Perioperative Anesthesia and Analgesia in Total Joint Arthroplasty Guidelines 2020

Opioids 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
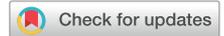
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The American Association of Hip and Knee Surgeons, The American Academy of Orthopaedic Surgeons (AAOS), The Hip Society, The Knee Society, and The American Society of Regional Anesthesia and Pain Medicine worked together to develop evidence-based guidelines on the use of opioids in primary total joint arthroplasty (TJA). The purpose of these guidelines is to improve the treatment of orthopedic surgical patients and reduce practice variation by promoting a multidisciplinary evidence-based approach on the use of opioids following primary TJA.

The combined clinical practice guidelines are meant to address common and important questions related to the efficacy and safety of opioids 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]. For each question, we have provided a recommendation, assessed the strength of the recommendation, and elaborated on the rationale of the recommendation, which should be interpreted in accordance with the AAOS Clinical Practice Guidelines and Systematic Review Methodology [1]. 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 preoperative opioid use affect patient reported outcomes, patient satisfaction, complications, opioid consumption after surgery, and/or risk for chronic opioid use?

Response/Recommendation

Preoperative opioid use is associated with inferior patient-reported outcomes, increased opioid consumption after surgery, an increased risk for chronic opioid use, and an increased risk of complications after TJA.

Strength of Recommendation: Moderate

Rationale

We reviewed 14 studies that evaluated the influence of preoperative opioid use on outcomes after TJA [2—15]. All studies were

assessed as low quality and thus a limited amount of meta-analyses were performed due to inconsistency in outcomes reported and the time points at which these outcomes were reported.

Nine studies evaluated the effects of preoperative opioid use on patient-reported outcomes [2,5–11,15]. Seven studies found that when compared to opioid-naïve patients, patients taking preoperative opioids had inferior patient-reported outcome scores in all outcomes measured [2,5–8,11,15]. Two of these studies were included in a direct meta-analysis with limited heterogeneity, which found that preoperative opioid use is associated with inferior pain scores postoperatively compared to opioid-naïve patients (0.52 standard mean difference; 95% confidence interval 0.28-0.76) [5,9]. Two studies found mixed effects of preoperative opioid use on patient-reported outcome scores. Hansen et al [9] found that preoperative opioid users had no difference in patient-reported outcome scores, but had significantly decreased range of motion following total knee arthroplasty (TKA) compared to opioid-naïve patients. Manalo et al [10] found no difference in range of motion after TKA or the University of California Los Angeles activity scores, but inferior visual analog scores among patients taking preoperative opioids compared to opioid-naïve patients.

Opioid consumption after TJA among patients taking opioids preoperatively was evaluated by 7 studies [2,4–7,9,14]. All 7 studies found that patients taking opioids preoperatively consume significantly more opioids after TJA compared to opioid-naïve patients. Seven studies evaluated chronic opioid use and found that preoperative opioid use is a major risk factor for chronic opioid use after TJA [4,6–8,12–14]. Due to heterogeneity of the time points at which opioid consumption was reported, a direct meta-analysis was not able to be completed.

Five studies compared complication rates after TJA between patients taking opioids preoperatively and opioid-naïve patients [5–9]. Three studies found that complications were more frequent among patients who took opioids preoperatively, while 2 studies found no difference between opioid-naïve patients and patients that took opioids preoperatively. Three studies found no difference in reoperation rates while 1 study found increased reoperation rates among patients taking opioids preoperatively [5–8]. It is the opinion of the workgroup that it is likely these studies were underpowered to detect differences in reoperation and revision rates between the 2 groups. The current literature suggests that complications are more common among patients taking opioids preoperatively, but is inconclusive regarding reoperation and revision rates.

Although all studies included are of limited quality, the workgroup upgraded this recommendation from limited to moderate. This recommendation was upgraded due to the consistency among a large number of low quality studies and the importance of reducing opioid use in light of the current opioid epidemic.

Guideline Question 2

For patients undergoing primary TJA who consume opioids preoperatively, does reducing opioid consumption prior to surgery affect patient-reported outcomes and/or opioid consumption after surgery?

Response/Recommendation

Reduction in opioid use prior to TJA may lead to improved patient-reported outcomes after TJA compared to patients who do not reduce opioid consumption prior to surgery.

