement. In addition, the publication of the systematic review and meta-analysis on opioids in primary hip and knee arthroplasties that supported the formulation of the Clinical Practice Guideline has undergone peer review for publication.

Disclosure Requirement

All authors or contributors to the Clinical Practice Guideline have provided a disclosure statement in accordance with the publicly available AAOS Orthopedic Disclosure Program. All authors and contributors attest none of the disclosures present are relevant to the Clinical Practice Guidelines. In accordance with the AAOS *Clinical Practice Guidelines and Systematic Review Methodology*, all authors and contributors attest none of the current disclosures are relevant to the Clinical Practice Guidelines and no prior relevant financial conflict was within a year of initiating work on the guideline.

FDA Clearance Statement

According to the FDA, it is the prescribing physician's responsibility to ascertain the FDA clearance status for all medications before use in a clinical setting.

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