Vancomycin Powder Use in Fractures at High Risk of Surgical Site Infection

Rabah Qadir, MD,[a] Timothy Costales, MD,[a] Max Coale, BA,[a] Alexandra Mulliken, BS,[a] Timothy Zerhusen, Jr, BS,[a] Manjari Joshi, MBBS,[b] Renan C. Castillo, PhD,[c] Anthony R. Carlini, MS,[c] and Robert V. O'Toole, MD[a]

Objectives: To determine if the use of intrawound vancomycin powder reduces surgical-site infection after open reduction and internal fixation of bicondylar tibial plateau, tibial pilon, and calcaneus fractures.

Design: Retrospective analysis.

Setting: Level I trauma center.

Patients: All fractures operatively treated from January 2011 to February 2015 were reviewed; 583 high-risk fractures were included, of which 35 received topical vancomycin powder. A previously published prospectively collected cohort of 235 similar high-risk fractures treated at our center from 2007 through 2010 served as a second comparison group.

Intervention: Topical vancomycin powder at wound closure.

Main Outcome Measurements: Deep surgical-site infection. Analyses used both univariate comparison of all patients and 1:2 matching analysis using both nearest neighbor and propensity-based matching.

Results: Compared with a control group of fractures treated during the same time period without vancomycin powder, the infection rate with vancomycin powder was significantly lower [0% (0/35) vs. 10.6% (58/548), $P = 0.04$]. Compared with our previously published historical infection rate of 13% for these injuries, vancomycin powder was also associated with significantly decreased deep surgical-site infection (0% vs. 13%, $P = 0.02$). These results agreed with the matched analyses, which also showed lower infection in the vancomycin powder group (0% vs. 11%–16%, $P \leq 0.05$).

Conclusions: Vancomycin powder may play a role in lowering surgical-site infection rates after fracture fixation. A larger randomized controlled trial is needed to validate our findings.

Key Words: vancomycin powder, deep infection, surgical-site infection, tibial plateau fracture, tibial pilon fracture, calcaneus fracture

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

(*J Orthop Trauma* 2021;35:23–28)

INTRODUCTION

Deep infection after treatment of high-energy fractures is a devastating complication, with incidence reported to be as high as 67%.[1] Certain high-risk injury patterns, such as tibial plateau, tibial pilon, and calcaneus fractures, have been reported to have infection rates higher than 50%.[2–5] More modern series have lower values, but large prospective trials still report infection rates of 11%–16% for these injury patterns, even with planned delayed definitive fracture treatment and modern interventions that are specifically geared toward decreasing infection.[6,7] Prevention of surgical-site infection after fracture fixation is paramount, considering that infections can result in substantial morbidity, health care resource utilization, and costs as high as $55,000–$270,000 per case in the United States.[8–10]

Recently, intrawound application of vancomycin powder has been shown to be effective in decreasing postoperative infection by multiple retrospective spine surgery studies[11–19] and a study of surgical site infection in patients with diabetes undergoing foot and ankle surgery.[20] In the setting of 1 study in spine trauma surgery, the use of intrawound vancomycin powder substantially decreased infection rates from 13% to 0%.[18]

Despite the promise of this technique as shown in spine surgery, few data exist examining the use of intrawound

Accepted for publication June 10, 2020.

From the [a]Department of Orthopaedics, R Adams Cowley Shock Trauma Center, University of Maryland School of Medicine, Baltimore, MD; [b]Division of Infectious Disease, R Adams Cowley Shock Trauma Center, University of Maryland School of Medicine, Baltimore, MD; and [c]Johns Hopkins Center for Injury Research and Policy, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

R. Qadir and his institution received research support funding for this work from AO North America. No other outside source of funding was obtained for this study. R. V. O'Toole is a paid consultant for CoorsTek, Imagen, and Smith & Nephew, receives stock options from Imagen, and receives royalties from CoorsTek, unrelated to this study. He is currently the Principal Investigator on Department of Defense–funded randomized controlled trial on the same topic. M. Joshi has received payment for consultancy and development of educational presentations from Pfizer, Forest, and Atox. Her institution has current grants from Atox. The remaining authors report no conflict of interest.