Strength of Recommendation: Limited

Rationale

One low quality study evaluated the influence of reducing preoperative opioid use on patient-reported outcome scores after TJA

[11]. In their retrospective case-control study, Nguyen et al found that patients on chronic opioids prior to TJA who reduced their opioid consumption by more than 50% prior to surgery had significantly better patient-reported outcome scores after TJA compared to patients who did not reduce their opioid intake prior to surgery. The percent change of improvement in patient-reported outcome scores was similar to a control group of opioid-naïve patients. Based on this low-quality evidence and the evidence presented above that demonstrates that patients on preoperative opioids have inferior outcomes compared to opioid-naïve patients, it is the opinion of the workgroup that reduction in preoperative opioid use may lead to improved patient-reported outcomes after TJA. This recommendation was upgraded from consensus to recommendation given the importance of reducing opioid use in light of the current epidemic.

Guideline Question 3

For patients undergoing primary TJA, does an opioid administered immediately prior to surgery affect postoperative pain, opioid consumption, and/or complications after surgery?

Response/Recommendation

An opioid administered immediately prior to surgery reduces postoperative pain and opioid consumption within the first 72 hours after TJA, but may increase the risk of complications, such as respiratory depression or sedation, especially if combined with other opioids administered intraoperatively or postoperatively.

Strength of Recommendation: Strong

Rationale

We reviewed 6 studies that compared the influence of an opioid administered pre-emptively immediately prior to TJA to placebo on postoperative outcomes after TJA [16–21]. Five studies are high quality and 1 is moderate quality. Three studies evaluated transdermal fentanyl patches placed 10-12 hours prior to surgery, 1 study evaluated intramuscular morphine, 1 study evaluated oral morphine, and 1 study evaluated intravenous morphine. A very limited amount of meta-analyses was performed due to inconsistency in outcomes reported and the time points at which these outcomes were reported.

All 6 studies reported visual analog pain scores within 72 hours after TJA after administration of an opioid pre-emptively prior to TJA. Four of the high quality studies found that an opioid administered pre-emptively prior to surgery resulted in lower VAS scores within 72 hours after TJA compared to placebo [16–19]. Three of these studies evaluated transdermal fentanyl and the fourth study evaluated intramuscular morphine. The 2 remaining studies, which evaluated intravenous morphine and oral morphine, found no difference in VAS scores compared to placebo [20,21].

All 6 studies evaluated opioid consumption within 72 hours after TJA. Five of the 6 studies found that administration of an opioid pre-emptively prior to TJA resulted in lower morphine consumption after TJA compared to placebo [16,18–21]. The other study found no difference in opioid consumption after TJA when comparing pre-emptive opioid administration to placebo [17]. Only one study evaluated range of motion after TJA and found no difference among patients who received a pre-emptive opioid prior to TJA compared to placebo [16].

Direct meta-analyses were performed to compare rates of nausea, vomiting, and urinary retention. The direct meta-analyses found no difference between patients who received a pre-

emptive opioid prior to TJA and placebo in rates of nausea (0.88 relative risk; 95% confidence interval 0.62-1.25), vomiting (0.60 relative risk; 95% confidence interval 0.33-1.10), and urinary retention (1.08 relative risk; 95% confidence interval 0.34-3.40). Four studies evaluated sedation and respiratory depression and found no difference between pre-emptive opioids and placebo [16,17,19,21]. However, it is the opinion of the workgroup that when combined with other opioids administered during the perioperative period, such as intraoperatively or postoperatively, opioids administered prior to surgery may increase the risk of complications including respiratory depression and sedation.

Guideline Question 4

For patients undergoing primary TJA, do opioids administered intraoperatively affect postoperative pain, opioid consumption, and/or complications?

Response/Recommendation

An opioid administered intraoperatively reduces opioid consumption, but does not affect postoperative pain within 72 hours after surgery. An opioid administered intraoperatively may increase the risk of complications, such as respiratory depression or sedation, especially if combined with other opioids administered preoperatively or postoperatively.

Strength of Recommendation: Moderate

Rationale

We reviewed 2 high quality studies that evaluated the influence of an opioid administered intraoperatively during primary TJA on postoperative pain, opioid consumption, and complications [22,23]. Given the differences in outcome measures utilized and the time points at which were measured at no meta-analyses could be performed.

Both studies evaluated postoperative opioid consumption after administering an intraoperative opioid during primary TJA. They both found that administering an intraoperative opioid reduced postoperative opioid consumption compared to placebo within the first 72 hours after surgery [22,23]. These 2 studies also evaluated VAS pain scores and found no difference between patients who received an intraoperative opioid and placebo within the first 72 hours postoperatively. Similarly, there was no difference in the rates of nausea or vomiting between patients who received intraoperative opioids and those who received placebo. However, it is the opinion of the workgroup that when combined with other opioids administered preoperatively or postoperatively, opioids administered during surgery may increase the risk of complications including respiratory depression and sedation. Given there is not significant evidence on the risk of complications associated with intraoperative opioid use, we downgraded this recommendation from a strong recommendation to a moderate recommendation.

