

**G49: Does administration of intravenous steroids (dexamethasone) during major orthopedic procedures increase the risk of subsequent Surgical Site Infection (SSI)/Periprosthetic Joint Infection (PJI)?**

Ibrahim Elganzoury, Armita Armina Abedi , Annette W-Dahl, Jean-Yves Jenny, Javad Mortazavi, Trifon Totlis, Dragan Radoičić, Vladislav Bartak, Azlina Amir Abbas, Ahmed Saeed Younis

**Response/Recommendations:** No. There is no concrete evidence linking intraoperative administration of intravenous low dose steroids to an increased risk of subsequent SSI/PJI.

**Strength of recommendations:** Weak

**Delegate Votes:**

**Rationale:**

In recent years there has been an interest in intravenous (IV) administration of steroids during surgery to reduce the incidence of nausea and pain [1]. During recent World Expert Meeting, administration of IV steroid during surgery was discussed and strongly endorsed [2]. The use of IV steroids had been shown to reduce the need of postoperative narcotics and pain medications after distal radius fixation, elbow fracture surgery and total joint arthroplasty. Patients treated with taper doses of IV steroids after these surgeries have shown to have less postoperative pain and improved range of motion[3][4][5]. Recent studies have demonstrated the effectiveness of perioperative high-dose steroid administration after total hip and knee arthroplasty in reducing postoperative inflammatory response, pain, nausea and vomiting and also accelerating postoperative rehabilitation [6][7][8]. However, there is insufficient data on the most optimal dose of IV steroids, considering side effects and the relation to surgical site infections (SSI) or periprosthetic joint infections (PJI). Further, contraindications for administration of IV steroids during surgery is not known [8]. One of the potential adverse effects of IV steroid relates to potential increase in subsequent SSI and/or PJI.

To evaluate the question posed here, we performed a comprehensive systematic review. All relevant literature were identified using MeSH terms and search of PubMed and Scopus databases. A total of 5,980 articles were identified on initial screening. After excluding duplicates, 5,128 publications remained. After further review, 83 studies were found to meet the inclusion criteria and were selected for full review and data extraction. We sub-grouped the studies into four groups: 1-single low dose (up to 10 mg dexamethasone) steroids 2-single high dose (more than 10 mg dexamethasone) steroids 3- multiple low dose steroids 4- multiple high dose steroids.

**Single Low-Dose IV Steroids:** The review of 15 publication in this category that reported in the rate of SSI showed that the incidence was comparable between the steroid group (1 event in 740 patients) and the placebo group (1 event in 737 patients), yielding a relative risk (RR) of 0.98 (95% confidence interval [CI]: 0.14 to 6.76) [9-23]. Additionally, six studies focusing on PJI outcomes showed no events in either the steroids group (0/272) or the placebo group (0/267) [14-16, 19-21].

**Single High-Dose IV Steroids:** Fourteen studies reported SSI outcomes with more events in the steroids group (8 events in 607 patients) compared to the placebo group (3 events in 611 patients), (RR: 1.99, CI: 0.71-5.60) [16, 24-36]. Furthermore, nine studies on PJI reported an increased incidence in the steroids group (9/384) compared to the placebo group (4/358) (RR: 2.2, CI: 0.72-6.76) [16, 28, 30-36].

**Multiple Low-Dose IV Steroids:** Thirteen studies on SSI outcomes observed a slightly higher number of events in the steroids group (5/640) versus the placebo group (3/638), with an (RR:1.45, CI: 0.45-4.66) [1, 11, 21, 35-44]. For PJI, three studies showed no events in the steroids group (0/84) and two events in the placebo group (2/92) (RR: 0.23; CI: 0.01-4.59) [37, 44-45].

**Multiple High-Dose IV Steroids:** Three studies on SSI outcomes reported one event in the steroids group (1/158) compared to none in the placebo group (0/160) (RR:3.12, CI: 0.13-74.85) [47-49].

For the SSI and PJI outcome, we have downgraded the evidence one level due to indirectness and two levels due to imprecision “insufficient number of events and short follow up period” so the evidence was downgraded from high to very low. Data from non RCTs trials and retrospective studies supported the results of our meta-analysis. Vournin et al. 2018 studied 18,872 total joint arthroplasties and found no statistically significant difference in PJI rate at about five years follow up between patients who received IV 5-10 mg dexamethasone and non-dexamethasone group (OR 1.05, 95% CI 0.71–1.54, P = 0.77) [50]. Also Klement et. al and Richardson et al. found no statistically significant difference in PJI risk after administration of 8-10 mg dexamethasone with total joint arthroplasty[51][52]. Godshow et al. 2019 showed that, in their retrospective cohort, administration of IV dexamethasone did not increase the risk of PJI neither affected the serum glucose level [53]. Jorgensen et al. in a prospective cohort study including 1,442 patients, who received a preoperative high dose steroids (125 mg methyl-prednisone) found no statistically significant increase in infections at three months follow up [54].