Presented in part at the Annual Meeting of the AAOS, March 1, 2016, Orlando, FL.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jorthotrauma.com).

Reprints: Robert V. O'Toole, MD, Department of Orthopaedics, R Adams Cowley Shock Trauma Center, University of Maryland School of Medicine, 22 South Greene St, T3R62, Baltimore, MD 21201 (e-mail: rotoole@som.umaryland.edu).

DOI: 10.1097/BOT.0000000000001863

vancomycin powder to reduce infection after open reduction and internal fixation of bicondylar tibial plateau, tibial pilon, and calcaneus fractures.[21] We therefore explored whether vancomycin powder decreases the incidence of deep surgical-site infection in these high-risk operatively treated fractures.

PATIENTS AND METHODS

After receiving institutional review board approval of the study protocol, we conducted a retrospective cohort study of all orthopaedic trauma surgery performed at a single level I trauma center from January 2011 to February 2015. We initially screened our trauma registry for the following injury patterns: OTA/AO type 41C tibial plateau, OTA/AO type 43B or 43C tibial pilon, and OTA/AO type 81A, 81B, or 81C calcaneus fractures.

We then individually reviewed each chart to screen for inclusion as an injury at high risk of sustaining a surgical-site infection. For the purpose of this study, we defined "high-risk" fractures as fractures requiring planned surgical delay and staged fracture fixation because of soft-tissue concerns. We included all closed and open injuries, including those requiring soft-tissue coverage and/or fasciotomies for compartment syndrome.

For plateau fractures, we excluded injuries not requiring initial external fixation and planned surgical delay to allow for swelling to resolve before fixation and for those that did not require fixation across both condyles. For pilon fractures, we excluded any injury that did not require initial ankle-spanning external fixation. For calcaneus fractures, we excluded any injury that was amenable to early (<10 days) fixation and any injury that could be fixed by percutaneous means not involving plate fixation.

Patients younger than 18 years and those who did not have a minimum follow-up duration of 6 months were also excluded. Six months were chosen as the minimum follow-up period because the previous work has shown that 85% of open fractures and 95% of closed fractures that presented with infection did so within that time frame.[22] Initially, 598 patients older than 18 years of age were eligible for the study. Fifteen were lost before attaining the required minimum of 6 months of follow-up, leaving 583 high-risk fractures for inclusion in the study.

In all patients, fixation surgery was performed by fellowship-trained orthopaedic trauma surgeons. During the study period, patients received intravenously administered cefazolin preoperatively and for 24 hours postoperatively for both open and closed fractures. Clindamycin was typically substituted for penicillin-allergic patients. Vancomycin was not typically used for intravenous prophylaxis at our institution. We did not use aminoglycosides for type III open fractures at our institution per our institutional protocol. Penicillin was added for barnyard-type open injuries.

Our treatment group consisted of all patients who received vancomycin powder and were treated from October 2012, when vancomycin powder began being used at our center at the discretion of the treating surgeon, to February 2015. Of the 35 patients identified as receiving vancomycin powder, all 35 patients were followed for at least 6 months and included in the study group; 23 were treated by 1 surgeon, and the remaining 12 were treated by 3 other surgeons. In this cohort, 1 g of vancomycin powder was applied topically to the surgical site directly in contact with the fixation device at the time of wound closure. The powder was not typically mixed with normal saline or any other material and was applied directly as a powder at the time of wound closure. We verified patients who received vancomycin powder by reviewing each operative note, intraoperative documentation, and pharmacy records. We were careful to distinguish those patients from patients who received vancomycin through antibiotic spacers or beads. No patients who received vancomycin powder were lost to follow-up.