Guideline Question 5

For patients undergoing primary TJA, do opioids administered after surgery affect postoperative pain, opioid consumption, patient-reported outcome scores, and/or complications?

Response/Recommendation

Scheduled opioid administration without multimodal analgesia within 72 hours after primary TJA reduces the need for additional opioid pain medications for breakthrough pain and may reduce postoperative pain within 72 hours after surgery, but providing scheduled opioids is discouraged. Scheduled opioid administration postoperatively may increase the risk of complications, such as respiratory depression and sedation, especially if combined with other opioids administered during the perioperative period.

Strength of Recommendation: Moderate

Rationale

Nine studies including 6 high quality studies and 3 moderate quality studies evaluated the influence of postoperative opioids on outcomes after primary TJA. A limited number of direct meta-analyses were performed due to inconsistency in outcomes reported and the time points at which these outcomes were reported.

Eight studies evaluated the postoperative consumption of opioids for breakthrough pain either delivered orally or with patient controlled analgesia between patients who received scheduled opioids postoperatively and patients who received placebo. All 8 studies found that the administration of scheduled opioids postoperatively reduced the consumption of opioids for breakthrough pain [24–31]. Two studies were included in a direct meta-analysis with moderate heterogeneity and found that patients who were administered scheduled opioids postoperatively routinely required less opioids for breakthrough pain compared to placebo (−0.54 standard mean difference; 95% confidence interval of −0.92 to −0.15).

All 9 studies evaluated postoperative pain and reported mixed results [24–32]. Three studies reported no difference in pain control between patients who received scheduled opioids postoperatively and placebo [25,26,31]. Three studies reported mixed results where some pain measures were improved among patients who received opioids scheduled postoperatively while other pain parameters were no different between these patients and placebo [28,29,32]. The final 3 studies found that opioids administered after primary TJA reduce postoperative pain compared to placebo [24,27,30].

Direct meta-analyses evaluating complications associated with postoperative opioid use compared to placebo found no differences between the 2 groups in rates of respiratory depression (−0.17 standard mean difference; 95% confidence interval −0.45 to 0.10), pruritus (1.01 relative risk; 95% confidence interval 0.70-1.47), nausea (1.30 relative risk, 95% confidence interval 1.03-1.65), vomiting (1.10 relative risk; 95% confidence interval 0.69-1.74), confusion (1.82 relative risk; 95% confidence interval 0.35-9.49), dizziness (1.50 relative risk; 95% confidence interval 0.60-3.71), headache (0.69 relative risk; 95% confidence interval 0.30-1.59), and constipation (1.71 relative risk; 95% confidence interval 0.82-3.59). Although the current literature does not demonstrate significant differences in rates of adverse events, it is the opinion of the workgroup that opioids pose significant risks to patients when not safely administered. The cumulative dose of opioids administered as well as the timing between opioid doses must be carefully monitored in TJA patients. Patients who receive excess opioid pain medication are at significant risk for adverse events such as sedation and respiratory depression. It is the recommendation of the workgroup that extended release opioids should be avoided to help mitigate this risk. In addition, it is the opinion of the workgroup that the lowest clinically effective dose of opioids be prescribed and administered to patients to help curb these adverse events in addition to the risk for chronic opioid dependence. Given the inconsistency in results with regards to postoperative pain as well as complications associated with postoperative opioid use this recommendation was downgraded from strong to moderate.

Guideline Question 6

For patients undergoing primary TJA, does the number of opioid pills prescribed at the time of discharge affect postoperative pain, opioid consumption, opioid refills, number of unused opioid pills, and/or complications including chronic opioid dependence?

Response/Recommendation

Prescribing lower quantities of opioid pills at discharge may lead to equivalent patient-reported outcomes, pain relief, reduced opioid consumption, and fewer unused opioid pills after TJA.

Strength of Recommendation: Moderate

Rationale

One high quality study evaluated the influence of the number of opioid pills prescribed at discharge after TJA on patient-reported outcome scores, pain control, and opioid consumption after TJA [33]. In their prospective blinded randomized controlled trial, Hannon et al found that patients who received 30 oxycodone immediate release pills (OxyIR) as opposed to 90 pills had equivalent patient-reported outcome scores and significantly fewer unused pills at 6 weeks postoperatively. Patients who received 90 OxyIR pills had on median 73 unused pills while patients who received 30 OxyIR pills had on median 15 unused pills. Opioid consumption within 6 weeks after surgery was equivalent between the 2 groups; however, regression analysis determined that being prescribed 90 OxyIR pills was independently associated with taking more oxycodone pills. Given the risks associated with diversion of unused opioid pills, it is the opinion of the workgroup that patients be prescribed the fewest number of opioid pills possible without jeopardizing pain control and clinical outcomes after TJA.

