



Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

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



Charles P. Hannon, MD, MBA ^{a, b, *}, Yale A. Fillingham, MD ^c, Mark J. Spangehl, MD ^d, Vasili Karas, MD ^e, Atul F. Kamath, MD ^f, William G. Hamilton, MD ^g, Craig J. Della Valle, MD ^e, AAHKS Anesthesia & Analgesia Clinical Practice Guideline Workgroup

^a Department of Orthopedic Surgery, Washington University in St. Louis, St. Louis, Missouri

^b Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota

^c Rothman Institute at Thomas Jefferson University, Philadelphia, Pennsylvania

^d Department of Orthopedic Surgery, Mayo Clinic, Phoenix, Arizona

^e Department of Orthopedic Surgery, Rush University Medical Center, Chicago, Illinois

^f Department of Orthopedic Surgery, Cleveland Clinic Foundation, Cleveland, Ohio

^g Department of Orthopaedic Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

ARTICLE INFO

Article history:

Received 25 January 2022

Received in revised form

8 March 2022

Accepted 12 March 2022

Available online 4 April 2022

Keywords:

periarticular injection

total joint arthroplasty

total knee arthroplasty

total hip arthroplasty

multimodal analgesia and anesthesia

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.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to <https://doi.org/10.1016/j.arth.2022.03.048>.

¹Denotes co-senior authors.

* Address correspondence to: Charles P. Hannon, MD, MBA, Washington University in St. Louis, 660 South Euclid Avenue, St. Louis, MO 63110.

<https://doi.org/10.1016/j.arth.2022.03.048>

0883-5403/© 2022 Elsevier Inc. All rights reserved.

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.

Acknowledgments

We would like to thank AAHKS for providing the funding and administrative support. We would like to thank Jayson Murray, Nicole Nelson, and Francisco Casambre from the AAOS Department of Research, Quality, and Scientific Affairs for their assistance with the analysis and guidance. Lastly, we thank the leadership of the AAHKS, AAOS, ASRA, and the Hip and Knee societies for help with organizational support.