## Conclusion:

Based on available data, administration of low dose IV steroids during major orthopedic surgeries does not seem to result in an increase in the rate of postoperative SSI/PJI. There is low evidence that administration of a single or multiple high-dose IV steroids during major orthopedic procedures may increase the risk of SSI/PJI. However, all studies available have a relatively small sample size, and are victim of type II statistical error, and carry immense heterogeneity. Thus, there is a need for large sized RCTs investigating the risk of SSI/PJI as a primary outcome in patients receiving perioperative IV steroids.

## References:

- [1] Teshome D, Fenta E, Hailu S. Preoperative prevention and postoperative management of nausea and vomiting in resource limited setting: A systematic review and guideline. *Int J Surg Open* 2020;27:10–7. <https://doi.org/10.1016/j.ijso.2020.10.002>.
- [2] Abedi AA, Parvizi J, Halawa M, Harty JA, Shao H, Hammad AS. Should Intravenous Corticosteroids Be Administered Routinely During Primary Knee or Hip Arthroplasty to Impart Analgesic and Anti-Inflammatory Properties? *J Arthroplasty*. 2024 Oct 20:S0883-5403(24)01091-X. doi: 10.1016/j.arth.2024.10.078. Epub ahead of print. PMID: 39437864.
- [3] Gottschalk MB, Dawes A, Hurt J, Spencer C, Campbell C, Toston R, et al. A Prospective Randomized Controlled Trial of Methylprednisolone for Postoperative Pain Management of Surgically Treated Distal Radius Fractures. *J Hand Surg Am* 2022;47:866–73. <https://doi.org/10.1016/j.jhsa.2022.06.008>.
- [4] Desai MJ, Matson AP, Ruch DS, Leversedge FJ, Aldridge JM, Richard MJ. Perioperative Glucocorticoid Administration Improves Elbow Motion in Terrible Triad Injuries. *J Hand Surg Am* 2016;41:S44–5. <https://doi.org/10.1016/j.jhsa.2016.07.080>.
- [5] Wagner ER, Hussain ZB, Karzon AL, Cooke HL, Toston RJ, Hurt JT, et al. Methylprednisolone taper is an effective addition to multimodal pain regimens after total shoulder arthroplasty: results