Our primary control group consisted of the remaining 548 fractures that did not receive vancomycin powder during the study time period. For further comparison, we additionally used a second previously published control group that had the same definition of high-risk plateau, pilon, and calcaneus fractures and was from the same institution (n = 235).[6] That group had been treated from April 2007 to November 2010 as part of a prospective randomized controlled trial investigating the effect of supplemental perioperative oxygen on surgical-site infection. The data represent high-quality prospectively collected data on surgical-site infection from a few years before the time point of this study. Because this study is not a randomized trial, we used both control cohorts as estimates of the baseline rate of surgical-site infection at this institution. The characteristics of all 3 cohorts are presented in Table 1.

Our primary outcome measure was deep surgical-site infection, which we defined in keeping with the Centers for Disease Control and Prevention (CDC) definition as postoperative infection requiring operative débridement with intraoperative identification that infection was deep to the subcutaneous layer. Superficial infections that required only antibiotic treatment or local wound therapy were not included in our outcome measure. We considered deep infection to be present regardless of the time after surgery, although the CDC definition has varied over time on this issue and considered surgical-site infection to be either within 90 days or 1 year of surgery depending on the version of the CDC guidelines. Consistent with the CDC guidelines, we included both culture-positive and culture-negative infections. All patients with infection were included regardless of the follow-up duration.

Statistical Analysis

All 3 cohorts were initially assessed for comparability using univariate and bivariate analyses. Subsets of the prospective and retrospective cohorts (both comprised only of control cases) were created for use as part of the primary analysis of outcomes. The matched control cases for each of the control cohorts were comprised of 70 cases (thus creating a 2:1 ratio of control to treatment cases). The process was repeated using matching ratios of 3:1 and 4:1 (105 and 140 cases, respectively) based on the literature, suggesting this range of ratios are best suited for managing the tradeoff between minimizing bias and maximizing sample size.[23,24]

TABLE 1. Characteristics of Cohorts

	Vancomycin Cohort (n = 35)	Prospective Cohort (n = 235)	Retrospective Cohort (n = 548)
Bone, n (%)			
Calcaneus	6 (17)	61 (26)	126 (23)
Pilon	10 (29)	91 (39)	208 (38)
Plateau	19 (54)	83 (35)	214 (39)
Tobacco use, n (%)	13 (37)	101 (43)	171 (31)
Diabetes, n (%)	6 (17)	18 (8)	57 (10)
Male, n (%)	22 (63)	173 (74)	354 (65)
Open fracture, n (%)	4 (11)	39 (17)	111 (20)
LOS, mean days (SD)	7.7 (7.8)	3.2 (3.4)	7.7 (9.9)
Age, mean years (SD)	42.3 (16.4)	42.7 (12.3)	46.1 (15.5)
Surgeon, n (%)			
A	0 (0)	12 (5)	28 (5)
B	5 (14)	10 (4)	80 (15)
C	3 (9)	49 (21)	124 (23)
D	5 (14)	50 (21)	138 (25)
E	22 (63)	64 (27)	121 (22)
F	0 (0)	10 (4)	27 (5)
G*	0 (0)	40 (17)	30 (5)

LOS, length of stay.
*Surgeons with fewer than 30 total cases across all cohorts are presented as group G.

At each ratio level, 2 matching techniques were used to create the resulting data sets. The first method used a nearest neighbor algorithm using the Mahalanobis distance as the metric for choosing cases. The second match used the propensity score of receiving the treatment as the distance measure.

All matching was performed on a set of 6 covariates available in all 3 cohorts: age, bone injured, open fracture status, diabetes status, sex, and tobacco use. In calculating the matching distances for the algorithms, the historical prospective control and retrospective control groups were separately joined to the single cohort of treatment cases. Distances were calculated for all possible combinations of treatment versus control cases in the joined set to select the matched cases. Both matching techniques are considered "greedy" because cases are matched in a particular order without replacement from the available control set. In situations with ties in the distances being matched, cases were selected in a random order. The matched data sets were then each compared with the joined, full cohorts used to create them and measures of balance among the covariates were assessed before and after the matching process.