References

- [1] American Academy of Orthopaedic Surgeons (AAOS) AAOS clinical practice guideline and systematic review methodology. <https://www.aaos.org/quality/research-resources/methodology/>; 2017 [accessed 01.05.20].
- [2] Pandazi A, Kanellopoulos I, Kalimeris K, Batistaki C, Nikolakopoulos N, Matsota P, et al. Periarticular infiltration for pain relief after total hip arthroplasty: a comparison with epidural and PCA analgesia. *Arch Orthop Trauma Surg* 2013;133:1607–12. <https://doi.org/10.1007/s00402-013-1849-8>.
- [3] Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalden RW, Bourne RB. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. *Clin Orthop Relat Res* 2010;468:2152–9. <https://doi.org/10.1007/s11999-009-1198-7>.
- [4] Liu W, Cong R, Li X, Wu Y, Wu H. Reduced opioid consumption and improved early rehabilitation with local and intraarticular cocktail analgesic injection in total hip arthroplasty: a randomized controlled clinical trial. *Pain Med* 2011;12:387–93. <https://doi.org/10.1111/j.1526-4637.2010.01043.x>.
- [5] Dimaculangan D, Chen JF, Borzio RB, Jauregui JJ, Rasquinha VJ, Maheshwari AV. Periarticular injection and continuous femoral nerve block versus continuous femoral nerve block alone on postoperative opioid consumption and pain control following total knee arthroplasty: randomized controlled trial. *J Clin Orthop Trauma* 2019;10:81–6. <https://doi.org/10.1016/j.jcot.2017.09.012>.
- [6] Motiffard M, Omidian A, Badiei S. Pre-emptive injection of peri-articular-multimodal drug for post-operative pain management in total knee arthroplasty: a double-blind randomized clinical trial. *Int Orthop* 2017;41:939–47. <https://doi.org/10.1007/s00264-016-3357-2>.
- [7] Hinarejos P, Capurro B, Santiveri X, Ortiz P, Leal J, Pelfort X, et al. Local infiltration analgesia adds no clinical benefit in pain control to peripheral nerve blocks after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2016;24:3299–305. <https://doi.org/10.1007/s00167-016-4187-x>.
- [8] Shi ZB, Dang XQ. Efficacy of multimodal perioperative analgesia protocol with periarticular medication injection and nonsteroidal anti-inflammatory drug use in total knee arthroplasty. *Niger J Clin Pract* 2018;21:1221–7. https://doi.org/10.4103/njcp.njcp_395_17.
- [9] Zhang S, Wang F, Lu Z, Li Y, Zhang L, Jin Q. Effect of single-injection versus continuous local infiltration analgesia after total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *J Int Med Res* 2011;39:1369–80. <https://doi.org/10.1177/147323001103900423>.
- [10] Barastegui D, Robert I, Palau E, Haddad S, Reverte-Vinaixa M, Lorente L, et al. Can local infiltration analgesia increase satisfaction in postoperative short-term pain control in total knee arthroplasty? *J Orthop Surg (Hong Kong)* 2017;25. <https://doi.org/10.1177/2309499017690461>. 2309499017690461.
- [11] Essving P, Axelsson K, Kjellberg J, Wallgren Ö, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. *Acta Orthop* 2010;81:354–60. <https://doi.org/10.3109/17453674.2010.487241>.
- [12] Ikeuchi M, Kamimoto Y, Izumi M, Sugimura N, Takemura M, Fukunaga K, et al. Local infusion analgesia using intra-articular double lumen catheter after total knee arthroplasty: a double blinded randomized control study. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2680–4. <https://doi.org/10.1007/s00167-012-2004-8>.
- [13] Nair VS, Radhamony NG, Rajendra R, Mishra R. Effectiveness of intraoperative periarticular cocktail injection for pain control and knee motion recovery after total knee replacement. *Arthroplast Today* 2019;5:320–4. <https://doi.org/10.1016/j.artd.2019.05.004>.
- [14] Niemeläinen M, Kalliovalkama J, Aho AJ, Moilanen T, Eskelinen A. Single periarticular local infiltration analgesia reduces opiate consumption until 48 hours after total knee arthroplasty. *Acta Orthop* 2014;85:614–9. <https://doi.org/10.3109/17453674.2014.961399>.
- [15] Solovyova O, Lewis CG, Abrams JH, Grady-Benson J, Joyce ME, Schutzer SF, et al. Local infiltration analgesia followed by continuous infusion of local anesthetic solution for total hip arthroplasty. *J Bone Joint Surg Am* 2013;95:1935–41. <https://doi.org/10.2106/jbjs.l.00477>.
- [16] Vendittoli P-A, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin M-C, et al. A multimodal analgesia protocol for total knee arthroplasty. *J Bone Joint Surg Am* 2006;88:282–9. <https://doi.org/10.2106/jbjs.e.00173>.
- [17] Kim TW, Park SJ, Lim SH, Seong SC, Lee S, Lee MC. Which analgesic mixture is appropriate for periarticular injection after total knee arthroplasty? Prospective, randomized, double-blind study. *Knee Surg Sports Traumatol Arthrosc* 2015;23:838–45. <https://doi.org/10.1007/s00167-014-3366-x>.
- [18] Aso K, Izumi M, Sugimura N, Okanoue Y, Kamimoto Y, Yokoyama M, et al. Additional benefit of local infiltration of analgesia to femoral nerve block in total knee arthroplasty: double-blind randomized control study. *Knee Surg Sports Traumatol Arthrosc* 2019;27:2368–74. <https://doi.org/10.1007/s00167-018-5322-7>.
- [19] Tziona D, Papaioannou M, Mela A, Potamianou S, Makris A. Local infiltration analgesia combined with a standardized multimodal approach including an adductor canal block in total knee arthroplasty: a prospective randomized, placebo-controlled, double-blinded clinical trial. *J Anesth* 2018;32:326–32. <https://doi.org/10.1007/s00540-018-2476-x>.
- [20] Zhou M, Ding H, Ke J. Adductor canal block in combination with posterior capsular infiltration on the pain control after TKA. *Ir J Med Sci* 2018;187:465–71. <https://doi.org/10.1007/s11845-017-1647-3>.
- [21] Zoric L, Cuvillon P, Alonso S, Demattei C, Vialles N, Asencio G, et al. Single-shot intraoperative local anaesthetic infiltration does not reduce morphine consumption after total hip arthroplasty: a double-blinded placebo-controlled