- of a randomized controlled trial: 2022 Neer Award winner. *J Shoulder Elb Surg* 2024;33:985–93. <https://doi.org/10.1016/j.jse.2023.12.016>.
- [6] Yue C, Wei R, Liu Y. Perioperative systemic steroid for rapid recovery in total knee and hip arthroplasty: A systematic review and meta-analysis of randomized trials. *J Orthop Surg Res* 2017;12:1–11. <https://doi.org/10.1186/s13018-017-0601-4>.
  - [7] Zhang LK, Zhu FB, Gao HH, Zhang L, Quan RF. Is intraoperative corticosteroid a good choice for postoperative pain relief in total joint arthroplasty? A meta-analysis of 11 randomized controlled trials. *Med (United States)* 2021;100:E27468. <https://doi.org/10.1097/MD.00000000000027468>.
  - [8] Hannon CP, Fillingham YA, Mason JB, Sterling RS, Casambre FD, Verity TJ, et al. The Efficacy and Safety of Corticosteroids in Total Joint Arthroplasty: A Direct Meta-Analysis. *J Arthroplasty* 2022;37:1898-1905.e7. <https://doi.org/10.1016/j.arth.2022.03.084>.
  - [9] Chen Y, Niu D, Wang Y, Zhao T, Xin W, Qian Q, et al. Perioperative Dexamethasone Split Between 2 Doses Further Reduced Early Postoperative Nausea and Vomiting Than Single-Dose Dexamethasone: A Randomized Blinded Placebo-Controlled Trial. 2024.
  - [10] Huang J-W, Yang Y-F, Gao X-S, Xu Z-H. A single preoperative low-dose dexamethasone may reduce the incidence and severity of postoperative delirium in the geriatric intertrochanteric fracture patients with internal fixation surgery: an exploratory analysis of a randomized, placebo-controlled trial. 2023;18(1)
  - [11] Kardash KJ, Sarrazin F, Tessler MJ, Velly AM. Single-dose dexamethasone reduces dynamic pain after total hip arthroplasty. 2008;106(4):1253-7. [6]
  - [12] Kim J-K, Ro DH, Lee H-J, Park J-Y, Han H-S, Lee MC. Efficacy of Systemic Steroid Use Given One Day After Total Knee Arthroplasty for Pain and Nausea: A Randomized Controlled Study. 2020;35(1):69-75.
  - [13] Lei Y-T, Xu B, Xie X-W, Xie J-W, Huang Q, Pei F-X. The efficacy and safety of two low-dose peri-operative dexamethasone on pain and recovery following total hip arthroplasty: a randomized controlled trial. 2018;42(3):499-505.
  - [14] Li D, Wang Q, Zhao X, Luo Y, Kang P. Comparison of Intravenous and Topical Dexamethasone for Total Knee Arthroplasty: A Randomized Double-Blinded Controlled Study of Effects on Dexamethasone Administration Route and Enhanced Recovery. 2021;36(5):1599-606.
  - [15] Li Q, Fang G, Liao W, Chen B, Yang Y, Liao J, et al. Intraoperative intravenous versus periarticular injection of glucocorticoids in improving clinical outcomes after total knee arthroplasty: A prospective, randomized and controlled study. 2024;32(2).
  - [16] Liu X-Y, Mou P, Cao J, Wang H-Y, Zeng W-N, Zhou Z-K. Effects of Dexamethasone on Postoperative Glycemic Control in Patients After Primary Total Joint Arthroplasty: A Randomized Double-Blind Controlled Trial. 2024;39(9):2213-20.
  - [17] Mo Y, Wang C, Yin D, Li F. Efficacy of Dexamethasone in Reducing Pain and Inflammation and Accelerating Total Hip Arthroplasty Postoperative Recovery: A Randomized Controlled Trial. 2024;39(4):589-95.
  - [18] Saini MK, Reddy NR, Reddy PJ, Thakur AS, Reddy CD. The application of low-dose dexamethasone in total knee arthroplasty: finding out the best route and dosage schedule. 2023;143(2):1005-12.
  - [19] Wagner ER, Hussain ZB, Karzon AL, Cooke HL, Toston RJ, Hurt JT, et al. Methylprednisolone

taper is an effective addition to multimodal pain regimens after total shoulder arthroplasty: results of a randomized controlled trial: 2022 Neer Award winner. 2024;33(5):985-93.