The entire process was repeated using a more parsimonious model (covariates: age, bone injured, and diabetes status). Infection rates were then compared between the matched data sets and the original treatment cohort. Results associated with the full model at a 2:1 match ratio are presented in Table 2 and Fig. 1. Additional results for all models and match ratios are available as **Supplemental Digital Content 1** (see **Table**, http://links.lww.com/JOT/B117). All analyses were performed using the R software package version 3.4.1, and the statistical significance was defined as a 2-sided P value of < 0.05.

RESULTS

In the 214 bicondylar tibial plateau fractures without vancomycin powder use 22 (10.3%) deep infections occurred. In 208 operatively treated tibial pilon fractures, 29 (14%) deep infections occurred. In 126 calcaneus fractures, 5 (4%) deep infections occurred. The overall deep infection rate associated with high-risk operatively treated fractures without vancomycin powder use was 10.6% (58 of 548 cases).

No (0%) infections occurred in 35 high-risk fractures treated with vancomycin powder compared with the retrospective control group during the same time period in which 58 deep infections occurred (10.6%) in similar high-risk fractures treated without vancomycin powder. This difference was statistically significant ($P = 0.04$). When comparing our vancomycin cohort with our prospective historical cohort in whom 31 deep infections occurred in 235 patients (13.2%), vancomycin powder significantly reduced the infection rate ($P = 0.02$). No side effects or wound healing problems were noted in the vancomycin powder group.

After matching our control groups for the 6 covariates, our vancomycin cohort was found to have an infection rate significantly lower than both prospective cohorts (0% vs. 16%, $P = 0.01$; and 0% vs. 14%, $P = 0.03$) (Table 2). Similarly, our vancomycin cohort had a lower infection rate than both matched retrospective cohorts (0% vs. 11%, $P = 0.05$; and 0% vs. 7%, $P = 0.17$), although the difference did not attain statistical significance for the propensity-matched cohort. Table 2 presents a comparison of infection rates among the study groups using 6 different combinations of analysis and control group. Infection rates and findings of statistical significance were similar across each of the match ratio levels used. In addition, results were generally consistent using a full or more parsimonious model for the matching

TABLE 2. Infection Rate by Cohort*

	Cases (n)	Infected (n)	Infection Rate (95% CI)	*P*†
Vancomycin cohort	35	0	0.00 (0.00–0.07)	—
Prospective (raw)	235	31	0.13 (0.09–0.18)	0.02
Prospective 2:1 (NN)	70	11	0.16 (0.09–0.26)	0.01
Prospective 2:1 (PS)	70	10	0.14 (0.08–0.24)	0.03
Retrospective (raw)	548	58	0.11 (0.08–0.13)	0.04
Retrospective 2:1 (NN)	70	8	0.11 (0.06–0.20)	0.05
Retrospective 2:1 (PS)	70	5	0.07 (0.03–0.15)	0.17

CI, confidence interval; NN, nearest neighbor matched using the Mahalanobis distance; PS, propensity score matched.
*Matched controls chosen based on the following covariates: age, bone injured, open fracture status, diabetes status, sex, and tobacco use. Where applicable, cohorts show ratio of matched controls to the original vancomycin cohort.
†Fisher's exact test.

process. One exception was the nearest neighbor matched comparison in the retrospective cohort where the parsimonious model comparisons had slightly lower infection rates that shifted findings from below to above the threshold for statistical significance. No adverse events attributed to the powder were noted in the vancomycin group nor were any wound healing problems documented in the medical records.