- randomized study. *Br J Anaesth* 2014;112:722–8. <https://doi.org/10.1093/bja/aet439>.
- [22] Hofstad JK, Winther SB, Rian T, Foss OA, Husby OS, Wik TS. Perioperative local infiltration anesthesia with ropivacaine has no effect on postoperative pain after total hip arthroplasty. *Acta Orthop* 2015;86:654–8. <https://doi.org/10.3109/17453674.2015.1053775>.
 - [23] Dobie I, Bennett D, Spence DJ, Murray JM, Beverland DE. Periarticular local anesthesia does not improve pain or mobility after THA. *Clin Orthop Relat Res* 2012;470:1958–65. <https://doi.org/10.1007/s11999-012-2241-7>.
 - [24] Murphy TP, Byrne DP, Curtin P, Baker JF, Mulhall KJ. Can a periarticular levobupivacaine injection reduce postoperative opiate consumption during primary hip arthroplasty? *Clin Orthop Relat Res* 2012;470:1151–7. <https://doi.org/10.1007/s11999-011-2108-3>.
 - [25] Lunn TH, Husted H, Solgaard S, Kristensen BB, Otte KS, Kjersgaard AG, et al. Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty. *Reg Anesth Pain Med* 2011;36:424–9. <https://doi.org/10.1097/aap.0b013e3182186866>.
 - [26] Busch CA, Shore BJ, Bhandari R, Ganapathy S, MacDonald SJ, Bourne RB, et al. Efficacy of periarticular multimodal drug injection in total knee arthroplasty. *J Bone Joint Surg Am* 2006;88:959–63. <https://doi.org/10.2106/jbjs.e.00344>.
 - [27] Villatte G, Engels E, Erivan R, Mulliez A, Caumon N, Boisgard S, et al. Effect of local anaesthetic wound infiltration on acute pain and bleeding after primary total hip arthroplasty: the EDIPO randomised controlled study. *Int Orthop* 2016;40:2255–60. <https://doi.org/10.1007/s00264-016-3133-3>.
 - [28] Krenzel BA, Cook C, Martin GN, Vail TP, Attarian DE, Bolognesi MP. Posterior capsular injections of ropivacaine during total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *J Arthroplasty* 2009;24:138–43. <https://doi.org/10.1016/j.arth.2009.03.014>.
 - [29] den Hartog YM, Mathijssen NMC, van Dasselaa NT, Langendijk PNJ, Vehmeijer SBW. No effect of the infiltration of local anaesthetic for total hip arthroplasty using an anterior approach: a randomised placebo controlled trial. *Bone Joint J* 2015;97-B:734–40. <https://doi.org/10.1302/0301-620x.97b6.35343>.
 - [30] Badner NH, Bourne RB, Rorabeck CH, Doyle JA. Addition of morphine to intra-articular bupivacaine does not improve analgesia following knee joint replacement. *Reg Anesth Pain Med* 1997;22:347–50. [https://doi.org/10.1016/s1098-7339\(97\)80010-7](https://doi.org/10.1016/s1098-7339(97)80010-7).
 - [31] Grosso MJ, Murtaugh T, Lakra A, Brown AR, Maniker RB, Cooper HJ, et al. Adductor canal block compared with periarticular bupivacaine injection for total knee arthroplasty. *J Bone Joint Surg Am* 2018;100:1141–6. <https://doi.org/10.2106/jbjs.17.01177>.
 - [32] Sigirci A. Pain management in total knee arthroplasty by intraoperative local anesthetic application and one-shot femoral block. *Indian J Orthop* 2017;51:280–5. <https://doi.org/10.4103/0019-5413.205688>.
 - [33] Nakai T, Nakamura T, Nakai T, Onishi A, Hashimoto K. A study of the usefulness of a periarticular multimodal drug cocktail injection for pain management after total hip arthroplasty. *J Orthop* 2013;10:5–7. <https://doi.org/10.1016/j.jor.2013.01.011>.
 - [34] Milani P, Castelli P, Sola M, Invernizzi M, Massazza G, Cisari C. Multimodal analgesia in total knee arthroplasty: a randomized, double-blind, controlled trial on additional efficacy of periarticular anesthesia. *J Arthroplasty* 2015;30:2038–42. <https://doi.org/10.1016/j.arth.2015.05.035>.
 - [35] Kampitak W, Tanavalee A, Ngarmukos S, Amarase C, Apihansakorn R, Vorapalux P. Does adductor canal block have a synergistic effect with local infiltration analgesia for enhancing ambulation and improving analgesia after total knee arthroplasty? *Knee Surg Relat Res* 2018;30:133–41. <https://doi.org/10.5792/ksrr.17.088>.
 - [36] Badner NH, Bourne RB, Rorabeck CH, Macdonald SJ, Doyle JA. Intra-Articular injection of bupivacaine in knee-replacement operations. Results of use for analgesia and for preemptive blockade. *J Bone Joint Surg Am* 1996;78:734–8. <https://doi.org/10.2106/00004623-199605000-00013>.
 - [37] Kelley TC, Adams MJ, Mulliken BD, Dalury DF. Efficacy of multimodal perioperative analgesia protocol with periarticular medication injection in total knee arthroplasty A randomized, double-blinded study. *J Arthroplasty* 2013;28:1274–7. <https://doi.org/10.1016/j.arth.2013.03.008>.
 - [38] Christensen CP, Jacobs CA, Jennings HR. Effect of periarticular corticosteroid injections during total knee arthroplasty. *J Bone Joint Surg Am* 2009;91:2550–5. <https://doi.org/10.2106/jbjs.h.01501>.
 - [39] Tsukada S, Wakui M, Hoshino A. The impact of including corticosteroid in a periarticular injection for pain control after total knee arthroplasty. *Bone Joint J* 2016;98-B:194–200. <https://doi.org/10.1302/0301-620x.98b2.36596>.
 - [40] Kwon SK, Yang IH, Bai SJ, Han CD. Periarticular injection with corticosteroid has an additional pain management effect in total knee arthroplasty. *Yonsei Med J* 2014;55:493–8. <https://doi.org/10.3349/ymj.2014.55.2.493>.
 - [41] Chia SK, Wernecke GC, Harris IA, Bohm MT, Chen DB, MacDessi SJ. Peri-articular steroid injection in total knee arthroplasty: a prospective, double blinded, randomized controlled trial. *J Arthroplasty* 2013;28:620–3. <https://doi.org/10.1016/j.arth.2012.07.034>.