- [20] Wu C, Luo D, Zhu Y, Zhao Q, Wang J, Dai Y. Efficacy of combining intravenous and topical dexamethasone against postoperative pain and function recovery after total knee arthroplasty: A prospective, double-blind, randomized controlled trial. 2023;31(2).
- [21] Yu Y, Lin H, Wu Z, Xu P, Lei Z, Mayr J. Perioperative combined administration of tranexamic acid and dexamethasone in total knee arthroplasty - benefit versus harm? 2019;98(34).
- [22] Wu Y, Lu X, Ma Y, Zeng Y, Bao X, Xiong H, et al. Perioperative multiple low-dose Dexamethasones improves postoperative clinical outcomes after Total knee arthroplasty. 2018;19(1).
- [23] Abdelhameed MA, Khalifa AA, Mahran MA, Kameel DN, Bakr HM, Abdelnasser MK. A Single Preoperative Low Dose of Dexamethasone Is Efficacious in Improving Early Postoperative Pain, Function, Nausea, and Vomiting After Primary Total Knee Arthroplasty: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Arthroplasty*. 2024 Nov 30:S0883-5403(24)01279-8. doi: 10.1016/j.arth.2024.11.061. Epub ahead of print. PMID: 39622426.
- [24] Lindberg-Larsen V, Ostrowski SR, Lindberg-Larsen M, Røvsing ML, Johansson PI, Kehlet H. The effect of pre-operative methylprednisolone on early endothelial damage after total knee arthroplasty: a randomised, double-blind, placebo-controlled trial. 2017;72(10):1217-24.
- [25] Aminmansour B, Khalili HA, Ahmadi J, Nourian M. Effect of high-dose intravenous dexamethasone on postlumbar discectomy pain. *Spine (Phila Pa 1976)*. 2006 Oct 1;31(21):2415-7. doi: 10.1097/01.brs.0000238668.49035.19.
- [26] An Y-Z, Xu M-D, An Y-C, Liu H, Zheng M, Jiang D-M. Combined Application of Dexamethasone and Tranexamic Acid to Reduce the Postoperative Inflammatory Response and Improve Functional Outcomes in Total Hip Arthroplasty. 2020;12(2):582-8.
- [27] Chan PK, Chan TCW, Mak CYH, Chan THM, Chan SHW, Wong SSC, et al. Pain Relief After Total Knee Arthroplasty with Intravenous and Periarticular Corticosteroid: A Randomized Controlled Trial. 2023;105(12):924-32.
- [28] Kluger MT, Skarin M, Collier J, Rice DA, McNair PJ, Seow MY, et al. Steroids to reduce the impact on delirium (STRIDE): a double-blind, randomised, placebo-controlled feasibility trial of pre-operative dexamethasone in people with hip fracture. 2021;76(8):1031-41.
- [29] Lei Y, Huang Z, Huang Q, Pei F, Huang W. Is a split-dose intravenous dexamethasone regimen superior to a single high dose in reducing pain and improving function after total hip arthroplasty? A randomized blinded placebo-controlled trial. 2020;102(11):1497-504.
- [30] Liu X-Y, Mou P, Cao J, Chen X-M, Wang H-Y, Zeng W-N, et al. The effect of a split-dose intravenous dexamethasone and a single high-dose on postoperative blood glucose after total joint arthroplasty: a randomized double-blind placebo-controlled trial. 2024;19(1).
- [31] Lunn TH, Andersen LO, Kristensen BB, Husted H, Gaarn-Larsen L, Bandholm T, et al. Effect of high-dose preoperative methylprednisolone on recovery after total hip arthroplasty: A randomized, double-blind, placebo-controlled trial. 2013;110(1):66-73.
- [32] Lunn TH, Kristensen BB, Andersen LØ, Husted H, Otte KS, Gaarn-Larsen L, et al. Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: A randomized, placebo-controlled trial. 2011;106(2):230-8.

- [33] Nielsen NI, Kehlet H, Gromov K, Troelsen A, Husted H, Varnum C, et al. High-dose steroids in high pain responders undergoing total knee arthroplasty: a randomised double-blind trial. 2022;128(1):150-8.
- [34] Shafiei SH, Siavashi B, Ghasemi M, Golbakhsh MR, Baghdadi S. Single High-Dose Systemic Methylprednisolone Administered Preoperatively Improves Pain Control and Sleep Quality After Total Hip Arthroplasty: A Double-Blind, Randomized Controlled Trial. 2022;16:733]
- [35] Xu H, Xie J, Yang J, Huang Z, Wang D, Pei F. Synergistic Effect of a Prolonged Combination Course of Tranexamic Acid and Dexamethasone Involving High Initial Doses in Total Knee Arthroplasty: A Randomized Controlled Trial. 2021;36(5):515-23.
- [36] Huang Z, Dong H, Ye C, Zou Z, Wan W. Clinical utilization of methylprednisolone in conjunction with tranexamic acid for accelerated rehabilitation in total hip arthroplasty. 2023;18(1).
- [37] McLawhorn AS, Poultsides LA, Sakellariou VI, Kunze KN, Fields KG, Jules-Elysée K, et al. Low-Dose Perioperative Corticosteroids Can Be Administered Without Additional Morbidity in Patients Undergoing Bilateral Total Knee Replacement: A Retrospective Follow-up Study of a Randomized Controlled Trial. 2022;18(1):48-56.22
- [38] Dissanayake R, Du HN, Robertson IK, Ogden K, Wiltshire K, Mulford JS. Does Dexamethasone Reduce Hospital Readiness for Discharge, Pain, Nausea, and Early Patient Satisfaction in Hip and Knee Arthroplasty? A Randomized, Controlled Trial. 2018;33(11):3429-36.23
- [39] Hatayama K, Terauchi M, Oshima A, Kakiage H, Ikeda K, Higuchi H. Comparison of Intravenous and Periarticular Administration of Corticosteroids in Total Knee Arthroplasty: A Prospective, Randomized Controlled Study. 2021;103(4):319-25.24
- [40] Lei Y, Huang Q, Xu B, Zhang S, Cao G, Pei F. Multiple Low-Dose Dexamethasone Further Improves Clinical Outcomes Following Total Hip Arthroplasty. 2018;33(5):1426-31.25
- [41] Lei Y, Huang Z, Huang Q, Huang W, Pei F. Repeat Doses of Dexamethasone up to 48 Hours Further Reduce Pain and Inflammation After Total Hip Arthroplasty: A Randomized Controlled Trial. 2020;35(11):3223-9.26]
- [42] Li D, Zhao J, Yang Z, Kang P, Shen B, Pei F. Multiple Low Doses of Intravenous Corticosteroids to Improve Early Rehabilitation in Total Knee Arthroplasty: A Randomized Clinical Trial. 2019;32(2):171-9.27
- [43] Li F, Huang X, Liu W, Huang W, Cheng J, Yin D. Dexamethasone with aggressive warming facilitates pain reduction, reduced blood loss, and quicker recovery after total hip arthroplasty. 2023;13(1).28
- [44] Lucero CM, García-Mansilla A, Zanotti G, Comba F, Slullitel PA, Buttarro MA. A Repeat Dose of Perioperative Dexamethasone Can Effectively Reduce Pain, Opioid Requirement, Time to Ambulation, and In-Hospital Stay After Total Hip Arthroplasty: A Prospective Randomized Controlled Trial. 2021;36(12):3938-44.29[30]
- [45] Sculco PK, McLawhorn AS, Desai N, Su EP, Padgett DE, Jules-Elysee K. The Effect of Perioperative Corticosteroids in Total Hip Arthroplasty: A Prospective Double-Blind Placebo Controlled Pilot Study. 2016;31(6):1208-12.30
- [46] Xu B, Ma J, Huang Q, Huang Z-Y, Zhang S-Y, Pei F-X. Two doses of low-dose perioperative dexamethasone improve the clinical outcome after total knee arthroplasty: a randomized controlled study. 2018;26(5):1549-56.31