DISCUSSION

Local antibiotic usage to reduce surgical-site infection is appealing to clinicians. Higher concentrations of antibiotics, that are well above the minimum inhibitory concentration and can stay in the local wound environment for some time, might be obtained with less risk of complication to remote organs as can occur with systemic intravenous use.[25] Traumatic musculoskeletal wounds consist of local tissue necrosis and hematoma that are potential nidi for infection and therefore increase the risk of surgical-site infection for fracture surgery. Moreover, systemic antibiotic delivery might be inadequate because the injuries contain local areas of tissue ischemia. Surgery, including open reduction and internal fixation, naturally adds to this ischemic insult rendering these wounds highly susceptible to infection. Local antibiotic delivery, such as that from vancomycin powder, theoretically would be useful in these settings.

This study assessed whether vancomycin powder decreases the incidence of deep surgical-site infection in 3 fractures known to have relatively high risk of infection. If vancomycin powder decreases surgical-site infections in this patient population and others, it could have an important public health benefit. Vancomycin powder is inexpensive (approximately $12 per application at our center). Furthermore, vancomycin powder is readily available in the operating room and takes little additional operative time to apply.

Vancomycin powder has been associated with decreased postoperative infection rates in multiple retrospective studies. Sweet et al[12] showed, in a retrospective cohort of 1732 patients who underwent thoracolumbar fusion, that when vancomycin powder was applied, infections dropped

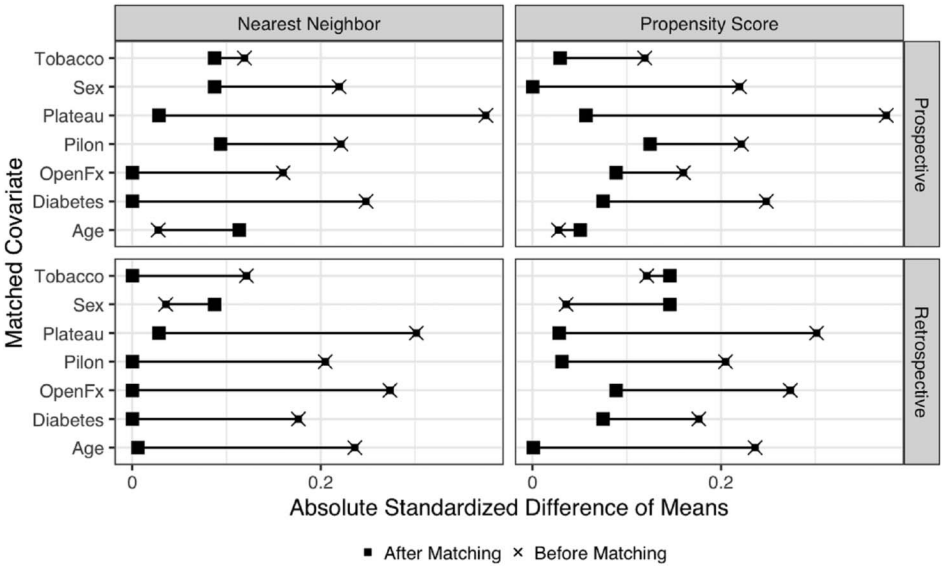

FIGURE 1. Covariate differences between treated and control cases before and after matching for prospective and retrospective cohorts.

from 2.6% to 0.2%. The authors applied a total of 2 g of vancomycin powder: 1 g was mixed in with bone grafting material to allow adherence to the microstructure of the graft and to minimize wound washout, and the remaining 1 g was sprinkled evenly in the deep and superficial portions of the wound during closure. At 2.5 years average follow-up, no adverse clinical outcomes or wound complications had occurred with vancomycin powder use. Our use of vancomycin powder for fracture surgery is similar to Sweet et al in that we applied the powder topically to deep and superficial portions of the wound during closure. We took extra care to ensure the powder was in direct contact with the fixation device. Retrospective spine studies have reproduced results similar to Sweet et al, reporting infection rates decreasing from 15% to 0% with no detrimental effects on the patients or implants.[11,14–17,26]