 - [42] Sean VVT, Chin PL, Chia SL, Yang KY, Lo NN, Yeo SJ. Single-dose periarticular steroid infiltration for pain management in total knee arthroplasty: a prospective, double-blind, randomised controlled trial. *Singapore Med J* 2011;52:19–23.
 - [43] Ikeuchi M, Kamimoto Y, Izumi M, Fukunaga K, Aso K, Sugimura N, et al. Effects of dexamethasone on local infiltration analgesia in total knee arthroplasty: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2014;22:1638–43. <https://doi.org/10.1007/s00167-013-2367-5>.
 - [44] Yue D, Wang B, Liu K, Guo W. Efficacy of multimodal cocktail periarticular injection with or without steroid in total knee arthroplasty. *Chin Med J (Engl)* 2013;126:3851–5.
 - [45] Iwakiri K, Ohta Y, Minoda Y, Kobayashi A, Nakamura H. Effect of peri-articular morphine injection for total hip arthroplasty: a randomised, double-blind trial. *Hip Int* 2018;29:245–52. <https://doi.org/10.1177/1120700018780067>.
 - [46] Iwakiri K, Ohta Y, Kobayashi A, Minoda Y, Nakamura H. Local efficacy of periarticular morphine injection in simultaneous bilateral total knee arthroplasty: a prospective, randomized, double-blind trial. *J Arthroplasty* 2017;32:3637–42. <https://doi.org/10.1016/j.arth.2017.07.020>.
 - [47] Miyamoto S, Sugita T, Aizawa T, Miyatake N, Sasaki A, Maeda I, et al. The effect of morphine added to periarticular multimodal drug injection or spinal anesthesia on pain management and functional recovery after total knee arthroplasty. *J Orthop Sci* 2018;23:801–6. <https://doi.org/10.1016/j.jos.2018.04.013>.
 - [48] Mauerhan DR, Campbell M, Miller JS, Mokris JG, Gregory A, Kiezbak GM. Intra-articular morphine and/or bupivacaine in the management of pain after total knee arthroplasty. *J Arthroplasty* 1997;12:546–52. [https://doi.org/10.1016/s0883-5403\(97\)90178-9](https://doi.org/10.1016/s0883-5403(97)90178-9).
 - [49] Schotanus MGM, Bemelmans YFL, van der Kuy PHM, Jansen J, Kort NP. No advantage of adrenaline in the local infiltration analgesia mixture during total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2017;25:2778–83. <https://doi.org/10.1007/s00167-015-3723-4>.
 - [50] Perets I, Walsh JP, Mu BH, Yuen LC, Ashberg L, Battaglia MR, et al. Intra-operative infiltration of liposomal bupivacaine vs bupivacaine hydrochloride for pain management in primary total hip arthroplasty: a prospective randomized trial. *J Arthroplasty* 2018;33:441–6. <https://doi.org/10.1016/j.arth.2017.09.013>.
 - [51] Suarez JC, Al-Mansoori AA, Kanwar S, Semien GA, Villa JM, McNamara CA, et al. Effectiveness of novel adjuncts in pain management following total knee arthroplasty: a randomized clinical trial. *J Arthroplasty* 2018;33:S136–41. <https://doi.org/10.1016/j.arth.2018.02.088>.
 - [52] Jain RK, Porat MD, Klingenstein GG, Reid JJ, Post RE, Schoifet SD. The AAHKS clinical research award: liposomal bupivacaine and periarticular injection are not superior to single-shot intra-articular injection for pain control in total knee arthroplasty. *J Arthroplasty* 2016;31:22–5. <https://doi.org/10.1016/j.arth.2016.03.036>.
 - [53] Johnson RL, Amundson AW, Abdel MP, Sviggum HP, Mabry TM, Mantilla CB, et al. Continuous posterior lumbar plexus nerve block versus periarticular injection with ropivacaine or liposomal bupivacaine for total hip arthroplasty. *J Bone Joint Surg Am* 2017;99:1836–45. <https://doi.org/10.2106/jbjs.16.01305>.
 - [54] DeClaire JH, Aiello PM, Warrity OK, Freeman DC. Effectiveness of bupivacaine liposome injectable suspension for postoperative pain control in total knee arthroplasty: a prospective, randomized, double blind, controlled study. *J Arthroplasty* 2017;32:S268–71. <https://doi.org/10.1016/j.arth.2017.03.062>.
 - [55] Alijanipour P, Tan TL, Matthews CN, Viola JR, Purtill JJ, Rothman RH, et al. Periarticular injection of liposomal bupivacaine offers No benefit over standard bupivacaine in total knee arthroplasty: a prospective, randomized, controlled trial. *J Arthroplasty* 2017;32:628–34. <https://doi.org/10.1016/j.arth.2016.07.023>.
 - [56] Amundson AW, Johnson RL, Abdel MP, Mantilla CB, Panchamia JK, Taunton MJ, et al. A three-arm randomized clinical trial comparing continuous femoral plus single-injection sciatic peripheral nerve blocks versus peri-articular injection with ropivacaine or liposomal bupivacaine for patients undergoing total knee arthroplasty. *Anesthesiology* 2017;126:1139–50. <https://doi.org/10.1097/ain.0000000000001586>.
 - [57] Barrington JW, Emerson RH, Lovall ST, Lombardi AV, Berend KR. No difference in early analgesia between liposomal bupivacaine injection and intrathecal morphine after TKA. *Clin Orthop Relat Res* 2017;475:94–105. <https://doi.org/10.1007/s11999-016-4931-z>.
 - [58] Hyland SJ, Deliberato D, Fada R, Romanelli M, Collins C, Wasielewski R. Liposomal bupivacaine versus standard peri-articular injection in total knee arthroplasty with regional anesthesia: a prospective, randomized controlled trial. *J Arthroplasty* 2018;34:488–94. <https://doi.org/10.1016/j.arth.2018.11.026>.
 - [59] Schumer G, Mann J, Stover M, Sloboda J, Cdebaca C, Woods G. Liposomal bupivacaine utilization in total knee replacement does not decrease length of hospital stay. *J Knee Surg* 2018;32:934–9. <https://doi.org/10.1055/s-0038-1673617>.
 - [60] Snyder MA, Scheuerman CM, Gregg JL, Ruhnke CJ, Eten K. Improving total knee arthroplasty perioperative pain management using a periarticular injection with bupivacaine liposomal suspension. *Arthroplast Today* 2016;2:37–42. <https://doi.org/10.1016/j.artd.2015.05.005>.

