

Ephedrine Use During Total Joint Arthroplasty Is Associated With Increased Risk of Periprosthetic Joint Infection

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INTRODUCTION: Total joint arthroplasty (TJA) is a common and generally successful surgery aimed at relieving pain and improving quality of life, but comes with several risks, including the serious complication of periprosthetic joint infection (PJI) which affects 2.0% to 2.4% of all total hip and knee arthroplasties respectively [1]. Increased risk for PJI has been linked to demographic factors [2], genetic factors [3], and perioperative variables [4] [5], but intraoperative vasopressor use has not been investigated as a risk factor. This study explores the potential relationship between intraoperative vasopressor administration (ephedrine, phenylephrine, or vasopressin) as a risk factor for 30-day and 90-day readmission along with PJI in TJA.

METHODS: In this retrospective study of 1,286 patients who underwent primary TJA (899 TKAs and 390 THAs) from our institution between 2020-2025, patients were categorized based on any intraoperative vasopressor use, as approved by our institutional review board. 562 patients (43.7%) were male. To identify the independent predictors of 30-day readmission, 90-day readmission, and PJI, multivariable logistic regression was used.

RESULTS SECTION: Out of the 1,286 patients included, 494 (38.4%) received no vasopressors intraoperatively, 557 (43.3%) received one vasopressor, and 235 (18.3%) received two or more. All-cause readmission rates for 30 and 90-days were not significantly different based on vasopressor use, however patients receiving two or more vasopressors had a higher risk of PJI within 90 days (0.2 vs. 0.5 vs. 2.1%, $p = 0.02$) regardless of anesthesia type (general vs. regional). The only independent predictor of increased 30-day readmission rate was undergoing a THA procedure rather than a TKA (OR = 4.32, 95% CI: 1.73 – 10.83, $p = 0.001$) while regional anesthesia was significantly protective (OR = 0.35, 95% CI: 0.14 - 0.84, $p = 0.025$). Regional anesthesia was also independently protective of PJI (OR = 0.14, 95% CI: 0.03 – 0.57, $p = 0.006$), while ephedrine administration was an independent predictor of increase PJI risk (OR = 1.05, 95% CI: 1.01 – 1.10, $p=0.025$).

DISCUSSION: In this study, administration of ephedrine intraoperatively was significantly associated with an increased risk for PJI which is a novel finding not reported in the literature. For each mg of ephedrine administered intraoperatively, PJI risk increased by 5%. Regional anesthesia was independently associated with reduced odds of 30-day readmission and PJI, which supports previously reported findings. Due to the retrospective nature of our study and the relatively small sample size, we achieved a statistical power of 76%, therefore further multi-center studies are required with larger sample sizes.

SIGNIFICANCE/CLINICAL RELEVANCE: This study indicates the impact of multidisciplinary intraoperative decisions such as vasopressor use on postoperative outcomes in TJA, and identifies intraoperative ephedrine administration as a potential risk factor for PJI.

REFERENCES:

- [1] Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty* 2012;27:61-65.e1. <https://doi.org/10.1016/j.arth.2012.02.022>.
- [2] Weinstein EJ, Stephens-Shields AJ, Newcomb CW, Silibovsky R, Nelson CL, O'Donnell JA, et al. Incidence, Microbiological Studies, and Factors Associated With Prosthetic Joint Infection After Total Knee Arthroplasty. *JAMA Netw Open* 2023;6:e2340457. <https://doi.org/10.1001/jamanetworkopen.2023.40457>.
- [3] Hijazi A, Hasan A, Pearl A, Memon R, Debeau M, Roldan M, et al. Genetic Polymorphisms Associated with Perioperative Joint Infection following Total Joint Arthroplasty: A Systematic Review and Meta-Analysis. *Antibiotics (Basel)* 2022;11:1187. <https://doi.org/10.3390/antibiotics11091187>.
- [4] Scigliano NM, Carender CN, Glass NA, Deberg J, Bedard NA. Operative Time and Risk of Surgical Site Infection and Periprosthetic Joint Infection: A Systematic Review and Meta-Analysis. *Iowa Orthop J* 2022;42:155–61.
- [5] Helwani MA, Avidan MS, Ben Abdallah A, Kaiser DJ, Clohisy JC, Hall BL, et al. Effects of regional versus general anesthesia on outcomes after total hip arthroplasty: a retrospective propensity-matched cohort study. *J Bone Joint Surg Am* 2015;97:186–93. <https://doi.org/10.2106/JBJS.N.00612>.

IMAGES AND TABLES:

Vasopressors Given	Sample Size (n)	30-day Readmission	90-day Readmission	PJI
0	494	2.0%	1.0%	0.2%
1	557	1.4%	2.0%	0.5%
2 or 3	235	3.8%	1.7%	2.1%
p-value	—	0.111	0.458	0.020

Table 1. Hospital readmission rates within 30 days for any reason, 90 days for any reason, and for periprosthetic joint infection (PJI) within 90 days for patients receiving 0, 1, or 2+ vasopressors intraoperatively as a combination of phenylephrine, vasopressin, and/or ephedrine. P-values calculated using chi-square tests for 30-day and 90-day readmission, and fisher's exact test for PJI. Significance = $p < 0.05$.

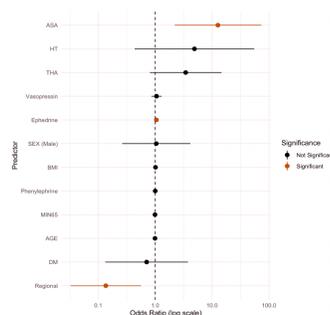


Figure 1. Forest plot of adjusted odds ratios (ORs) and 95% confidence intervals (CI) for hospital readmission within 90 days due to periprosthetic joint infection (PJI), derived from multivariable logistic regression.