Surprisingly, little clinical work has studied the use of vancomycin powder in the orthopaedic trauma patient, in whom implant-related infections have historically been relatively high compared with other orthopaedic subspecialties. Recently, basic science work has supported the concept.[27] Surgical-site infection rates have varied over time. Ruffolo et al[28] presented the largest series of bicondylar tibial plateau fractures, reporting an overall 27.9% major complication rate with 23.6% deep infections in 140 patients. Earlier literature reported infection rates for high-energy tibial plateau fractures between 5% and 80%.[5,29–32] Similarly, pilon fractures have reported infection rates from 5% to 40%.[2,29–32] Calcaneus fractures are associated with soft-tissue complications and infections in the range of 0%–20%.[33–35] Regardless of the precise rate of current infection, it is recognized that these high-risk surgical cases are at risk for surgical-site infection and have recently been the subject of at least 2 prospective trials attempting to reduce infection rates (negative pressure wound therapy and supplemental oxygen).[6,7] Our data suggest that perhaps vancomycin powder is another technique for clinicians to consider for reducing infection rates.

Vancomycin powder might be particularly useful in cases of orthopaedic trauma. It has been reported that 56% of implant-related infections in orthopaedic trauma surgery at a single center involved *Staphylococcus aureus (S. aureus)*,[22] of which 58% (32% of all infections) were methicillin-resistant *S. aureus*. The addition of other antibiotics could possibly provide broader coverage and better reduction; we have no experience with other types of intrawound antibiotic powder to date.

Strengths of our study include the novelty of this investigation within orthopaedic fracture surgery. Furthermore, we used an easily verifiable outcome measure (deep surgical-site infection by CDC criteria) through a retrospective review in a fracture type that has been identified in prospective trials as being at risk for infection.[6,7] Our retrospective control group and historical prospective comparison group were both established at the same institution with the same surgeons. Finally, our sample size was large enough to show statistical significance for our primary outcome measure in several matched data sets. Rigorous statistical matching techniques and more than 1 control group were used. All analyses consistently indicated the vancomycin powder group to have a lower rate of surgical-site infection.

Study limitations include those typical of all retrospective studies. First, although the control groups are both large and we showed statistically and clinically significant findings, the study group is relatively small, preventing subgroup analyses. We cannot address questions outside our study design, such as the performance of vancomycin powder when intravenous antibiotics are not also administered, because all patients received intravenous antibiotics in both groups. Despite statistically significant findings, results are limited by the sample size as the treatment group included just 35 patients. Furthermore, although the statistical comparisons were largely consistent in their results, some variability in the retrospective propensity matched comparisons exists. This might be due to a paradox where propensity matching could increase the matched distances between paired cases, thus augmenting imbalance, particularly in situations where a large number of unmatched cases are set aside.[36] Of note, our statistical matching technique, although robust, did not carve out in detail the OTA/AO fracture type and specific Gustilo classification subgroups of open fractures. Considering the relatively homogeneous nature of this high-risk group in both fracture type and Gustilo classification, we believe that neither factor is likely to produce important changes to our findings, but these characteristics could be explored in larger future studies. In addition, potential selection bias exists in the selection of which patients received vancomycin powder. The powder was first used by 1 surgeon, and then others began to use it. It was not used as part of any trial, so the use was in no way protocolized, introducing potential for selection bias. Another limitation is that neither control group was ideal: 1 had higher quality data in that it was from a prospective trial on surgical-site infection, but from an earlier period of time; the other was from a similar time interval but was retrospective in nature. Regardless of which group is compared, the trends are consistent, and an infection rate of 0% with vancomycin powder use in this high-risk population is a provocative finding.

These data do not definitively answer the question regarding efficacy of intrawound vancomycin powder, just as the retrospective spine studies do not answer its efficacy in spine surgery. We believe these data provided reasonably compelling evidence to help justify a large multicenter prospective trial such as the VANCO Study.[37] Of note, all patients reported in the current study precede initiation of the VANCO trial at our site.