- [61] Dysart SH, Barrington JW, Gaizo DJD, Sodhi N, Mont MA. Local infiltration analgesia with liposomal bupivacaine improves early outcomes after total knee arthroplasty: 24-hour data from the PILLAR study. *J Arthroplasty* 2018;34:882–886.e1. <https://doi.org/10.1016/j.arth.2018.12.026>.
- [62] Mont MA, Beaver WB, Dysart SH, Barrington JW, Gaizo DJD. Local infiltration analgesia with liposomal bupivacaine improves pain scores and reduces opioid use after total knee arthroplasty: results of a randomized controlled trial. *J Arthroplasty* 2018;33:90–6. <https://doi.org/10.1016/j.arth.2017.07.024>.
- [63] Johnson J, Deren M, Chambers A, Cassidy D, Koruprolu S, Born C. Biomechanical analysis of fixation devices for basicervical femoral neck fractures. *J Am Acad Orthop Surg* 2019;27:e41–8. <https://doi.org/10.5435/jaaos-d-17-00155>.
- [64] Andersen KV, Nikolajsen L, Haraldsted V, Odgaard A, Søballe K. Local infiltration analgesia for total knee arthroplasty: should ketorolac be added? *Br J Anaesth* 2013;111:242–8. <https://doi.org/10.1093/bja/aet030>.