- [47] Li F, Huang X, Liu W, Huang W, Wang C, Yin D. Application of dexamethasone combined with tranexamic acid in perioperative period of total hip arthroplasty. 2022;101(42):E31223.
- [48] Li B, Yang X, Liu F, Huang H, Zhang B, Li X, Lu Q, Liu P, Fan L. Effect of Perineural or Intravenous Betamethasone on Femoral Nerve Block Outcomes in Knee Arthroplasty: A Randomized, Controlled Study. *Orthop Surg*. 2024 Apr;16(4):873-881. doi: 10.1111/os.14018.
- [49] Xu H, Zhang S, Xie J, Lei Y, Cao G, Pei F. Multiple Doses of Perioperative Dexamethasone Further Improve Clinical Outcomes After Total Knee Arthroplasty: A Prospective, Randomized, Controlled Study. 2018;33(11):3448-54.
- [50] Vuorinen MA, Palanne RA, Mäkinen TJ, Leskinen JT, Huhtala H, Huotari KA Infection safety of dexamethasone in total hip and total knee arthroplasty : a study of eighteen thousand , eight hundred and seventy two operations. *Int Orthop*. 2019 Aug;43(8):1787-1792. doi: 10.1007/s00264-018-4156-8.
- [51] Klement MR, Wilkens HS, Fillingham YA, Manrique J, Austin MS, Parvizi J. Intraoperative Dexamethasone Reduces Readmission Rates Without Affecting Risk of Thromboembolic Events or Infection After Total Joint Arthroplasty. *J Arthroplast* n.d.;33:3252–6. <https://doi.org/10.1016/j.arth.2018.05.016>.
- [52] Richardson AB, Bala A, Wellman SS, Attarian DE, Bolognesi MP, Grant SA, et al. Perioperative Dexamethasone Administration Does Not Increase the Incidence of Postoperative Infection in Total Hip and Knee Arthroplasty: A Retrospective Analysis. *J Arthroplasty* 2016;31:1784–7. <https://doi.org/10.1016/j.arth.2016.01.028>.
- [53] Godshaw BM, Mehl AE, Shaffer JG, Meyer MS, Thomas LC, Chimento GF. The Effects of Peri-Operative Dexamethasone on Patients Undergoing Total Hip or Knee Arthroplasty : Is It Safe for Diabetics ? *J Arthroplasty* 2019;34:645–9. <https://doi.org/10.1016/j.arth.2018.12.014>.
- [54] Jørgensen CC, Pitter FT, Kehlet H. Safety aspects of preoperative high-dose glucocorticoid in primary total knee replacement. *Br J Anaesth* 2017;119:267–75. <https://doi.org/10.1093/bja/aex190>.