The initial data found by this study suggest that vancomycin powder might play a role in lowering the rate of surgical-site infection after fracture fixation surgery. A larger randomized controlled trial is needed to validate our findings; however, if confirmed, this technique might provide another important tool for fracture surgeons to help reduce the rate of a potentially devastating complication.

ACKNOWLEDGMENTS

The authors thank Dori Kelly, MA, senior editor and writer, for professional article editing.

REFERENCES

1. Buckholz RW, Heckman JD, Court-Brown C, et al. *Rockwood and Green's Fractures in Adults*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
2. Teeny SM, Wiss DA. Open reduction and internal fixation of tibial plafond fractures: variables contributing to poor results and complications. *Clin Orthop Relat Res.* 1993;292:108–117.
3. Heier KA, Infante AF, Walling AK, et al. Open fractures of the calcaneus: soft-tissue injury determines outcome. *J Bone Joint Surg Am*. 2003; 85:2276–2282.
4. Thornton SJ, Cheluitte D, Ptaszek AJ, et al. Treatment of open intra-articular calcaneal fractures: evaluation of a treatment protocol based on wound location and size. *Foot Ankle Int*. 2006;27:317–323.
5. Young MJ, Barrack RL. Complications of internal fixation of tibial plateau fractures. *Orthop Rev*. 1994;23:149–154.
6. Stall A, Paryavi E, Gupta R, et al. Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: a randomized controlled pilot trial. *J Trauma Acute Care Surg*. 2013;75: 657–663.
7. Stannard JP, Volgas DA, McGwin G III, et al. Incisional negative pressure wound therapy after high-risk lower extremity fractures. *J Orthop Trauma*. 2012;26:37–42.
8. Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med*. 2004;350:1422–1429.
9. Qadir R, Sidhu S, Ochsner JL, et al. Risk stratified usage of antibiotic-loaded bone cement for primary total knee arthroplasty: short term infection outcomes with a standardized cement protocol. *J Arthroplasty*. 2014; 29:1622–1624.
10. Kapadia BH, McElroy MJ, Issa K, et al. The economic impact of periprosthetic infections following total knee arthroplasty at a specialized tertiary-care center. *J Arthroplasty*. 2014;29:929–932.
11. O'Neill KR, Smith JG, Abtahi AM, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. *Spine J.* 2011;11:641–646.
12. Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. *Spine (Phila Pa 1976)*. 2011;36:2084–2088.
13. Bridwell KH, Anderson PA, Boden SD, et al. What's new in spine surgery. *J Bone Joint Surg Am.* 2013;95:1144–1150.
14. Gans I, Dormans JP, Spiegel DA, et al. Adjunctive vancomycin powder in pediatric spine surgery is safe. *Spine (Phila Pa 1976).* 2013;38:1703–1707.
15. Strom RG, Pacione D, Kalhorn SP, et al. Decreased risk of wound infection after posterior cervical fusion with routine local application of vancomycin powder. *Spine (Phila Pa 1976).* 2013;38:991–994.
16. Pahys JM, Pahys JR, Cho SK, et al. Methods to decrease postoperative infections following posterior cervical spine surgery. *J Bone Joint Surg Am.* 2013;95:549–554.
17. Caroom C, Tullar JM, Benton EG Jr, et al. Intrawound vancomycin powder reduces surgical site infections in posterior cervical fusion. *Spine (Phila Pa 1976).* 2013;38:1183–1187.
18. Godil SS, Parker SL, O'Neil KR, et al. Comparative effectiveness and cost-benefit analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma. *J Neurosurg Spine.* 2013;19:331–335.