Guideline Question 7

For patients undergoing primary TJA, does tramadol affect postoperative pain, opioid consumption, and/or postoperative complications and how does its efficacy compare to other opioid medications?

Response/Recommendation

Tramadol administered within 24 hours after surgery may reduce postoperative pain and opioid consumption after TJA within 72 hours after surgery, but may be associated with adverse events such as dizziness and dry mouth.

Strength of Recommendation: Moderate

Rationale

Three studies evaluated the effects of tramadol on postoperative pain, opioid consumption, and complications after primary TJA. One high quality study compared the use of tramadol vs a placebo for treatment of pain after TJA [34]. Another high quality study compared tramadol to placebo and to paracetamol with codeine [35]. One additional high quality study compared tramadol to other opioid medications for treatment of pain after TJA. There were mixed results among all studies on the effects of tramadol on pain, patient-reported outcome scores, opioid consumption, and adverse events after TJA.

Both studies that compared tramadol to a non-opioid control found that there was no difference in pain relief between control and tramadol [34,35]. However, each study found different results with regards to opioid consumption. Stiller et al [34] found that intravenous tramadol 100 mg/mL administered every 6 hours for 24 hours after surgery led to 31% lower morphine consumption in TKA patients measured via a morphine patient controlled analgesia device. Stubhaug et al [35] found that after THA the addition of either 50 mg or 100 mg oral tramadol did not result in any change in opioid consumption when compared to placebo. When compared to paracetamol with codeine, both 50 mg and 100 mg oral tramadol resulted in less efficacious pain relief and opioid consumption. Pang et al [36] found that tramadol reduced opioids administered via a patient controlled analgesic device compared to placebo.

Adverse events including dizziness, dry mouth, and nausea were more common among patients who received tramadol compared to placebo. A direct meta-analysis of 2 studies found that rates of dry mouth (1.97 relative risk; 95% confidence interval 1.04-3.75) and dizziness (1.50 relative risk; 95% confidence interval 1.12-2.00) were more common among patients who took tramadol compared to placebo [35,36].

Given the conflicting evidence with regards to opioid consumption, the fact that 2 studies evaluated intravenous tramadol which is not approved by the Food and Drug Administration in the United States, and that there was inconclusive evidence comparing the efficacy of tramadol to other opioids, the strength of the recommendation was downgraded to moderate.

Areas for Future Research

The best available evidence includes high and moderate quality data; however, there remain many limitations in the formulation of the clinical practice guidelines on the use of opioids after primary TJA. Given the poor outcomes after primary TJA among patients who take chronic opioids prior to surgery, we recommend future research on innovative and effective ways at reducing chronic opioid use prior to TJA. Future research should evaluate whether reducing chronic preoperative opioid use leads to improved postoperative outcomes including postoperative pain, opioid consumption, opioid dependence, and functional outcomes.

Opioids administered during the perioperative period (eg, immediately preoperatively, intraoperatively, and postoperatively) reduce the need for additional opioid consumption and postoperative pain. However, there is significant heterogeneity in the route, dose, frequency, and type of opioids administered in the current literature. For example, in the studies reporting on opioids administered preoperatively, most investigate transdermal fentanyl while only 2 other studies evaluate intravenous and oral opioids. In addition, many of the studies included did not utilize a multimodal analgesic regimen. Future research should focus on determining the role of opioids in a modern multimodal anesthesia and analgesia protocol after TJA. This would include determining what opioids should be administered, the route, dose, frequency, and duration of treatment. Future research should also focus on how many pills should be prescribed after discharge and ways to help patients wean from taking opioids after surgery.

With the advent of the opioid crisis in the United States, tramadol has been considered a safer alternative to other traditional opioid pain medications for treatment of postoperative pain. However, there remains limited literature on its efficacy in a modern multimodal analgesia protocol. Future research is warranted to determine the type of tramadol that should be administered (eg, immediate vs extended release), the dosage, frequency, and duration of treatment. In addition, there is a paucity of literature on oral tramadol, which requires further study. Further investigation is also warranted into the side effects associated with

tramadol use and whether these side effects are further compounded when traditional opioids are also administered.

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 American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, and the Hip and Knee Societies. The AAOS Evidence-Based Quality and Value Committee reviewed the Clinical Practice Guideline draft for endorsement. Additionally, 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 Orthopaedic Disclosure Program. All authors and contributors attest that none of the disclosures present are relevant to the Clinical Practice Guidelines.

Acknowledgments

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