19. Tubaki VR, Rajasekaran S, Shetty AP. Effects of using intravenous antibiotic only versus local intrawound vancomycin antibiotic only versus local intrawound vancomycin antibiotic powder application in addition to intravenous antibiotics on postoperative infection in spine surgery in 907 patients. *Spine (Phila Pa 1976).* 2013;38:2149–2155.
20. Wukich DK, Dikis JW, Monaco SJ, et al. Topically applied vancomycin powder reduces the rate of surgical site infection in diabetic patients undergoing foot and ankle surgery. *Foot Ankle Int*. 2015;36:1017–1024.
21. Singh K, Bauer JM, LaChaud GY, et al. Surgical site infection in high-energy peri-articular tibia fractures with intra-wound vancomycin powder: a retrospective pilot study. *J Orthop Traumatol*. 2015;16:287–291.
22. Torbert JT, Joshi M, Moraff A, et al. Current bacterial speciation and antibiotic resistance in deep infections after operative fixation of fractures. *J Orthop Trauma*. 2015;29:7–17.
23. Lewallen S, Courtright P. Epidemiology in practice: case-control studies. *Commun Eye Health.* 1998;11:57–58.
24. Linden A, Samuels SJ. Using balance statistics to determine the optimal number of controls in matching studies. *J Eval Clin Pract.* 2013;19:968–975.
25. Tennent DJ, Shiels SM, Sanchez CJ Jr, et al. Time-dependent effectiveness of locally applied vancomycin powder in a contaminated traumatic orthopaedic wound model. *J Orthop Trauma.* 2016;30:531–537.
26. Qadir R, Ochsner JL, Chimento GF, et al. Establishing a role for vancomycin powder application for prosthetic joint infection prevention: results of a wear simulation study. *J Arthroplasty.* 2014;29:1449–1456.
27. Hovis JP, Montalvo R, Marinos D, et al. Intraoperative vancomycin powder reduces Staphylococcus aureus surgical site infections and biofilm formation on fixation implants in a rabbit model. *J Orthop Trauma.* 2018;32:263–268.
28. Ruffolo MR, Gettys FK, Montijo HE, et al. Complications of high-energy bicondylar tibial plateau fractures treated with dual plating through 2 incisions. *J Orthop Trauma.* 2015;29:85–90.
29. Blauth M, Bastian L, Krettek C, et al. Surgical options for the treatment of severe tibial pilon fractures: a study of three techniques. *J Orthop Trauma*. 2001;15:153–160.
30. McFerran MA, Smith SW, Boulas HJ, et al. Complications encountered in the treatment of pilon fractures. *J Orthop Trauma.* 1992;6:195–200.
31. Wyrsh B, McFerran MA, McAndrew M, et al. Operative treatment of fractures of the tibial plafond: a randomized, prospective study. *J Bone Joint Surg Am.* 1996;78:1646–1657.
32. Grose A, Gardner MJ, Hettrich C, et al. Open reduction and internal fixation of tibial pilon fractures using a lateral approach. *J Orthop Trauma*. 2007;21:530–537.
33. Benirschke SK, Kramer PA. Wound healing complications in closed and open calcaneal fractures. *J Orthop Trauma*. 2004;18:1–6.
34. Bibbo C, Patel DV. The effect of demineralized bone matrix-calcium sulfate with vancomycin on calcaneal fracture healing and infection rates: a prospective study. *Foot Ankle Int*. 2006;27:487–493.
35. Koski A, Kuokkanen H, Tukiainen E. Postoperative wound complications after internal fixation of closed calcaneal fractures: a retrospective analysis of 126 consecutive patients with 148 fractures. *Scand J Surg*. 2005;94:243–245.
36. King G, Nielsen R. Why propensity scores should not be used for matching. *Polit Anal.* 2019;27:435–454.
37. O'Toole RV, Joshi M, Carlini AR, et al. Local antibiotic therapy to reduce infection after operative treatment of fractures at high risk of infection: a multicenter, randomized, controlled trial (VANCO study). *J Ortho Trauma* 2017;31:S18–S24.